In the Name of

GOD

the Compassionate,
the Merciful

The 22nd International Congress of Asia-Pacific Blood and Marrow Transplantation

The 4th International and 7th National Congress on Stem Cells and the 2nd Annual Nursing Congress on Hematopoietic Stem Cell Transplantation

Iran-Tehran-Espinas Palace Hotel
28-30 Oct 2017

سرشناسه: کنگره سالیانه آسیا و اقیانوسیه خون و پیوند مغز و استخوان
عنوان و نام پدیدآور :
The 22nd International Congress of Asia-Pacific Blood And Marrow Transplantation
The 4th International and 7th National Congress on Stem Cells and the 2nd Annual Nursing Congress on Hematopoietic Stem Cell Transplantation
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شناسه افزوده: مرکز تحقیقات هماتولوژی، آنکولوژی و پیوند سلول‌های بنیادین

The 22nd International Congress of Asia-Pacific Blood And Marrow Transplantation

The 4th International and 7th National Congress on Stem Cells and the 2nd Annual Nursing Congress on Hematopoietic Stem Cell Transplantation

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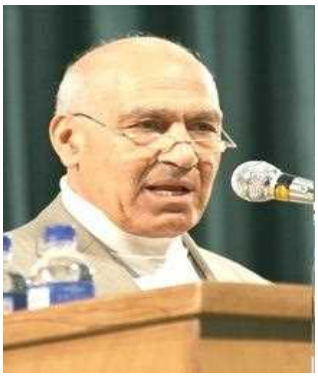
Message of Congress President



Dear participants

It is my very great privilege to welcome you all to the 22nd International Congress of the Asia-Pacific Blood and Marrow Transplantation (APBMT) this year in Tehran, Iran.

I would like to extend an especially warm welcome to our distinguished guests, members of the APBMT, all academic professionals, outstanding scholars and honorable speakers from all around the world. We are extremely delighted to receive all of you for this outstanding gathering this year.

I hope we can use this conference as a great opportunity to bring together renowned experts in new and emerging areas of Hematology-Oncology and stem cell transplantation research from around the world to share knowledge and ideas on behalf of improving hematopoietic stem cell transplantation and regenerative medicine.

As well, aspire to let our common interests on behalf of learning science and overcoming this war called “cancer” through defying the current unfortunate proposed barricades and barriers between countries by opening our doors for collaborating for the greater good of humanity in the pursuit of improving quality of life. For science does not know borders, and education is enlightening and beneficial for all.

Even though, with all the advancements and triumphs of medicine today, there still is a great deal to be achieved. That is why I am so humbled to have so many exceptional participants and contributors this year. So that we can use this exceptional opportunity to share and learn from each other.

We hope you will enjoy the scientific presentations by internationally renowned experts in this field.

Again, I welcome you to the 22nd Interational Asia-Pacific Blood and Marrow Transplantation Congress. Thank you all for your attendance.

Sincerely,

Dr. Ardeshir Ghavamzadeh, MD
Congress President

About the APBMT

The Asia-Pacific Blood and Marrow Transplantation Group (APBMT) is an international organization involved in the transplantation of hematological stem cells. The purpose of this organization is to allow all countries of the Asia-Pacific region to cooperate and collaborate by sharing basic and clinical research. Originally, transplant physicians from the countries of China, Hong Kong, India, Indonesia, Japan, South Korea, Malaysia, Taiwan, Thailand and Australia / New Zealand initiated the APBMT in 1990. They held early APBMT meetings in China and Japan from 1990 to 1994. Since then, plenary meetings have been held 14 times in the past 19 years, occurring annually since 2004 (refer to the Annual Meetings). In 2000, the APBMT planned to have a transplantation-case registry system as a symbol of unity; in consequence, the APBMT Registry (consists of the annual Activity Survey and the annual Outcome Registration) was initiated in 2006. Since this moment, the annual Activity Surveys were performed three times, as seen through our home page as well as our report-booklets. In 2006, the APBMT established their own structures in an attempt to preserve and expand their activities, which are consisted of the Executive Board, Scientific Committee, Regular Members, Supporting Members, Tentative Attendees and the Secretarial Office/ Data Center (located in Japan). In 2009, the APBMT secured the bylaws as well as confirmed the APBMT as one of the founding members of the Worldwide Network for Blood and Marrow Transplantation (WBMT). The APBMT is now comprised of 21 countries/ regions (Australia, Bangladesh, Cambodia, China, Hong Kong, India, Indonesia, Iran, Japan, South Korea, Malaysia, Mongolia, Myanmar, New Zealand, Pakistan, Philippines, Singapore, Sri Lanka, Taiwan, Thailand and Vietnam), and it is expanding its activities through its annual congresses (Australia in 2011, India in 2012, Vietnam in 2013, China in 2014, Japan in 2015 and Singapore in 2016), registration systems and working groups under the collaboration with the member societies of the WBMT.


22nd Asia-Pacific Blood and Marrow Transplantation
APBMT 2017
22nd APBMT 2017
28-30 October 2017
Espinas Palace Hotel,Tehran, Iran
Ardeshir Ghavamzadeh MD
Congress President
Kamran Alimoghaddam MD
Congress Scientific Secretary Co-Chair
Marjan Yaghmaei PhD
Congress Executive Secretary Co-Chair
Mazyar Shadman MD
Congress Executive Secretary
Co-Chair for International Affairs
www.apbmt2017.org

ABSTRACTS


22nd Asia-Pacific Blood and Marrow Transplantation
APBMT 2017
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28-30 October 2017
Espinas Palace Hotel,Tehran, Iran
Ardeshir Ghavamzadeh MD
Congress President
Fariba Bolourchifard
Scientific Secretary of Nursing
Ashrafsadat Mousavi
Executive Secretary of Nursing
www.apbmt2017.org

Congress Venue

The 22nd International Congress of APBMT will take place in Tehran, Iran from October 28 to 30, 2017 at the Espinas Palace Hotel Conference Hall.
Alley No. 33, Abedi St., Behroud Sq., Payam Blvd, Yadegar Imam Highway, Tehran www.palace.espinashotels.com
The Espinas Palace Hotel is located in the northwest region of Tehran. Access to the Espinas Palace Hotel is directly via the Yadegar Emam Highway, through the exclusive road. Another feature of this hotel is the use of the Air Taxi (Heli Board) to transfer guests from the airport to the hotel.

- 57 minutes from the Imam Khomeini International Airport by car
- 23 minutes from the Mehrabad International Airport by car
- 500 on-site parking spaces and quick access to major highways
- Nearby restaurants and cafes

Tourist Attractions

Tabiat Bridge: Modarres Highway, Abbas Abad, Tehran, Iran
***4.5 miles** from the Espinas Palace Hotel*

Milad Tower: Private Road of Milad Tower, Northern Angle of Hemmat Cross Shahid Sheikh Fazlollah Nouri Highway, Tehran
***3.5 miles** from the Espinas Palace Hotel*

Darband: Tehran, Iran
***4.7 miles** from the Espinas Palace Hotel*

Tajrish Bazaar: Tajrish Market, Tajrish Square, Tehran
4.2 miles from the Espinas Palace Hotel

Sadabaad Palace: Shahid Fallahi, Tehran
4.1 miles from the Espinas Palace Hotel

Golestan Palace: Arq Square, Tehran
8.6 miles from the Espinas Palace Hotel

ABSTRACTS

Tehran Bazaar: Panzdah-E-Khordad St., Tehran
8.8 miles from the Espinas Palace Hotel

National Museum of Iran: Emam Khomeini Ave., Si-e-Tir corner, Tehran
8.0 miles from the Espinas Palace Hotel

Niavaran Palace Complex: Tehran, Iran
6.6 miles from the Espinas Palace Hotel

Carpet Museum of Iran: Beside Laleh Park, Tehran
5.7 miles from the Espinas Palace Hotel

Reza Abbasi Museum: Shariati Street, Tehran
6.2 miles from the Espinas Palace Hotel

Committee list

Ardeshir Ghavamzadeh MD - Congress President
Kamran Alimoghaddam MD - Congress Scientific Secretary Co-Chair

Scientific Committee

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- Ahmad Ahmadzadeh/Iran
- Ahmad Tamadoni/Iran
- Ali Ghasemi/Iran
- Ali Unal/Turkey
- Amir Abbas Hedayatiasl/Iran
- Amir Ali Hamidiyeh/Iran
- Antonia Muller/Switzerland
- Ardeshir Ghavamzadeh/Iran
- Babak Nejati/Iran
- Behjat Kalantari/Iran
- Francois Lefrere/France
- Ghasem Janbabayee/Iran
- Gholamreza Bahoosh/Iran
- Hans Jochem Kolb/Germany
- He Huang/China
- Hossein Kamranzadeh/Iran
- Kamran Alimoghaddam/Iran
- Kevin Hay/USA
- Koichi Miyamura/Japan
- Lalindra Gooneratne/Sri Lanka
- Mahshid Mehdizadeh/Iran
- Mani Ramzi/Iran
- Marjan Yaghmaie/Iran
- Mazyar Shadman/USA
- Mehrdad Payandeh/Iran
- Mohamad Reza Eshghi/Iran
- Mohamad Reza Ostadali/Iran
- Mohamad Vaezi/Iran
- Mohamed Lotfy Sorror/USA
- Nicolaus Kröger/Germany

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- Ong Tee Chuan/Malaysia
- Rahim Asghari/Iran
- Rainer Storb/USA
- Raymond Leonard Powles/England
- Riccardo Saccardi/Italy
- Saeed Mohammadi/Iran
- Sahar tavakoli/Iran
- Seyed Asadollah Mousavi/Iran
- Seyed reza Safaee nodehi/Iran
- Shahin Shamsian/Iran
- Shinichiro Okomato/Japan
- Tahereh Rostami/Iran
- Tannaz Bahri/Iran
- Yoshihisa Kodera/Japan

Committee list

Marjan Yaghmaie PhD - Congress Executive Secretary Co-Chair
Mazyar Shadman MD-Congress Executive Secretary Co-Chair for International Affairs

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- Tahereh Mirfallah,MSc

Scientific Secretary of Nursing

Fariba Bolourchifard Scientific Secretary of Nursing
Ashrafsadat Mousavi Executive Secretary of Nursing

Scientific Committee

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- Alireza Nikbakht
- Arezo Rasti
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- Fariba Bolourchifard
- Fariba Tahsili
- Farzaneh Solymani
- Fatemeh Irannejad
- Hamidreza Masoumi
- Hayedeh Noktehdan
- Hooman Shahsavari

ABSTRACTS

- Leila Sayadi
- Mahin Sabz Alipour sarab
- Mahvash Agahi
- Malihe Khosravi
- Masoumeh Rashidi
- Masoumeh Saljughi
- Massoud Nezameddini
- Mitra Zandi
- Omolbanin Bakhti
- Parvin rezaei
- Roghayeh Kouhi
- Saeed Mohammadi
- Sakineh Ghorbani
- Shadan Pedramrazi
- Shokouh Varaei
- Soraya Moomivand
- Wang Ting
- Zahra Behboodi Moghadam

Detailed Program

22nd International Congress of Asia – Pacific
Blood and Marrow Transplantation

APBMT Program

Day 1 – Saturday, October 28, 2017

TIME	PROGRAMME	SPEAKER
7:30-8:00	The Recitation of the Holy Quran , National Anthem of the Islamic Republic of Iran	
8:00-8:30	Welcome & Opening Remarks	Ardeshir Ghavamzadeh, Kamran Alimoghaddam
8:30-10:10	Plenary 1: APBMT/ WBMT Joint Session: Transplantation reports in the Asian pacific region & the progress of BMT in the world and Asian pacific region	Chairpersons: Ardeshir Ghavamzadeh, Shinichiro Okamoto
8:30-8:45	The progress of BMT in the Islamic Republic of Iran	Ardeshir Ghavamzadeh
8:45-9:00	The report of transplantation in all 15 BMT centers of Iran in the last five years	Abbas Hajifathali, Mani Ramzi, Mehrdad Payandeh
9:00-9:20	The current status and future challenges of the Asia-Pacific Blood and Marrow Transplantation Group (APBMT)	Shinichiro Okamoto
9:20-9:30	The history, current status and future trends of WBMT	Yoshihisa Kodera
9:30-9:40	The report of transplantation in China in five recent years	He Huang
9:40-9:50	The advance of HSCT after the enforcement of "The Act for Appropriate Provision of Hematopoietic Stem Cells to be Used in Transplantations" in Japan	Yoshihisa Kodera
9:50-10:00	Outcome of autologous hematopoietic stem cell transplants for multiple myeloma in a single center in Sri Lanka	Lalindra Gooneratne

10:00-10:10	The report of transplantation in Malaysia in five recent years	Ong Tee Chuan
10:10-10:30	Coffee Break	
10:30-13:00	Plenary 2: Educational session of immunotherapy & gene therapy in the transplantation era: CART-Cell	Chairpersons: He Huang, François Lefrere
10:30-10:50	The first results of gene therapy in the area of hemoglobinopathies	François Lefrere
10:50-11:10	New and old targets for CART-Cell	Antonia Müller
11:10-11:30	Clinical experience with CD19 CAR for lymphoid malignancies	Kevin Hay
11:30-11:50	Advanced CD19-CART therapy for acute lymphocytic leukemia and B cell Lymphoma/ China Perspective	He Huang
11:50-12:10	Toxicity of CART therapy	Kevin Hay
12:10-12:30	Panel Discussion	He Huang, Kevin Hay, Antonia Muller, François Lefrere
12:30-14:00	Prayer & Lunch Break	
14:00-16:00	Plenary 3: Haploidentical and other related transplantations/ MRD in the post transplantation Era	Chairpersons: Raymond Leonard Powles, Mohamed Sorror
14:00-14:20	Haploidentical hematological stem cell transplantation as a front line therapy for adult Acute Lymphocytic Leukemia	He Huang
14:20-14:40	A comparison between gene therapy and haploidentical stem cell transplantation for SCID syndrome	François Lefrere
14:40-15:00	Incorporating patient health in the decision-making about the treatment of Acute Myeloid Leukemia	Mohamed Sorror
15:00-15:20	MRD in Philadelphia Positive ALL patients post-transplant	Koichi Miyamura
15:20-15:40	Place of Stem Cell Transplants for accidental irradiation incidents	Raymond Leonard Powles
15:40-16:00	Panel Discussion	Mohamed Sorror, He Huang, Koichi Miyamura, Raymond Leonard Powles
16:00-16:30	Coffee Break	
16:00-17:30	Poster Presentation	

Detailed Program

Day 2 - Sunday, October 29, 2017

TIME	PROGRAMME	SPEAKER
8:30-10:00	Plenary 4: Transplantation in Pediatrics & the quality of HSCT	Chairpersons: Amir Ali Hamidieh, Amir Abbas Hedayati Asl
8:30-8:50	NK Cell-Derived Exosomes enhance NKs anti-Neuroblastoma activity in a preclinical study: Future NK cell therapy for relapsed Neuroblastoma after HSCT	Amir Ali Hamidieh
8:50-9:10	Transplantation outcome in Pediatric Philadelphia positive ALL patients	Amir Abbas Hedayati Asl
9:10-9:25	Reduced-Intensity Conditioning Hematopoietic Stem Cell Transplantation in Leukocyte Adhesion Deficiency Type I: A Single Center Experience	Tahereh Rostami
9:25-9:45	Insurance approval of mesenchymal stem cell therapy for steroid refractory acute GVHD in Japan	Koichi Miyamura
9:45-10:00	Panel Discussion	Amir Ali Hamidieh, Amir Abbas Hedayati Asl, Tahereh Rostami, Koichi Miyamura
10:00-10:30	Coffee Break	
10:30-13:00	Plenary 5: Transplantation in older and non-malignant patients/ MRD in the Transplantation Era	Chairpersons: Mehrdad Payandeh, Rainer Storb
10:30-10:50	Transplantation in older patients	Rainer Storb
10:50-11:10	Comorbidities and age in Allogeneic Hematopoietic Cell Transplantation	Mohamed Sorror
11:10-11:30	Transplantation for patients with non-malignant blood disorders	Rainer Storb
11:30-11:50	Persistent challenge of the detection of minimal residual disease	Koichi Miyamura
11:50-12:10	Transplantation in patients with comorbid diseases	Mehrdad Payandeh

12:10-12:30	Panel Discussion	Rainer Storb, Mohamed Sorror, Mehrdad Payandeh, Koichi Miyamura,
12:30-14:00	Prayer & Lunch Break	
14:00-16:00	Plenary 6: Pre and Post transplantation treatment:{Allogeneic, Autologous, NK cell and DLI}	Chairpersons: Riccardo Saccaradi, Mahshid Mehdizadeh, Mazyar Shadman
14:00-14:20	Prophylactic and pre-emptive DLI	Hans Jochem Kolb
14:20-14:40	Transplant for double or triple hit lymphoma and their management	Mazyar Shadman
14:40-15:00	HSCT for Multiple Sclerosis	Riccardo Saccaradi
15:00-15:20	Post-transplant maintenance in lymphoid malignancies	Mazyar Shadman
15:20-15:40	International accreditation and quality of HSCT: the JACIE experience	Riccardo Saccardi
15:40-16:00	Panel Discussion	Mazyar Shadman, Hans Jochem Kolb, Riccardo Saccaradi, Mahshid Mehdizadeh
16:00-16:30	Coffee Break	APBMT Business Meeting (Amiran Hall 1)
16:00-17:30	Poster Presentation	Meetin Business Meeting (Amiran Hall 1)

Detailed Program

Day 3 – Monday, October 30, 2017

TIME	PROGRAMME	SPEAKER
8:30-10:00	Plenary 7: An educational session of cell therapy and regenerative medicine, GVHD and transplantation in non-malignant diseases	Chairpersons: Kamran Alimoghaddam, Rainer Storb, Nicolas Kröger
8:30-8:45	Graft-versus-host disease and graft-versus-tumor effects	Rainer Storb
8:45-9:00	Chronic GVHD and immune function post allo-HSCT	Antonia Müller
9:00-9:15	Treatment options for steroid refractory GVHD	Nicolas Kröger
9:15-9:30	Daratumumab in conjunction with ABMT (Cancer Centre London Experience)	Raymond Leonard Powles
9:30-9:45	Role of ATG in preventing GVHD after allogeneic SCT	Nicolaus Kröger
9:45-10:00	Panel Discussion	Nicolas Kröger, Rainer Storb, Raymond Leonard Powles, Antonia Muller
10:00-10:30	Coffee Break	
10:30-13:00	Oral Presentations from submitted abstracts	Chairpersons: Seyed Asadollah Mousavi, Mohamad Vaezi, Hossein Kamranzadeh
10:30-10:45	Autologous cord blood transplantation in children with Acquired Severe Aplastic Anemia	Sun Yuan
10:45-11:00	Successful treatment with granulocyte transfusion and early neutrophil engraftment in allogeneic transplant patients with febrile neutropenia	Ali Unal
11:00-11:15	Multiple Myeloma: Allogeneic or Autologous Hematopoietic Stem Cell Transplantation	Sahar Tavakoli

11:15-11:35	Pedigree analysis: a tool for finding matched donors in patient's' second and third degrees relatives	Mohammad Reza Ostadali
11:35-11:50	Evaluation of HLA-identical sibling allogenic peripheral blood stem cell transplantation for acute myelogenous leukemia at BTH, Vietnam	Van Man Huynh
11:50-12:05	Outcomes of co-transplantation of mesenchymal and hematopoietic stem cells compared to hematopoietic stem cell transplantation alone in beta thalassemia patients	Hossein Ranjbar
12:05-12:15	Hepatogenic differentiation of IPS cells on an aligned Polyether sulfone compared to random nanofibers	Maryam Kabir Salmani
12:15-12:25	Mild hypotxia and bone marrow mesenchymal stem cells enhance the expansion and homing of human cord blood CD34+ stem cells	Fatemeh Mohammadali
12:25-12:35	Expansion of umbilical cord blood hematopoietic stem cells on biocompatible nanofiber scaffolds as a co-culture with bone marrow derived mesenchymal stem cells	Majeed Mokhtari
12:35-13:00	Questions & Answers	

Detailed Program

Nursing Program

Day 1 – Saturday, October 28, 2017

TIME	PROGRAMME	SPEAKER
Chair	Ardeshir Ghavamzadeh, Ashraf Alsadat Mousavi, Fariba Bolourchifard, Zahra Monjamed, Mahin Saeidi, Seyed Masoud Nezamedini, Ebrahim Khadem, Hayde Noktedan	
800 –8:15	Welcome Remarks	Ardeshir Ghavamzadeh
8:15-8:45	Update in the nursing care of BMT	Ashraf Alsadat Mousavi
8:45-9:05	Key note lecture on the evaluation of transplantation in patient safety	Masoud Nezamedini
9:05-9:25	Key note lecture on complementary medicine	Ebrahim Khadem
9:25-9:40	Palliative care	Hayde Noktedan
9:40-10:10	The preparatory establishment of hematopoietic stem cell transplantation nursing follow-up platform in Peking University Hematology Institute	Wang Ting
10:10-10:30	Coffee Break	
Chair	Bolourchifard, Monjamed, Naghavi, Sayadi, Manokian, Shahsavari, Ting	
	How do I care for…?	
10:30-10:50	Complications involving thalassemia major (incongruence of the blood groups)	Bahar Naghavi
10:50-11:10	Complications involving MM (renal failure)	Leila Sayadi
11:10-11:30	Complication s involving lymphoma (tumor lysis)	Arpi Manokian
11:30-11:50	DIC	Hooman Shahsavari
11:50-12:30	Comprehensive use of multiple strategies to prevent perianal infection after hematopoietic stem cell transplantation	Wang Ting
12:30-14:00	Prayer & Lunch Break	

Chair	Roddehghan, Naghavi, Bolourchifard, Bakhty, Torkaman, Tahsili, Hoseini, Amini	
	Panel	
14:00-15:30	Oral Care in Hematopoietic Stem Cell Transplantation (The Challenges)	Zahra Roddehghan Naghavi, Bolourchifard, Omolbanin Bakhty, Fariba Tahsili, Ashraf Alsadat Hosseini, Leila Torkaman, Wang Ting, Fariba Gayed Amini, Esfandiyar Asgari
15:30-16:00	Coffee Break	
Chair	Nikhbakht, Manokian, Bolourchifard , Haziny, Zahra Shahryari, Maryam Mashhadi Reza, Ting	
	Discussion	

16:00-17:30	Ethics in HSCT	Alireza Nikhbakht, Arpi Manokian, Fariba Bolourchifard, Abdolrahim Haziny, Wang Ting
17:30-17:37	The effect of education on self-care behaviors of gastrointestinal side effects in patients undergoing chemotherapy	Ehsan Abadi Pishe
17:37-17:44	Another start for a new life without pain	Mozhdeh Tanha Maafi
17:44-17:51	Extravasation of cytotoxic agents	Vida Chehri
17:51-18	The effect of self-care education on the complication of nausea and vomiting in patients undergoing chemotherapy	Shokoh Varaei

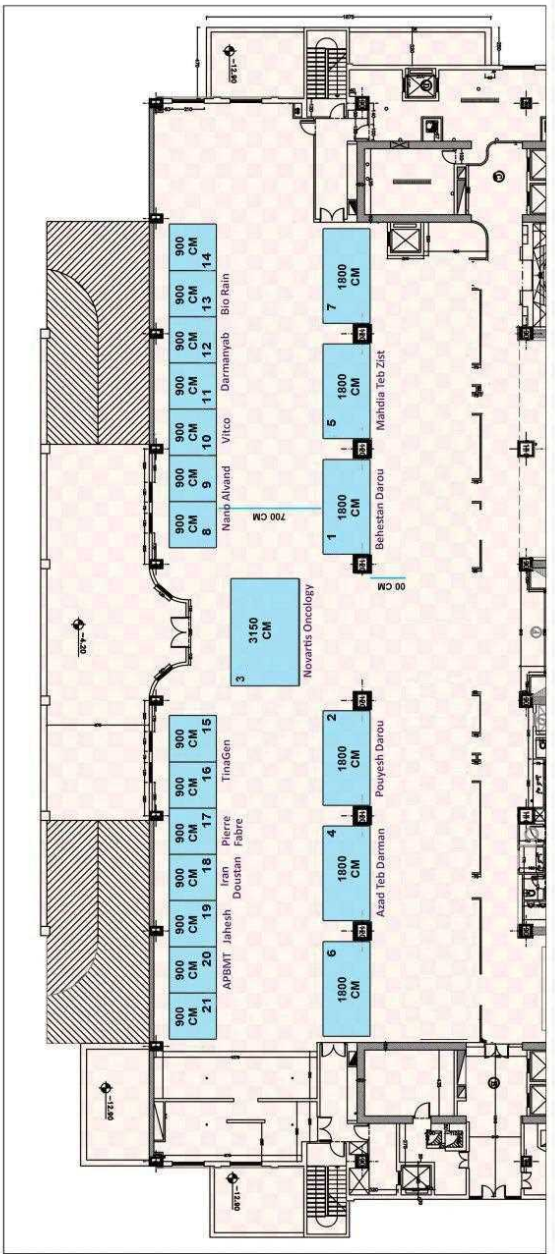
Detailed Program

Day 2 – Sunday, October 29, 2017

TIME	PROGRAMME	SPEAKER
Chair	Bolourchifard, Zandi, Noktedan, Rashidi, Monjamed, Maryam Rahmani, Tahmineh Naji	
8:00 –10:00	Adolescence & Adult Sessions Back to the life (Experiences and Perspectives of Patients)	Bolourchifard, Mitra Zandi, Noktedan, Masoumeh Rashidi, Zahra Monjamed, Naghavi, Naji, Firouzeh Heidari, Khalilzadeh
10:00-10:30	Coffee Break	
Chair	Bolourchi Fard, Behbodi, Pedram, Solymani, Irannejad	
10:30-11:30	Panel Discussion Sex Problem	Zandi, Bolourchifard, Zahra Behboodi, Shadan Pedramrazi Farzaneh Soleimanian, Fatemeh Irannejad Ting, Rashidi
Chair	Bolourchifard, Monjamed, Masomi, Khosravi, Rezaee, Naghavi	
	Early infections	Hayedeh Noktedan
11:30-11:55	Prophylaxis in fungal disease	Hamidreza Taghvaye Masoumi
11:55-12:15	Bacterial Resistance in the transplant ward	Malihe Khosravi
12:15-12:40	Respiratory Viruses in the transplant ward	.Parvin Rezaee
12:40-13:00	CMV in the transplant ward	Bahar Naghavi
13:00-14:00	Prayer & Lunch Break	
Chair	Bolourchifard, Rasti, Agahi, Kohi, Mohammadi	
	How to Understand Blood Tests? and Apheresis	
14:00-14:30	Full blood counts	Arezo Rasti
14:30-15:00	Liver and renal function tests	Mahvash Agahi
15:00-15:30	Chemotherapy standards	Roghayeh Kohi
15:30-16:00	Apheresis in small body weight	Saeed Mohammadi

16:00-16:30	Coffee Break	
Chair	Bolourchifard, Ghorbani, Saljoghi, Moomivand, Mohammadi	
	Cell source & transplant	
16:30-17:00	Autologous	Sakineh Ghorbani
17:00-17:30	Allograft	Masoumeh Saljogh
17:30-18:00	Alternative Donor	Soraya Moomivand

Exhibition Hall Map



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Medical Oral

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Blood and Marrow Transplantation

Current Status and Future Challenges of APBMT

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The Asia-Pacific Blood and Marrow Transplantation Group (APBMT) is an international organization which is involved in hematological stem cell transplantation (HSCT), sharing their information and cooperating with basic and clinical research in Asia-Pacific countries. It has been almost a quarter century since APBMT was founded in 1990. Currently twenty one countries/regions are participating in APBMT Group. APBMT has kept growing in terms of the numbers of participating countries/regions, the level of science, and the strength of our collaboration. As opposed to the transplant societies in both America and Europe, our group consists of countries where the disease for which transplantation are indicated, the infrastructure for supporting transplantation, financial background, and endemic of infectious diseases vary significantly. fAccordingly, the challenges in HSCT vary among our region.

One of our most important challenges is to increase sites to perform HSCT and the access to it. According the APBMT survey 2013, the rate of transplant is less than 50 per 10 million populations in the vast majority of Asia-Pacific countries/regions which accounts for more than 50% of the world's population. Among the reasons that have contributed to this huge supply and need discrepancies, the lack of trained personnel and the ability of the healthcare system to cover the cost of HSCT. The APBMT vision for the forthcoming years encompasses this important issue. We are aiming to provide emerging countries with training opportunities in HSCT and ensuring the quality of HSCT among Asia-pacific area. We believe that the important factors for establishing a successful and sustainable HSCT program will require careful forward planning with realistic timelines, adequate financial support, good business plan, appropriate infrastructure, sufficient well trained staffs and visionary leadership.

As opposed to the majority of Asia-Pacific countries/lesions, the field of HSCT is shifting toward transplants being done in elderly patients with more co-morbidity as the societies are aging rapidly. Such patients require more medical care per patient including long-term care after transplant. Also, introduction to a verity of active novel targeting agents into clinical practice is accelerating. Thus, positioning HSCT wisely within the therapeutic paradigm shift is crucial issues. The important project related to this issue is to steering the HSCT Registry in Asia (APBMT Transplant Outcome Registry). It is eagerly needed to set-up platform to design and promote clinical study and to collaborate with other international organizations related with HSCT.

These are the big challenges of APBMT, however, I remain optimistic and I believe great enthusiasm for hematopoietic stem cell transplantation and the passion of Asian peoples have undoubtedly contribute significantly to achieve this goal in the very near future.

The history, current status and future trends of WBMT

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The history, current status and future trends of WBMT Yoshihisa Kodera, for WBMT Aichi Medical University School of Medicine Japan Purpose: To deepen the understanding of Worldwide Network for Blood and Marrow Transplantation (WBMT). Materials and methods: The level 1 data from WBMT (WBMT annual reports and the other published articles from WBMT) were summarized. Results: 1. WBMT started under the collaboration of 4 registry-based international societies, EBMT, CIBMT, APBMT and WMDA in Lyon in 2007, and currently it involves 24 international societies. 2. Mission is to promote excellence in stem cell transplantation (SCT), stem cell donation, cellular therapy (CT) and accreditation through collaboration of existing international societies using coordination, communication and advocacy. The purpose of this cooperation is to engage exclusively in charitable, scientific, and educational activities and endeavors including specifically, but not limited to, promoting and fostering, among the many scientific and clinical disciplines, the exchange and diffusion of information and ideas relating to SCT and CT and encouraging investigations on these matters. The focus of the Network is to collaboratively advance the field of SCT and CT while not pre-empting the activities of its member societies. 3. Headquarter was set in Bern, Switzerland. Blanches were set in Minneapolis, USA（Administrative Office）, Leipzig, Germany, Basel, Switzerland, Nagoya, Japan, San Paulo, Brazil and Cape Town, South Africa. WBMT is a NGO of Switzerland and in official relation with WHO. Executive Committee is consisted of 6～7（including 1 secretary）persons. Board is consisted of 24 voting members. 4. The WBMT products until this moment were the followings; a. Global survey of Hematopoietic Stem Cell Transplantation b. Setting Global Transplant Center Number (GTCN) c. Four Workshops for emerging countries with WHO d. Joint session with Tandem Meeting, EBMT Meeting and recently APBMT Meeting 5. WBMT consider the followings as the future aspects; a. To continue Global Activity Survey b. To continue the activities of the current Standing Committees c. To keep the relationship with WHO d. To keep organizing WBMT/WHO Joint Workshop e. To strengthen the fund f. To organize APBMT/WBMT, LABMT/WBMT, AFBMT/WBMT Joint Session in each annual meeting g. To move toward the global patient/donor outcome registration Discussion: Ten years has passed since WBMT initiated its activities. Through its activities, WBMT has created not only the network of existing international societies but also the network of physicians/co-medicals, health experts and policy makers at the global level. We are convinced that this network could contribute to support and promote the peaceful relations among countries as well as the further advances of HSCT in the world.

The report of hematopoietic stem cell transplantation in China

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Hematopoietic stem cell transplantation (HSCT) is a potentially curative strategy for hematologic malignancies, solid malignancies and other non-malignant diseases. This regimen has benefited patients since its first emergence over 50 years ago. It is employed with increasing frequency worldwide. A total of 68,146 HSCT (31,926 allogeneic, 47%; 36,220 autologous, 53%) were reported by 1566 teams from 77 of the 79 countries worldwide known to have performed HSCT for the year 2012. Here we report the activity of HSCT in China from 2008 to 2016.

Altogether there were 21884 HSCTs (allogeneic: 16,631 (76%); autologous: 5,253 (24%)) performed from 1 January 2008 to 30 June 2016. Among them, 39% were female and 61% were male. The numbers of autologous and allogeneic HSCTs increased continually during the study period. The number of autologous HSCTs was smaller than the number of allogeneic HSCTs, although the relative proportion of autologous HSCTs increased. There were 121 (10.5%) autologous HSCTs performed in 2008 and 1,142 (24.3%) in 2015. Disease indications for autologous HSCT were: lymphoma 45%, multiple myeloma 27%, AML 14%, ALL 4% and POEMS syndrome 4%. For allogeneic HSCT, a continued rapid increase in haploidentical related donors (HRD) , and slower growth for unrelated donors, matched-related donors (MRD) and cord blood transplantation (CBT). The proportion of HRD among allogeneic HSCTs increased from 29.6% (313/1,062) in 2008 to 48.8% (1,939/3,975) in 2015 while the proportion of MRD HSCTs decreased from 48.1% (511/1,062) to 33.0% (332/3,975). The proportion of unrelated donor HSCTs among allogeneic HSCTs decreased from 20.4 (216/1,062) to 13.6% (540/3,975) while the proportion of CBTs was increased from 2.1% (22/1,062) to 4.2% (184/3,975). HSCTs have been increasing continuously for all indications except chronic myelogenous leukemia. Severe aplastic anemia is a common HSCT indication among non-malignant diseases in China. The number of cases of allogeneic HSCT for this disorder has increased annually, from 59 (5.6%) in 2008 to 569 (14.3%) in 2015.

In conclusion, there are more allogeneic than autologous HSCTs in China. Major increases were observed in MRD HSCT while the proportion of unrelated donor HSCTs and MRD HSCTs were decreased.

Advance of HSCT after the enforcement of "The Act for Appropriate Provision of Hematopoietic Stem Cells to be Used in Transplantations" in Japan

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Advance of HSCT after the enforcement of "The Act for Appropriate Provision of Hematopoietic Stem Cells to be Used in Transplantations" in Japan Yoshihisa Kodera, for JMDP, JCBBN, JDCHCT and JSHCT Department of Promotion for Blood and Marrow Transplantation Aichi Medical University School of Medicine Purpose: To understand the importance and the impact of the act for hematopoietic stem cell transplantation (HSCT). Materials and methods: The act was analyzed from the view of major impact to the on-going HSCT in Japan. Results: 1. The main points of the act. a. The act mandated to receive the accreditation by the national government for the organizations related to HSCT. b. The act stipulated the roles of preexisted organizations, Japan Marrow Donor Program (JMDP) and Japan Cord Blood Bank Network (JCBBN). c. The act newly built two organizations, The Supportive Organization for HSCT (in Japanese Red Cross Society: JRCS) and The Japanese Data Center for Hematopoietic Cell Transplantation (JDCHCT). d. The act mandated the obligations of the national and the regional governments to support the activities of HSCT. e. The act asked The Japan Society for Hematopoietic Cell Transplantation (JSHCT) to collaborate with these 4 organizations. 2. The main impacts of the act. a. Each organization including JSHCT played own proper roles resulting the avoidance of job duplication. b. JMDP concentrated on adult donor recruitment and coordination. c. JCBBN concentrated on cord blood collection, storage and procurement. d. JRCS concentrated on donors' HLA typing and donor-patient HLA matching. e. JDCHCT concentrated on making the national HSCT data which were opened to all the citizens. f. JSHCT concentrated to authorize transplant specialists (physicians, nurses, institutional HSCT coordinators) and transplant/harvest centers. g. The financial status of JMDP and JCBBN was stabilized. Discussion: To make a national level acts for HSCT is essential for 1. Effective operation of HSCT, 2. Stabilization of the financial status related to HSCT and 3. Regulation for the additional appearance of new organizations related to HSCT.

Outcome of autologous haematopoietic stem cell transplants for multiple myeloma in a single center in Sri Lanka

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Introduction: Multiple myeloma (MM) accounts for about 1% of cancers and about 10% of haematological malignancies. Reported incidence of MM (likely to be underestimated) in Sri Lanka is about 1.2/100,000 population/year. The standard of care for transplant eligible patients is induction therapy followed by an autologous haematopoietic stem cell transplant (ASCT). We report the outcome of patients with MM at one year follow up post transplant at the first HSCT centre established in Sri Lanka.

Method: A retrospective analysis of 5 patients with MM a year after undergoing an ASCT at Asiri Central Hospital, Colombo, Sri Lanka was performed.

Results: Three males and 2 females. Age range at transplant 38-65 years (average 50.2 years). Two patients each with IgG and IgA myeloma, 1 with light chain (k) myeloma. ISS stage: 3 x stage I, 1 each in stage II & III. All received bortezomib based induction (3x CyBorD, 2x VTD). One received Len Dex as second line and 1 thalidomide maintenance until HSCT. Pre transplant: 4 x VGPR, 1x CR. Stem cell dose range $2.8x10^6$/kg to $8.1x10^6$/kg CD34 (average $5.5x10^6$). Melphalan 200mg/m^2 conditioning (dose reduced in 2 patients due to renal impairment).Neutrophil engraftment on D+11 (3 patients), D+10 (2 patients). Platelet engraftment D+11 (all patients). Maintenance not given for ISS I (3 patients), Thalidomide maintenance given for ISS II & III. 1 year post HSCT 4 patients in CR, 1 remained in VGPR.

Conclusions: All patients engrafted by D+11 in spite of varying stem cell doses (lowest $2.8x10^6$/kg). As per the literature all our patients had a PFS of at least 1 year with frontline ASCT.

The report of transplantation in Malaysia in five recent years

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Malaysia started Hematopoetic Stem Cell Transplantation (HSCT) in year 1987, first performed in pediatrics patients, subsequently in adult patients since 1993. Data from the National Transplant Registry showed that up to 31 December 2015, a total of 3626 HSCT have been performed (allogeneic and autologous). There were 401 HSCT performed in year 2015 by 8 transplant centers in the country. Malaysia performed HSCT for both malignant and non-malignant Hematology diseases, source of donor including matched sibling donor, haploidentical family donor and alternative donor including Matched unrelated donor and cord blood. More details on HSCT, including problems and challenges of HSCT in Malaysia will be discussed further in the presentation.

First results of gene therapy In the hemoglobinopathies area

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The hemoglobinopathies are the most prevalent monogenetic disorders in the world. Beta-thalassemia major (β-Thal$_M$) and sickle cell disease are genetic disorders caused by mutations in both alleles of the β-globin genes that result in a failure to produce functional β-globin. This defect or mutation in β-globin are responsible for chronic hemolytic anemia, ineffective erythropoiesis and many others well-known complications. Standard therapy consists in red blood cell transfusions and iron chelation therapy that has dramatically improved patient survival. However, despite this supportive care, both life expectancy and quality of life remain impaired. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the main curative option, but is dependent on the existence of an HLA-identical sibling donor. Moreover, allogeneic HSCT is associated with a 5-20% mortality rate, depending upon the risk category, that mainly results from graft versus host disease (GVHd) - an immune conflict between the donor's immune cells donor and the recipient. The best outcomes of allogeneic HSCT patients are usually observed in young children transplanted with HLA-identical siblings donor with a full myeloablative conditioning regimen while results of HSCT in other settings (i.e. reduced intensity conditioning regimen, unrelated or mismatch donor) remains disappointing.Gene therapy which consists in the *ex vivo* transduction of a corrected copy of a β-globin gene into autologous hematopoietic stem cells (HSCs) is an interesting alternative to allogeneic HSCT in the absence of an appropriate donor. Thanks to its autologous nature, this treatment manages to overcome the GVHd pitfall. Success of gene therapy for hemoglobinopathies is here presented raising the question of developing this approach in a larger scale.

New and old targets for CAR-T cells

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Chimeric antigen receptor T (CAR-T) cells have attracted great attention in recent years and have entered the clinic. CART-T cells directed against CD19, which is expressed on the majority of B-cell malignancies, are generated by several companies and are now commercially available.
Major efforts are underway to develop CAR-T cells also for other, CD19-negative malignancies. Key problem in the generation of new CAR-T cells is target selection. While CD19-directed CAR-T cells eradicate all cells of the B-lineage (malignant and healthy), the loss of healthy B cells can be managed routinely in the clinic. However – the majority of other known tumor-associated antigens are also expressed on healthy cells and tissues. Due to their strong reactivity CAR-T cells can detect and attack even cells with lowest levels of antigen expression on their surface. At this point, this so called off-target toxicity hampers the translation of many CAR-T cells into clinical testing and application. Strategies to overcome this problem are (i) the search for tumor-specific antigens, that are expressed on tumor cells exclusively, (ii) the development of ways to turn CAR-T cells on and off on demand. Here, we provide an overview of new CAR-T cells directed against tumor antigens expressed on acute myeloid leukemias and solid tumors. Moreover, strategies to control the reactivity of CAR-T cells, once infused into the patient will be discussed (suicide genes and other methods to switch-off the “living drug”).

Clinical outcomes of CD19-specific chimeric antigen receptor-modified (CAR)-T cell adoptive immunotherapy

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Lymphodepletion chemotherapy followed by transfer of CD19-specific chimeric antigen receptor-modified (CAR)-T cells has led to high response rates in relapsed/refractory (R/R) B cell acute lymphoblastic leukemia (B-ALL), B cell non-Hodgkin's lymphoma (NHL), and chronic lymphocytic leukemia (CLL). Preclinical work at our institution demonstrated that CD19 CAR-T cells manufactured from a 1:1 ratio of $CD4^+$:$CD8^+$ CAR-T cells provided a synergistic enhancement in anti-tumor activity. Furthermore, formulation of CAR-T cells in a defined composition was expected to increase the uniformity of the product and improve the ability to establish relationships between CAR-T cell dose and clinical outcomes. Therefore, we enrolled R/R B-ALL, NHL, and CLL patients in a single center phase I/II clinical trial (clinicaltrials.gov NCT01865617) of lymphodepletion chemotherapy followed by CD19 CAR-T cells formulated in a 1:1 $CD4^+$:$CD8^+$ ratio and infused at one of three different dose levels (DL; DL1, $2x10^5$; DL2, $2x10^6$; and DL3, $2x10^7$ CAR-T cells/kg). In the initial dose finding stage, the maximum tolerated dose (MTD) for a first infusion of CAR-T cells was defined as DL1 in high marrow burden (>5%) B-ALL and DL2 in all other patients. Thirty-four of 36 patients with B-ALL completed response assessment at approximately 3 weeks after CAR-T cell infusion, with 32 (94%) achieving a minimal residual disease (MRD) negative complete remission (CR) by bone marrow flow cytometry. Higher marrow tumor burden and infused CAR-T cell dose led to increased CAR-T cell *in vivo* expansion. A subset of patients who received CAR-T cell infusion after cyclophosphamide (Cy)-based lymphodepletion without fludarabine (Flu) achieved complete remission, but subsequently relapsed in association with loss of CAR-T cell persistence due to a $CD8^+$ T cell mediated anti-transgene immune response. Addition of Flu to the lymphodepletion regimen improved CAR-T cell expansion and persistence, and disease-free and overall survival. Thirty-nine of 41 patients with NHL completed response assessment. Of the 20 patients who received Cy/Flu followed by the MTD of CAR-T cells, the overall response rate (ORR) was 80% (CR 10/20, 50%; partial response [PR] 6/20, 30%). Similar to in B-ALL, the addition of Flu to Cy lymphodepletion improved CAR-T cell persistence and progression free survival. Of 24 patients with high-risk CLL, 20 received Cy/Flu and CAR-T cells at or below the MTD. Nineteen patients underwent response assessment at 4 weeks after CAR-T cell infusion. The ORR at 4 weeks was 74% (CR 4/19, 21%; PR 10/19 53%),

with clearance of any detectable bone marrow disease by flow cytometry in 15/17 patients (88%) who had marrow disease prior to CAR-T cells. The response rates in patients with ibrutinib-refractory disease were similar. Patients with PR by IWCLL 2008 imaging criteria did not have inferior progression-free survival to those in CR, suggesting that size criteria may be inadequate to assess the early response to CD19 CAR-T cell therapy in CLL. IGH deep sequencing was performed on bone marrow from 12 of these 15 patients with no detectable disease by flow cytometry, and demonstrated no detectable malignant clone in 7 patients (58%). Absence of the malignant clone by IGH sequencing was associated with 100% progression free and overall survival (median follow-up 6.6 months).

Advanced CART19 therapy for acute lymphocytic leukemia and B-cell lymphoma

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Patients with relapsed/refractory acute lymphocytic leukemia (R/R ALL) and lymphoma have a very poor prognosis under current therapeutic modalities. Allo-HSCT is considered the only curative option for patients with R/R ALL and salvage allo-HSCT has been applied to these patients. Nevertheless, according to results of recent clinical trials, the high relapse rate and poor OS still remain a great challenge. Thus, re-induction remission is an urgent issue to improve clinical outcomes of patients with R/R ALL and lymphoma.

Chimeric antigen receptor modified T cells against CD19 (CART19s) have shown promises as a novel therapy for R/R ALL patients in clinical trials. Consistently high anti-leukemia efficacy of CART19 from several different institutions have been demonstrated. CART19 products prepared by each institution differ in several respects, including CAR design, T-cell activation and transduction methods etc. Various infused CART19 doses, lymphodepleting chemotherapy regimens and patient populations have been attempted in clinical protocols. Different lymphodepleting chemotherapies prior to CART19 infusion were administered but no consistent lymphodepleting regimen has been established currently.

In this report, the clinical trial of CART19 therapy for CD19+ acute lymphocytic leukemia and lymphoma in our center is presented. We enrolled 30 consecutive patients with R/R ALL and 6 R/R B-cell lymphoma with 4-1BB/CD3-ζ co-stimulated CART19s, evaluating the efficacy and safety profiles in Chinese patients. All the 36 patients received CART19 infusion at doses of 1.1×106/kg to 9.8×106/kg. 27 patients with ALL and 3 patients with B-cell lymphoma achieved complete remission 1 month after CART19 infusion. CART19 expanded and persisted in peripheral blood and bone marrow. 11 patients with ALL underwent subsequent haploidentical hematopoietic stem cell transplantation. 28 patients (77.8%) suffered from cytokine release syndrome (CRS). The Grade 3 CRS developed in 11 patients (39.3%) and was associated with a higher disease burden on day -1 and number of previous relapse. Also recent advances in CART19 generation, infused CART19 doses, lymphodepleting chemotherapy regimens and diagnosis as well as treatment of CART19-associated complications based on current clinical trials are summarized in order to pursue an optimal CART-based therapeutic strategy.

Toxicities of chimeric antigen receptor-modified (CAR)-T cell adoptive immunotherapy: Cytokine Release Syndrome and Neurotoxicity

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Chimeric antigen receptor-modified (CAR)-T cells targeting CD19 have produced excellent outcomes in relapsed/refractory (R/R) B cell acute lymphoblastic leukemia (B-ALL) and promising results in R/R B cell non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL). These results have led to successful multicenter trials, the first US Food and Drug Administration (FDA) approvals for an anti-CD19 CAR-T cell product (tiagenlecleucel-T), and the development of CAR-T cell therapies targeting other antigens. However, CAR-T cell activation *in vivo* by encounter with the target antigen can also be associated with cytokine release syndrome (CRS) and neurotoxicity. CRS presents with fever and hypotension, and in severe cases can lead to multi-organ dysfunction, capillary leak, intensive care unit (ICU) admission, and rarely, death. Neurologic adverse events (AEs) after CAR-T cell therapy have been poorly understood, and include severe headaches, delirium, transient aphasia, decreased level of consciousness, seizures, or cerebral edema. An improved understanding of the presentations of these toxicities will enable safe CAR-T cell use in future trials.

We conducted a single center phase I/II clinical trial of lymphodepletion chemotherapy followed by anti-CD19 CAR-T cells formulated in a 1:1 $CD4^+$:$CD8^+$ ratio at one of three different dose levels (DL; DL1, $2x10^5$; DL2, $2x10^6$; and DL3, $2x10^7$ CAR-T cells/kg) in patients with R/R B-ALL, NHL, and CLL (clinicaltrials.gov, NCT01865617) at our institution. Of the 133 patients who completed toxicity assessment, CRS developed in 70% with the majority of presentations being mild to moderate (58% grade 1-2, 4% grade 3, 8% grade ≥4). Fever was the first objective sign of CRS. Neurologic AEs of any grade occurred in 40% (19% grade 1-2, 16% grade 3, 5% grade ≥4). All grade ≥3 neurotoxicity occurred after CRS development (median 4.5 days). The most common neurologic AE was delirium with preserved alertness (66%), followed by headache (55%), language disturbance (34%), and decreased level of consciousness (25%). Rare events included coma requiring ventilator support (6 patients), seizures (4 patients), acute cerebral edema (2 patients), and intracranial hemorrhage (ICH, 1 patient). In the majority of cases, toxicity was transient and resolved. The maximum tolerated dose (MTD) for a first infusion of CAR-T cells was defined as DL1 in high marrow burden (>5%) B-ALL and DL2 in all other patients. DL3 was excessively toxic as a first infusion with 5/12 patients (42%) having grade ≥4

CRS or neurotoxicity. Twenty-six patients (20%) were administered tocilizumab and/or dexamethasone to treat CRS and/or neurotoxicity; all patients receiving tocilizumab and/or dexamethasone had grade ≥3 CRS and/or neurotoxicity, with the exception of 2 patients who had progressive grade 2 CRS. Toxicity-directed intervention with tocilizumab and/or dexamethasone was successful in all except 6 patients who died, four of whom received CAR-T cell infusion at higher that the MTD during dose-finding.

In multivariable analyses, we found that factors associated with increased *in vivo* CAR-T cell expansion such as higher bone marrow $CD19^{+}$ tumor burden, cyclophosphamide and fludarabine (Cy/Flu) lymphodepletion, and higher infused CAR-T cell dose were associated with the development of CRS and/or neurotoxicity. Logistic regression analyses of the relationships of CRS, neurotoxicity, and anti-tumor response with peak in vivo blood CAR-T cell counts indicated that a therapeutic window can be defined in B-ALL, in which there is a high probability of CR with an acceptable risk of serious toxicity. Targeting of a peak CAR-T cell count within this window could be achieved by risk-adapted CAR-T cell dosing, in which patients with high burden B-ALL receive a low dose of CAR-T cells and those with low burden B-ALL receive a high dose of CAR-T cells. Anti-tumor response was closely associated with increasing peak CAR-T cell counts in NHL and CLL patients with lymphadenopathy. In these patients, CAR-T cell dose reduction would decrease the incidences of CRS and neurotoxicity, but this would occur at the expense of anti-tumor efficacy. We therefore sought a strategy to maintain peak CAR-T cell counts by identifying patients at the highest risk of toxicity who may benefit from early intervention to prevent subsequent toxicity. High fever and serum IL-6, IL-15, MCP-1 and IL-10 within the first 36 hours of infusion was associated with subsequent toxicity and provided the basis for classification tree algorithms to identify these patients soon after CAR-T cell infusion but prior to the development of grade ≥3 toxicity.

Our results demonstrate that CRS and neurotoxicity are common AEs after CAR-T cell therapy, however, they are well tolerated in most patients who receive an optimized lymphodepletion regimen and CAR-T cell dose. Effective therapies are available, and the development of early intervention strategies will further improve the safety of CD19 CAR-T cells, and potentially of CAR-T cells targeting other malignancies.

Haploidentical Hematological Stem Cell Transplantation as Front Line Therapy For Adult Acute Lymphocytic Leukemia

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Compared to pediatric acute lymphoblastic leukemia (ALL), the outcome of adult ALL is still poor with the long-term survival reaching only 35-50%. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) and chemotherapy are the main post-remission therapies. Several trials have been constructed to compare allo-HSCT with chemotherapy as the optimal post-remission therapy for adult ALL, but the outcome is still controversial. Especially with the introduction of pediatric inspired therapy into adult ALL recent years, the role of allo-HSCT in adult ALL should be further investigated.

The detection of minimal residual disease (MRD) has been widely used to identify patients with poor prognosis. More and more data in adult ALL recent years confirmed the prognostic role of MRD at multiple time points. And therefore, MRD has now been incorporated into the risk stratification system to identify patients with high relapse risk as transplant candidates in first CR. Patients with high levels of MRD would benefit from allo-HSCT when compared to chemotherapy alone in several prospective trials.

Matched sibling donor (MSD) has always been the first selection for allo-HSCT. With the improvement in transplant technologies, the outcome of unrelated donor (URD) HSCT and haploidentical (HID) HSCT is now approaching to MSD HSCT. And the results from different groups recent years suggested that the outcomes of URD/HID HSCT were comparable to MSD HSCT. In some studies, HID HSCT was even more preferred than MSD HSCT in high risk patients because of a superior GVL effect. But the data of direct comparison between HID HSCT and chemotherapy was still rare. Some recent results suggested that for patients having no MSD, the outcome of HID HSCT was better than chemotherapy alone, but this conclusion needs to be further validated.

Overall, the results of HID HSCT progressed greatly during the past decade, which were comparabe to MSD HSCT and no worse than chemotherapy alone as post-remission therapy. HID HSCT could be selected as a front line therapy for adult ALL in CR1, especially for those with MRD positive remission.

A comparison between gene therapy and haploidentical stem cell transplantation for SCID syndrome

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X-linked severe combined immunodeficiency (SCID-X1) is the most frequent genetic form of SCID resulting in the absence of T and NK lymphocytes. If untreated patients lead to death within the first year of life. Allogenic bone marrow transplantation is the gold standart therapy but is dependant on the availability of a suitable HLA-compatible donor. Alternative mismatch and haplo-identical donors can represent an alternative but highly increase the vital risks. SCID-X1 is caused by genetic defects concerning the IL2 receptor. In the absence of HLA compatible donor, a gene therapy via a transduction of a corrected copy of the gene in autologous stem cell can represent an alternative solution to bone marrow transplantion using an at high risk non-identical donor. The present paper challenges the two options through a comparative clinical and biological study in term of hematopoietic and immunological reconstitution and global pronostic.

Incorporating patient health in the decision-making about treatment of Acute Myeloid Leukemia

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The utility of comorbidities assessed prior to treatment for AML is unknown. We retrospectively collected comorbidities and laboratory data from 1079 pts with newly diagnosed AML who received therapy at 5 institutions. HCT-CI comorbidities were evaluated per HCT-CI standard comorbidity definitions. Newly evaluated comorbiditiesincluded including hyperlipidemia, hypertension, deep venous thrombosis, gastroesophageal reflux disease, hypothyroidism, hypoalbuminemia, thrombocytopenia,neutropenia, anemia, elevated lactate dehydrogenase (LDH), smoking, and alcohol intake. Patients (1079) were randomly divided into a training (n=710) and a testing set (n=369). In the training set, the unadjusted hazard ratios(HRs) for 1-year overall mortality were calculated for each comorbidity as well asall adjustment factors: gender, age, race, cytogeneticrisks, regimen intensity, WBC, blast count, and marrow blast percentages. Only factors that were associated with overall mortality at a significance level of P<.10 proceeded to the multivariate model. Each comorbidity that entered the multivariate model was then adjusted for the effect of other comorbidities as well as gender, age, cytogenetic-risks, and regimen intensity. The adjusted HRs were employedas weights for individual comorbidities. In the validation set, augmenting the HCT-CI with the three new covariates: platelets, albumin, and LDH yielded the highest predictive power among all other comorbidity indices. An AML-composite model was designed and validated from augmented HCT-CI, age, and cytogenetics. Then, we used the AML-composite model to define distinct prognostic groups, and within each, compared 2-year mortality rates according to whether patients received intensive or non-intensive therapy. Per the composite model grouping, pts had better survival rates if they received intensive therapy, although the differences were not statistically significant in patients with composite scores ≥10. Results persisted among patients aged 70-79 years old. Although results seem better with intensive therapy, less than 50% ofpatients with composite scores 4 given such therapies were predicted to be alive at 2 years, suggesting thatrandomization between novel intensive and novel non-intensive therapies might be worthwhile.

MRD in Philadelphia positive ALL patients post-transplant

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Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph^+ALL) arises from t(9;22)(q34;q11.2) that results in BCR-ABL fusion protein. Ph^+ALL is more common in older patients (25%-35%) and is associated with highly aggressive disease. Before the era of imatinib, leukemia-free survival (LFS) with intensive chemotherapy alone was very low and allogeneic stem cell transplantation (allo-HSCT) was the only curative treatment. However, even with allo-HSCT, hematological relapse remained a major obstacle, because the majority of patients received it with a substantial burden of leukemia at allo-HSCT due to resistance to chemotherapy.

In the early 1990s, the detection of minimal residual disease (MRD) in Ph^+ALL patients was performed using a polymerase chain reaction (PCR). An earlier study using qualitative PCR suggested that BCR-ABL chimeric messenger RNA (BCR-ABL) detected by PCR after allo-SCT indicates imminent hematological relapse. This study also found that MRD negativity just before allo-HSCT suggested long-term LFS after allo-HSCT. However, qualitative PCR gives only limited information and does not allow precise analysis of tumor load kinetics. Thus, the development of quantitative MRD detection has been strongly desired. A decade later, quantitative PCR was introduced and we could start sequential monitoring of the amount of leukemia.

The introduction of imatinib, a selective BCR-ABL tyrosine kinase inhibitor (TKI), in the early 2000's was a revolutionary step in the management of Ph^+ALL as well as CML and a shift in the paradigm for the management of cancer in general. A high CR rate was observed with imatinib-based chemotherapy increased the number of patients who were eligible for allo-SCT. Moreover, intensified consolidation therapy reduced early relapse rates following induction therapy and resulted in improved OS and EFS rates following chemotherapy only. However, several studies showed that PFS was better in patients who received HSCT than those who did not. Even the era of next-generation TKIs, allo-HSCT is still the standard therapy for those tolerant of this procedure.

After transplantation, a substantial number of patients still showed a relapse of leukemia. Although it is ideal to perform allo-HSCT under MRD negative conditions, this is sometimes difficult to achieve, despite the administration of TKI. There are some reports of post-transplant imatinib administration, but its efficacy and administration methods are still controversial. Recently, there have been some

reports of post-transplant imatinib administration, but its efficacy and administration methods are still controversial.

In a Chinese study, 62 patients initiated imatinib therapy post-HSCT and 20 patients did not. Ten patients (16.1%) terminated imatinib therapy owing to AEs. Among the patients in the imatinib and non-imatinib groups, the estimated 5-year relapse rate was 10.2% and 33.1% (p = 0.016), and the 5-year probability of disease-free survival (DFS) was 81.5% and 33.5% (p = 0.000) with the median follow-up of 31 months and 24.5 months, respectively. Multivariate analysis identified imatinib maintenance therapy post-HSCT as an independent prognostic factor for DFS (p = 0.000, hazard ratio [HR] =4.8) and overall survival (OS) (p = 0.000, HR = 6.2). They concluded that the relapse rate can be reduced and DFS may be improved in Ph $^{+}$ ALL patients with imatinib maintenance therapy after allo-HSCT.

In our study, we analyzed 34 Ph^{+}ALL patients retrospectively including 7 receiving post-transplant imatinib administration. OS was significantly better in patients with post-transplant administration (66.7% vs. 29.6% at 3 years, p=0.03), with no significant difference in leukemia-free survival (LFS) (0% vs. 29.6% at 3 years, p=0.29). The median duration of negative minimal residual disease (MRD) in patients with post-transplant imatinib administration was 6 months in the pre-emptive administration group, where imatinib was administered upon detecting MRD after allo-HSCT. In the prophylactic administration group, imatinib was administered as soon as possible after allo-HSCT, and the median duration of MRD was 12 months. In all patients whose observation periods were longer than one year, MRD became positive in both groups leading to hematological relapse. We therefore concluded that post-transplant imatinib administration is not an ideal treatment for Ph^{+}ALL patients whose MRD is positive at allo-SCT.

A German Group prospectively compared prophylactic administration of imatinib with intervention upon molecular relapse to evaluate the effect of post-transplant imatinib administration. MRD became positive in both groups, leading to hematological relapse. Prophylactic imatinib significantly reduced the incidence of molecular recurrence after SCT compared with MRD-triggered imatinib (40% vs 69; P.0.046). Median duration of PCR negativity was 26.5 and 6.8 months, respectively (P.0.065). Five-year survival in both groups was high (80 and 74.5%), despite premature discontinuation of imatinib in the majority of patients because of poor tolerability. They concluded that post-transplant imatinib administration is not an ideal treatment for Ph^{+}ALL patients. On the contrary, all patients who received imatinib upon appearance of BCR-ABL and promptly achieved a molecular response remained in remission for the duration of imatinib treatment.

In conclusion, all patients with Ph^{+}ALL are candidates for the post-transplant TKIs to reduce the risk of relapse and MRD monitoring should start 4 weeks after allo-HSCT

and continue every month during the first year of treatment. Patients with undetectable MRD after allo-HSCT may be treated prophylactically or, alternatively, may be monitored and administered a TKI only after the detection of MRD (preemptive strategy). Post-transplant TKI administration seems inadequate to achieve long-term LFS and a further improvement in therapeutic strategies before allo-HSCT is warranted. In terms of a cure for Ph^+ALL, MRD at allo-SCT may produce a profound impact on long-term LFS, indicating that post-transplant intervention seems to have some limitations.

NK Cell-Derived Exosomes enhance NKs anti-Neuroblastoma activity in a preclinical study: Future NK cell therapy for relapsed Neuroblastoma after HSCT

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Background: There is little information on strategies for treatment of relapses occurring after haploidentical hematopoietic stem cell transplantation (HSCT) performed for high-risk neuroblastoma (NB). Within the last decade, HSCT strategies have been combined with adoptive cellular therapies using natural killer (NK) cells. Until now a number of cytokines have been studied to activate and expand NK cells *ex vivo*. Recently it has been known immune cell-derived exosomes can increase immunity against tumors. In this experiment, we have studied the NKs effectiveness on the NB after expansion and then incubation with NK-derived exosomes.

Methods: The exosomes were derived from two populations of NKs: 1) Naïve NKs and, 2) NKs previously exposed to NB cells (Nx). Also, we have studied the NB derived exosomes (NB-Ex) on NK function. The molecular load of the characterized exosomes (by means of nanoparticle tracking analysis, flow cytometry, scanning electron microscopy and western blot) from NKs exposed to the NB was revealed their expression of NCRs in addition to CD56, NKG2D, and KIR2DL2 receptors. These exosomes (Nx) were used to treat NKs and then administered to NB cells both *in vitro* and *in vivo*. Thirty-five nude mice were divided into 5 groups (ILs, NKs, Cytokine activated NKs, NB-Ex, Nx, Cytokine activated NK-Ex) and injected sub cutaneously with 1 million SK-N-SH cells to develop tumors.

Results: Our results revealed some kind of NKs education by the exosomes. This education from NKs previously exposed to NB cell-derived exosomes caused efficient and greater cytotoxicity against NB tumors, but NB-Ex acts as tumor promoters by providing a tumor supporting niche. The 90-day survival in mice models that were treated with only cytokines was zero. In contrast, the survival rate for Nx-ANKs, CANKs, and Nx-CANKs groups were 56%, 71%, and 86%, respectively (*P<0.05).

Conclusion: This method of preparing exosomes has a dramatic effect on activation of NKs against neuroblastoma in the preclinical model and could be translated in human clinical trials for pediatric patients suffering from relapse of high-risk neuroblastoma after HSCT, in the near future.

Transplantation Outcome in Pediatric Philadelphia Positive ALL Patients

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Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) remained until recently the molecular genetic abnormality associated with the worst outcome. Hematopoietic stem cell transplant (HSCT) was considered the treatment of choice, however, recent data have indicated that chemotherapy plus tyrosine kinase inhibitor (TKI) maybe an alternative effective therapy.

In pediatric patients with ALL, the Philadelphia chromosome translocation is uncommon, with a frequency of less than 5%. However, it is classified as a high or very high risk, and only 20-30% of Ph+ children with ALL are cured with chemotherapy alone. Allogeneic hematopoietic stem cell transplantation from a closely matched donor cures 60% of patients in first complete remission. Recent data suggest that chemotherapy plus TKIs may be the initial treatment of choice for Ph+ ALL in children. However, longer observation is required to determine whether long-term outcome with intensive imatinib and chemotherapy is indeed equivalent to that with allogeneic related or alternative donor HSCT.

Because Ph+ ALL is rare in children, the question of whether HSCT could be a dispensable part of their therapy may not be answered for some time. An international multicenter study is needed to answer the question of whether imatinib plus chemotherapy could replace sibling allogeneic HSCT in children with Ph+ ALL. The challenges in the treatment of Ph+ ALL are the selection of appropriate pre-transplantation therapy, the minimization of transplantation toxicity, the correct use of TKIs after transplantation and the appropriate use of and response to BCR/ABL monitoring.

Trials comparing chemotherapy and HSCT must obtain sufficient data about therapy and stratify the analysis to assess the outcomes of best-chemotherapy with best-HSCT approaches.

Reduced-Intensity Conditioning Hematopoietic Stem Cell Transplantation in Leukocyte Adhesion Deficiency Type I: A Single Center Experience

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Introduction: Pediatric patients with leukocyte adhesion deficiency type-I (LAD-I), a rare autosomal recessive primary immunodeficiency disorder, experience severe and recurrent lifethreatening bacterial infections. Allogeneic haematopoietic stem cell transplantation (HSCT) offers the possibility of curative therapy although the conditioning regimen used for HSCT in LAD-I is still a controversial issue. This study provides evaluation of outcome of the LAD-I pediatric patients who underwent Reduced-Intensity Conditioning (RIC) HSCT.

Patients and Methods: Twenty four patients (14 female) with severe LAD-I who received 26 HSCTs between Februay 2007 and September 2016 at our center were enrolled . The median age at HSCT was 30 months (range:4months -14years). Patients received bone marrow (n=9), peripheral blood progenitor cells (n=14) or umbilical cord blood grafts (n=3) from HLA-matched related donors (n=18), mismatched related or unrelated donors (n=4), unrelated fully matched donors (n=1) and haploidentical relative donors (n=1). RIC regimen was provided with Fludarabine, Melphalan and anti-thymocyte immunoglobulin. Cyclosporine A and Prednisolon were used as graft-versus-host disease (GvHD) prophylaxis.

Result: Engraftment occurred in 23/26, of which one patient experienced graft rejection.The median times to neutrophil and platelet engraftments were 12 days (range: 10 - 23days) and 15 days (range: 10 - 32days), respectively. With a median follow-up of 43 months (range: 2 - 95months), overall survival (OS) was 70.8%.The main causes of death were GvHD and infection. Acute GvHD occurred in ten patients (4 grade I-II, 6 grade III-IV) and 3 patients also developed chronic GvHD. There were no significant differences in acute GvHD occurence and also OS regarding to the stem cell sources. At this time,10 patients with full chimerism and 6 patients with mixed chimerism are alive and disease free.

Conclusion: HSCT offers long term benefit in LAD-1 and should be considered as an early therapeutic option if a suitable HLA-matched stem cell donation is available. As pre-transplant infections in primary immunodeficient patients especially those affected by LAD-1 lead to rise in mortality rate, RIC regimen is found to be safe and mixed donor chimersim appears sufficient to prevent significant symptoms.

Insurance Approval of Mesenchymal Stem Cell for acute GVHD in Japan: Need of Follow up for Some Remaining Concerns

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Acute graft versus host disease (aGVHD) is a major obstacle following allogeneic hematopoietic stem cell transplantation. Steroid is the standard treatment for aGVHD grade II-IV; however, nearly half of patients developed steroid refractory aGVHD. Many drugs have been proposed, but no standard therapy has yet to be determined. This is because of the resistance to these drugs also of infections due to prolonged immunosuppressive states. Over the past decade a new approach using mesenchymal stem cell (MSC) has been emerging in Japan and western countries. MSCs have unique characteristics such as specific immunosuppressive properties, no immunogenicity on their own and supportive activity for hematopoiesis. Most of the published trials have reported a favorable effect in acute GVHD, but phase III trial failed to reach the primary endpoint, however, subgroup analyses found significant effects on gut and liver GVHD in the patients with MSCs infusion. In Japan several institutes are trying developed MSC for clinical use in post HSCT patients. However, several limitation make it difficult to use of MSC in clinical practice. Recently we conducted a phase II/III study using MSC (JR-031) for patients with steroid-refractory grade III or IV aGVHD. From the feasible clinical results, JR-031 was approved by PMDA as the first product which meets the Act to Revise the Pharmaceutical Affairs Act and the Act to Ensure the Safety of Regenerative Medicine. The cost of one series of the treatment is more than ten million yen. Now we encounter the new issues such as cost, indication, safety and efficacy. Mechanism of MSC has still unclear and potential concerns about ectopic tissue formation and MSC related malignancy in-vivo remain. In conclusion, MSC infusions are well tolerated and show some benefit in part of patients without adverse safety effects, however longer-term follow-up is needed to be more certain of this.

Transplantation in Older Patients

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The concept of allogeneic hematopoietic cell transplantation (HCT) was born in the aftermath of the atomic bomb explosions leading up to and following the end of World War II. The idea was simple: eliminate malignant blood cancer, say, leukemia, with the highest tolerated doses of total body irradiation (TBI) or an equivalent chemotherapeutic agent, and then rescue and cure the patient with an infusion of marrow from a healthy donor. While this approach has worked well in younger, medically fit patients, older individuals and those with comorbidities were unable to tolerate the toxicities associated with the high-intensity conditioning regimens. Yet, older individuals have the highest prevalence of hematologic malignancies. In order to get around this quandary and to treat this heretofore unserved patient population, reduced-intensity or minimal-intensity conditioning regimens for HCT have been introduced which, in large part, rely on graft-vs.-tumor effects for eradication of the underlying malignancy.

This presentation will review the results obtained with the novel regimens in older patients, which have been encouraging. One interesting finding is that comorbidities rather than physiological age turned out to be a most important risk factor for non-relapse mortality. Existing challenges include post-transplantation disease relapse and balancing graft-vs.-host disease and graft-vs.-tumor effects

Comorbidities and Age in Allogeneic Hematopoietic Cell Transplantation

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In order to enhance our ability to evaluate comorbidities before allogeneic HCT, an HCTCI was developed by modifying another non-transplant index, the Charlson comorbidity index (CCI). The study included 1055 patients with different hematologic diseases. Integer weights of comorbidities were calculated based on adjusted hazard ratios (HRs) from Cox proportional hazard models of NRM. In the validation set, the HCT-CI scores captured more patients with comorbidities compared to the CCI. The index could potentially be used to guide selection of conditioning regimens.

The HCT-CI score has been extensively validated in several retrospective and prospective multi-center studies. Overall, 25 studies could prove the validity of HCT-CI score but 8 did not. Limited sample size was evident in most of the disagreeing studies. However, in two recent large prospective studies, the HCT-CI was shown to predict both NRM and OS after allogeneic HCT given to patients in Italy or United States.

Additionally, the HCT-CI score could predict risks of development of certain posttransplant complications such as grades III-IV acute GVHD and subsequent mortality. In another study, higher pretransplant HCT-CI scores were associated with impaired physical

health, increased depression, increased distress, and diminished social support among longterm survivors. The index can best be used in combination with other variables such as Karnofsky performance status (KPS), relapse risks, the EBMT risk score, and the Instrumental Activities of daily Living.

A potential limitation of the index was the weak agreement on comorbidity coding by evaluators at different institutions. Therefore,a systematic methodology for reviewing medical charts and consistent guidelines for comorbidity coding were summarized in a web based calculator (www.hctci.org). This brief training program resulted in improvement of inter-rater reliability among different evaluators.

Two recent modifications were introduced tothe HCT-CI to improve its discriminative power. In a study of 3,033 recipients of allogeneic HCT, A score of 1 was assigned to age of ≥40 years to form a composite comorbidity/age index. In another study, weights were developed for low albumin, low platelets, and high ferritin values to develop an augmented HCT-CI.

Transplantation for Patients with Non-malignant Disorders

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This presentation will review the history and current results of allogeneic hematopoietic cell transplantation (HCT) for various, serious, non-malignant blood diseases. These include immunodeficiency disorders, severe aplastic anemia, marrow failure syndromes, and hemoglobinopathies. HCT donor choices range from HLA-identical siblings to HLA-matched unrelated volunteers, cord blood, and HLA-haploidentical relatives. For some diseases and donor/host combinations, 100% long-term survivals have been accomplished. Current efforts are focused on designing HCT conditioning regimens with minimal short- and long-term toxicities and improving prevention and control of graft-vs.-host disease.

Persistent Challenge of detection of minimal residual disease

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At diagnosis, patients with acute leukemia may have a total of approximately 10^{12} leukemia cells in the body. Complete hematological remission (CR) has been used as the standard target point of remission induction therapy of acute leukemia for the last forty years. However, even if the CR is achieved, there still could exist as many as 10^{10} leukemia cells in the patient body. Thus patients with 10^{10} leukemia cells are treated on the same regimens as those with much lower levels, perhaps with no leukemia cells at all. Minimal residual disease (MRD) is a term describing leukemia cells which can not be found by conventional cyto-morphologic criteria whose detection power is 10^{-2} (one cell among 100 leukemia cells). Polymerase chain reaction (PCR) based methods which amplified leukemia specific sequences was developed late 80's with detection power of 10^{-5} to 10^{-6}. Using this qualitative method, a large number of studies have shown that detection of MRD somewhat correlates with clinical outcome. Detection of MRD during the initial induction therapy is now one of the most important prognostic factors in childhood acute lymphoid leukemia (ALL). Similarly, MRD detected after transplant for Ph+ALL always resulted in hematologic relapse within a few months. However, MRD does not always mean hematological relapse near future. We found that MRD detected within 1 year after transplant for chronic myelogenous leukemia (CML) turn to negative. Likewise, in the patients with acute myeloid leukemia (AML) with t(8;21) who has long-term disease free survival, MRD is often detected. Furthermore, BCR-ABL and BCL2-IgH genes are detected in normal healthy volunteers. Taken together, the clinical significance of MRD detected by qualitative PCR methods is still controversial. It gives the limited information and does not allow precise analysis of tumor load kinetics. Thus the development of the quantitative MRD detection has been strongly desired.

Since early 90's, many investigators have tried to establish this quantitative MRD detection. This can be achieved by two main techniques. Flow cytometry (FCM) based detection using leukemia-associated aberrant antigens and real time quantitative PCR (RQ-PCR) based techniques using tumor specific DNA/RNA sequences. Leukemia can be regarded as malignant counterparts of cells in immature and more mature stages of hematopoiesis, respectively. Most ALL cells indeed have immuno-phenotype comparable to those of normal immature lymphoid cells. Malignant cells also display aberrant or unusual antigen expression, which are the results of cross-linage expression of antigens, maturational asynchronous expression of antigen, antigen over expression, absence of antigen expression and ectopic antigen expression. Single

antibodies are not suitable for distinguishing leukemia from normal cells, thus the detection of leukemia cells by FCM with 3 colors has been studied. In general, FCM analysis can detect one malignant cell in 10^2-10^4 cells.

"Leukemia specific gene sequences" detected by RQ-PCR are divided into three groups. One group is leukemia specific gene resulting from the chromosomal abnormalities. The second group is antigen-receptor gene. The antigen receptor gene comprises several discontinuous germ line segments that undergo rearrangement in lymphoid cells. The uniqueness of the rearrangement derives from the use of one of the many gene segments. Because such rearrangements are clonal, analysis of immunoglobulin and T-cell receptor gene configurations can be used to track the persistence of leukemia clones whose rearrangements were determined at diagnosis. In addition, fused genes such as BCR-ABL are also used for monitoring MRD in ALL. The third group is target genes which are over-expressed or ectopic-expressed. The Wilms' tumor gene (WT1) has been suggested as a powerful parameter for MRD in leukemia. Individual WT1 transcript kinetics was exclusively dependent on disease progression, treatment and subsequent disease outcome. Moreover, gradually rising WT1 levels over a period of weeks and months paralleled long-term disease progression and appeared to be a prognostic indicator for subsequent clinical relapse.

Each method has several limitations. In first, RQ-PCR for chimeric gene are applicable in only small part of leukemia. In second, detection of the immunoglobulin and T-cell receptor (TCR) gene rearrangements needs time and laborious work requiring a design of corresponding primers take 3–4 weeks. In addition, the evolution of additional clones beyond the first or index clone during therapy cannot be detected. FCM requires experienced technicians and sometimes does not achieve a deep sensitivity.

Recently, a next generation sequencing (NGS)-based method has been developed in an attempt to overcome these limitations. However, the number of published studies that have tested the clinical utility of this novel method is very small. The NGS method uses a set of universal primers, thus avoiding the laborious processes of primer designing and testing of patient-specific rearrangements. Moreover, this method has a higher sensitivity than other methods, with sensitivity values approaching 10^{-6}, which may allow more accurate predictions of clinical outcomes. Recently FCM methods developed 6 colors analysis resulting the more accurate detection of MRD and furthermore it is now applied for detection of MRD in multiple myeloma which exhibit the more complexed antigen presentation.

Finally before measuring MRD come into the general clinical fields, standardization is the most important and urgent issue. One decade ago, in the field of BCR-ABL detection, each investigator used his/her own methodologies of RQ-PCR regarding to the choice of the sample (PB or BM), methods of RQ-PCR such as the nucleotide

sequence of primers/probe, control genes (ABL, GAPDH, G6PD, -actin or HPRT) and the expression of data. Recently the standardization program of RQ-PCR has been completed in Europe and IS (International standard) is introduced. In addition new kits, which is based on this protocol, is now available. It contains the primer/probe sets and the diluted plasmids for the leukemia specific gene and the control gene (ABL). Now we are in front of door where every doctors can measure the amount of MRD like number of white blood cell.

Transplant in patients with comorbid disease

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Modifications in immunosuppressive therapies, improvements in clinical supportive care, and introduction of reduced-intensity conditioning (RIC) regimens have led to an increased indication of transplant to patients who were otherwise not previously eligible for AHSCT with a myeloablative conditioning regimen (MA), such as the elderly .Alternatively, in practice series of option can support HSCT in elderly .Patients and donors were matched for HLA-A, -B, and -C antigens by either intermediate resolution DNA typing or high-resolution techniques .Matching for HLA-DRB1 and -DQB1 was at the allele level. Patients received infection prophylaxis according to standard guidelines .Nevertheless, AHSCT continues to have a significant morbimortality rate.

Three main factors influence mortality and survival rates after AHSCT: the primary disease per se, donor type, and patient-related factors, such as the presence of comorbidities. Comorbidity indexes have been developed to evaluate the impact of these comorbidities on different clinical situations, including cancer and HSCT .Charlson's Comorbidity Index (CCI) and the Adult Comorbidity Evaluation (ACE-27) are valuable tools in predicting mortality in cancer patients.

However, CCI has shown a low sensitivity for this purpose in AHSCT. In an attempt to improve the assessment of the comorbidity risk profile in AHSCT patients, the Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) was developed. The HCT-CI included a larger number of pre-transplant comorbidities compared to CCI and provided a better predictability of transplant-related mortality (TRM) and overall survival (OS. (In developing countries, data on the impact of comorbidities on AHSCT outcomes remain scarce. Therefore, we aimed at evaluating, in this presentation the HCT-CI and the ACE-27 indexes as predictors of AHSCT complications.

Prophylactic and preemptive DLI

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Allogeneic stem cell transplantation is a most successful treatment of leukemia and other hematological malignancies. The combination of T cell depleted transplantation with subsequent transfusion of donor lymphocytes (DLI) for restitution of T cells prevents acute GVHD and improves graft-versus-leukemia effects. The effect of DLI has been shown in patients with relapse of chronic myelogenous leukemia (CML), myeloma and acute myeloid leukemia. The pattern of response indicates a role of myeloid derived dendritic cells of leukemia/host origin. Lasting responses were seen in cytogenetic/molecular and hematological relapse of CML; some patients remained in remission for more than 20 years. However late relapses were seen that responded again to DLI. Improved responses were seen with low dose interferon-a and the combination of interferon-a and GM-CSF followed by DLI. Contrary to animal studies clinical treatments could be complicated by acute and chronic GVHD. Prevention of GVHD was best achieved by delayed treatment and repeated DLI in escalating doses. In transformed relapses of CML and relapses of AML responses were less and in most cases not sustained. A rapid pace of the disease and inability of blasts to differentiate to dendritic cells were unfavorable fort he response. As a rule responses to DLI may be delayed and repeated treatments may be required. Prophylactic and preemptive DLI may control the disease in patients transplanted in remission and surviving withlout relapse for more than 6 months. In non-myeloid malignancies bispecific trifunctional antibodies may be necessary to direct T-cells towards the tumor cells. Postgrafting treatment with targeted drugs may also be helpful.

Transplant for double or triple hit lymphoma and their management

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Diffuse large B-Cell Lymphoma (DLBCL) - the most common type of lymphoma- is an aggressive but potentially curable disease. Advancement in understanding of molecular characteristics of lymphoma has improved our ability to identify subgroups of DLBCLs with poor overall survival and inferior response to standard treatment. Double-hit (DHL) lymphomas are lymphomas with evidence of myc and either bcl-2 or bcl-6 translocations. Triple hit lymphomas (THL) are defined as lymphomas with all three (myc, bcl-2 and bcl-6) rearrangements. The recent (2016) revision of the World Health Organization (WHO) classification for lymphoma has created a separate category for these lymphomas as "high-grade B-cell lymphoma with translocations involving myc and bcl-2 or bcl-6". Number of studies have demonstrated poor outcomes in patients with DHL or THL when standard frontline treatment regimens like R-CHOP are used. Subsequently and in the absence of randomized clinical trials, the standard of care shifted to more aggressive induction regimens like dose-adjusted R-EPOCH, HyperCVAD and similar protocols instead of R-CHOP. In many cases, consolidation with high dose therapy followed by autologous stem cell transplant (ASCT) has been utilized in patients who achieve complete remission after induction (CR1). A recent multi-institutional retrospective analysis did not show a meaningful clinical benefit from ASCT in first CR if an intensive induction was used for initial treatment but use of ASCT translated to improved outcomes if R-CHOP was the induction. Given the retrospective nature of the data, a detailed discussion with patients about pros and cons of ASCT in CR1 is recommended but in many institutions including ours, ASCT is no longer recommended to DHL/THL patients in CR1 after intensive induction. Patients should be aware of extremely poor outcomes after relapse and participation in clinical trials are highly recommended. Retrospective data has shown inferior clinical outcomes after ASCT in DLH/THL patients who achieve a second remission after relapse (CR2). Interestingly and taking to account the limitation of retrospective data, DHL does not seems to be an independent adverse marker for inferior outcome after allogeneic SCT and this modality should highly be considered for eligible patients with relapsed/ refractory DHL/THL. Most importantly, novel therapeutic approaches like chimeric antigen receptors (CAR) T cells targeting lymphoma markers (CD19, CD20,etc), antibody-drug conjugates, bispecific antibodies and novel combination of targeted agents, antibodies with or without chemotherapy are being tested in clinical trials.

HSCT for Multiple Sclerosis

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Intense immunosuppression followed by autologous haematopoietic stem cell transplantation (AHSCT) is a treatment now considered by the neurological community as a possible strategy for aggressive forms of multiple sclerosis (MS). In the past years it was barely taken into account by the majority of MS experts, for its low profile of safety and the absence of prospective randomized controlled studies. More recently, while the randomized controlled trials are still lacking, numerous studies have been published that convincingly demonstrate its undeniable efficacy in the more aggressive forms of MS.

In the majority of relapsing multiple sclerosis patients the disease can be quite easily controlled by the already available and approved therapies. There are however some aggressive cases that continue to have clinical and MRI activity in spite of the treatment. These are the cases that likely can take advantage by intense immunosuppression followed by autologous haematopoietic stem cell transplantation

Several studies support the notion of a qualitative immune resetting after the procedure and have suggested mechanisms potentially underlying the powerful treatment effects that last well beyond recovery of immune cell numbers. Indeed, open uncontrolled studies have shown suppression of any detectable form of MS disease activity for 4-5 years in 70-80% of patients treated with AHSCT, higher rates than those achieved by other therapies for MS in separate studies. Superiority of AHSCT over mitoxantrone at suppressing MRI activity has been shown in one randomised controlled trial. The initially high treatment-related mortality (3.6% in studies until 2005) has considerably decreased in recent years (0.5% in studies from 775

An evidence already exists to support the use of AHSCT for treatment of patients with aggressive relapsing MS and those with treatment-refractory relapsing MS who failed to respond to high-potency approved DMT because of lack of efficacy.

Post transplant maintenance in lymphoid malignancies

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Autologous stem cell transplant (ASCT) after conditioning with high dose chemotherapy or radiation is commonly used for treatment of high-risk lymphoid malignancies. ASCT is considered standard of care in patients with diagnosis of diffuse large B-cell lymphoma (BLBCL) or Hodgkin Lymphoma (HL) in second remission and some experts consider it standard for patients with mantle cell lymphoma (MCL) after achievement of first remission. While this approach has resulted in significant improvement in patient outcomes, relapse after ASCT is common and occurs in significant number of patients ranging 40-60% depending on the histology and clinical situation. One strategy to prolong the duration of response in these patients is maintenance therapy using novel agents with high disease activity and low rate of side effects. In the past decade, number of active anti-lymphoma agents have been introduced to the field and are increasingly used for treatment of lymphoma either as part of combination with chemotherapy agents or as monotherapy. These agents are of particular interest in the maintenance setting given their minimal toxicity profile.

Maintenance studies using monoclonal anti CD-20 antibodies (like rituximab) for patients with DLBCL after ASCT have not shown a clinically significant benefit and therefore such use of agents is not currently recommended for this indication. While not approved for DLBCL, Bruton tyrosine kinase (BTK) inhibitor, ibrutinib has been shown to be more active in a subset of DLBCL patients with activated B cell type (ABC). As a result, a US intergroup study is currently ongoing to assess the potential benefit of ibrutinib maintenance therapy after ASCT for ABC type DLBCL patients. In recent years antibody drug conjugate brentuximab vedotin (BV) has been approved for Hodgkin lymphomabpatients in the relapsed setting. Evidence from a prospective randomized study has demonstrated improved progression-free survival for high-risk HL patients who received BV maintenance after ASCT compared to the standard of care arm. Another group of novel therapeutic agents for HL is checkpoint inhibitors and anti PD-1 antibodies nivolumab and pembrolizumab have both shown significant activity in relapsed HL. Currently, a multicenter study investigates the efficacy and toxicity of combination of nivolumab and BV for HL patients in the post ASCT setting. Lastly, for MCL patients who undergo ASCT, role of rituximab maintenance has been studied and an overall survival (OS) benefit has been shown with rituximab maintenance after ASCT. This practice-changing finding has led to other studies using

anti CD20 antibodies and other novel agents (proteasome inhibitors, immunomodulatory agents, etc) to further improve the outcomes.

In summary, as more novel targeted agents become available for treatment of lymphoid malignancies, new studies will be required to understand and determine the optimal regimen for maintenance therapy in the post-ASCT setting in order to improve the OS without compromising quality of life.

International accreditation and quality of HSCT: the JACIE experience

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The complexity of transplantation as a medical technology and the frequent need for close interaction and interdependence between different services and teams including external providers (donor registries, typing laboratories etc.) distinguishes it from many other medical fields. Approximately 20 years ago this complexity led to efforts by transplantation professionals to standardise processes based on consensus as a way to better manage the inherent risks of this treatment. In the regard, haematopoietic stem cell transplantation (HSCT) was, and continues to be, a pioneer in the area of quality and standards.

The Foundation for Accreditation of Cellular Therapy (FACT) and the Joint Accreditation Committee – ISCT & EBMT (JACIE) stand out as examples of profession-driven initiatives to improve quality in transplantation and which have subsequently been incorporated by third parties like healthcare payers (heath insurers, social security) and competent authorities (authorisation of treatment).

In the presentation an overview of where these initiatives came from, the format of the standards and the philosophy underlying these schemes will be given. Specific practical issues such as viability of products and validation of processes will be discussed along with some practical examples to illustrate the relevance of the standards to day-to-day work. In the second part, an explanation of future developments including the 7th edition of the FACT-JACIE Standards, new standards for immune receptor cells and benchmarking of clinical outcome.

Graft-vs.-Host Disease and Graft-vs.-Tumor Effects

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Graft-vs.-host (GVH) reactions occur after immunocompetent hematopoietic cells are infused into a histoincompatible immunocompromised host. Targets of GVH reactions include hematopoietic cells, and this conveys graft-vs.-tumor (GVT) effects in patients with blood cancers and skin, gut, and liver epithelia, where GVH reactions cause graft-vs.-host disease (GVHD). It was recognized early on in both animal experimentation and the first human transplants that avoiding GVHD negated GVT effects, which then led to death from the underlying malignancy for which the transplant was carried out. On the other hand, permitting GVHD and thereby enabling GVT effects risked serious damage in skin, gut, and liver, and death from associated infections. A precise way how to balance these two competing immunological reactions and establish graft-vs.-host tolerance while maintaining GVT effects has eluded us to this day. The recently introduced minimal-conditioning regimens for transplantation to treat older patients with hematologic malignancies rely in large part on GVT effects. Given the minimal nature of these regimens, they have allowed for the purest determination of GVT effects apart from conditioning, and the best determination of GVHD not augmented by regimen-related toxicities. For control of GVHD and also to enable engraftment, patients receive post-grafting immunosuppression, which is slated not to exceed 6 months after transplantation. The hope is that, once immunosuppression has been discontinued, “the brakes will be taken off” the immune cells so that powerful GVT effects will occur. In part, these hopes were fulfilled; nevertheless, disease relapse in patients with advanced hematologic malignancies has remained the primary cause of failure of allogeneic HCT followed closely by GVHD. This presentation will review improved GVHD prevention, with particular focus on avoiding serious acute GVHD, which is not associated with GVT effects but, rather, with an unacceptably high non-relapse mortality. The report will also show that the level of disease burden at the time of transplantation is a major predictor of relapse. Targeted radio-immunotherapy with a novel, powerful, short-lived alpha-emitting radionuclide added to existing conditioning regimens, promises to increase tumor cell kill before transplantation without adding toxicity. Combining this approach with improved GVHD prevention is likely to reduce the risks of both relapse and non-relapse mortality from GVHD and improve overall long-term survival.

Chronic GVHD and Immune Function Post Allo-HCT

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Chronic Graft-vs-Host-disease (GVHD) is one major complication following allogeneic hematopoietic cell transplantation (HCT) that, with increasing age of patients, use of unrelated donors, and better survival during the early phase post-HCT, is continuously increasing in incidence. Besides major impairment of quality of life, caused by classical cGVHD symptoms (diarrhea, painful dry eyes and mouth, etc.) patients suffer frequently from infections that constitute the major cause of death in this patient cohort. Because these patients are usually given several immunosuppressant drugs infectious complications are often ascribed to this medication. In contrast, the way lymphoid tissues are affected by alloreactivity, and which role the damage of these tissues has on immune reconstitution and function post allo-HCT is poorly understood. While it is commonly believed that donor T cells are important for immune protection as donor immunity can be transferred into the recipient during an allo-HCT, the clinical observation that GVHD has a major impact on immune function has long been known. Here, we present and summarize findings on immune reconstitution in the context of GVHD in mice and humans.

Treatment Option for Steroid Refractory GVHD

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Allogeneic stem cell transplantation is a potentially curative treatment for a variety of hematologic malignancies and non malignant diseases. However, about half of the patients receiving transplantation are subsequently exposed to increased morbidity and mortality.
One of the major complication is the by donor T cells mediated acute and chronic graft-versus host disease (GvHD), which resulted in high morbidity and also mortality and is associated with reduced quality of life.
Despite better understanding of the pathogenesis of acute graft-versus-host disease (aGVHD) and the increasing prophylactic treatment option with a wider array of immunosuppressive medication, about 30-50% of our patients that undergo allogeneic hematopoietic cell transplantation develop grade 2-4 aGVHD and about 40 to 50% will become steroid refractory. Acute GVHD patients who are refractory to standard steroid treatment have a dismal long-term prognosis with only 5-20% overall survival.
If GvHD become steroid refractory alternative treatment options are antithymocyte globulin, alemtuzumab , mycophenolate mofetil, anti-IL receptor antibodies, TNF alpha antibodies , pentostatin or etarnercept has been used alone or in combination but treatment success is limited. Controversial results were report for mesenchymal stroma cells in treatment of steroid refractory GvHD. More recently, JAK inhibition by ruxolitinib resulted in high response rate in steroid refractory acute and chronic GvHD in a retrospective study. More recently encouraging results were report about fecal transplantation in a limited number of patients.

Daratumumab in conjunction with ABMT, Cancer Centre London Experience

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Daratumumab is a human IgGK1k monoclonal antibody with high affinity to CD38 that has in the last 2 years in the US (and last year in Europe) been increasingly used in a real-world setting of standard clinical care; albeit with huge restrictions because of cost in spite of having clear cut proven efficacy.

We report the challenges of introducing its use into a busy myeloma clinical practice in the UK in a private care healthcare insurance setting at a time when it is not part of the UK National Health provision for treatment with results of 25 patients treated over a period of 18 months, with entry including patients who have previously relapsed some from all approved treatment options. The challenges include management of potentially severe infusion related reactions in a High Dependency setting, the difficult of alerting the blood transfusion service to difficulties in cross matching blood, the difficulty of interpreting MRD and bone marrow IP, and the interference the daratumumab has in assessing response in IgGK myeloma patients. This latter problem requires a protein reference laboratory to distinguish between myeloma IgGK with the same mobility as Daraumumab IgGK. We will discuss that Daratumumab has an effect on the levels of 'normal' immunoglobulins and 'normal' free light chains that requires that these tests are interpreted in a more sensitive way than normally.

It is into this background we will discuss how we have piloted insertion of an autologous stem cell transplant into the monthly daratumumab maintenance pathway

Role of ATG in preventing GvHD

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Allogeneic stem cell transplantation (allo-SCT) is a potentially curative treatment for a wide range of hematologic malignancies. However, about half of the patients receiving transplantation are subsequently exposed to increased morbidity and mortality. Furthermore, donor immune cells contained in the graft can also target healthy host tissues causing acute and chronic graft-versus-host-disease (GVHD), which is associated with reduced quality of life.

Polyclonal anti-thymocyte globulins (ATG) or Anti-lymphocyte globulin (ALG) from the rabbit have been introduced about 50 years ago into the allo-SCT setting. The use of these globulins reflects a form of in vivo T-cell depletion, which concomitantly depletes host T-cells that have survived the conditioning regimen. This reduces the risk of rejection while similarly depleting newly infused donor T-cells, thus potentially reducing GVHD.

Randomised studies with or without ATG or ALG in unrelated stem cell transplantation has been shown to reduce the risk of acute and chronic graft-versus-host disease, while the effect on reduction of chronic GvHD was more striking. Furthermore this did not lead to a higher incidence of relapse. The role of ALG in HLA-identical sibling transplantation was recently confirmed by a significant reduction of chronic GvHD in AML and ALL patients without increase of relapse.

Meta-analyses were conducted and provide evidence of ATG/ALG favorable outcomes in patients undergoing allo-SCT

A recent network analysis between ATG and ALG showed that ATLG seems to be the best option to prevent chronic and acute GVHD. Both formulations show similar efficacy in TRM while ATG tends to be the better treatment option regarding survival.

Multiple Myeloma: Allogeneic or Autologous Hematopoietic Stem Cell Transplantation?

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Introduction: Autologous stem cells transplantation (auto-HCT) is an accepted method in multiple myeloma (MM) patients, but usually it is not curative. The issue of allogeneic hematopoietic stem cells transplantation (allo-HCT) is challenging yet for myeloma. We investigated allo-HCT in MM and compared with auto-HCT.

Patients and Methods: In this retrospective study, we recruited 272 patients from January 2011 to January 2015 (218 (80.15%) patients in autologous group and 54 (19.85%) in allogeneic group). We performed allogeneic HCT with peripheral blood stem cells source in our center for patients who are relatively young (less than 55 years old) with good performance, have match sibling donor and accepted allogeneic HCT. The conditioning regimens in autologous and allogeneic groups was Melphalan 200 mg/m2 only and Fludarabine 30 mg/m2 plus Melphalan 140mg/m2 in 5 days respectively. GVHD prophylaxis consisted of Methotrexate and Cyclosporine. The outcomes then compared between two groups using log-rank and Gray tests and cox proportional hazard regression.

Results: The median follow-up in the autologous and allogeneic group was 17.02 months. Three years disease-free survival of auto-HCT was 38.61% (CI: 27.37%, 49.72%) and 68.88% (CI: 50.74%, 81.47%) for allo-HCT patients (P-value = 0.0363).
Three years overall survival of auto-HCT was 77.26% (CI: 66.08%, 85.16%) and 82.15% (CI: 64.92%, 91.44%) for allo-HCT patients (P-value = 0.6363) showing no significant statistical difference between two groups.
Mortality rate was 11.01% for auto-HCT and for allo-HCT was 12.96%. The most common cause of death between two groups was relapse of primary disease. Three year relapse incidence was 20.83% (CI: 9.04%, 35.30%) for allo-HCT and 54.33% (CI: 42.02%, 65.09%) for auto-HCT (Gray's test p-value = 0.018). The three year TRM incidence was 10.36% (CI: 2.92%, 23.33%) and 7.01% (CI: 3.14%, 12.98%) in allogeneic and autologous patients respectively (Gray's test p-value = 0.42).

Conclusion: Despite there was no statistically significant difference between two groups in terms of OS but DFS and relapse incidence was meaningfully better in allogeneic group. So, perhaps the reason of non-significant OS improvement in allogeneic group is higher early death due to higher TRM. We suggest that this study needs longer follow up to see whether allo-HCT resulted in OS improvement.

Pedigree Analysis: a Tool for Finding Matched Donors in Patients' Second and Third Degree Relatives

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The most available matched stem cell donors are patients' siblings. In countries that consanguineous marriage is legitimated there is possible to find matched donors in the patient relatives other than siblings. In western countries such a donors could be found by chance and after extended family HLA typing. The basis of finding matched other relatives in western countries is common HLA haplotypes in their population and any patient that have such haplotypes has a (small) chance of having matched other relatives. In consanguineous marriages there is additional chance of shared HLA haplotypes between patients' father's and mother's family. The most frequent of such donors are patients' parents. By limited family HLA typing and extending HLA pedigree to the parents' families we have found 253 matched stem cell donors during 2006 to the end of 2016. For some of the patient international search for unrelated donors couldn't find any matched donor throughout the world. In conclusion, pedigree analysis is a valuable tool for finding matched donors in patients who had no matched sibling donor and their parents are related.

Successful Treatment with Granulocyte Transfusion and Early Neutrophil Engraftment in Allogeneic Transplant Patients with Febrile Neutropenia

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Background and Aim: Febrile Neutropenia is very severe and urgent early complication after bone marrow transplantation before engraftment. Infection delays engraftments. In this study we evaluated the effect and outcome of Granulocyte transfusion on febrile neutropenia and neutrophil engraftment in patients receiving allogeneic transplantation.

Methods: Between 2015-2016, five patients receiving allogeneic bone marrow transplantation (BMT) were treated with granulocyte transfusion at the time of febrile neutropenia before engraftment. The reasons for the use of the granulocyte transfusion were prolonged febrile neutropenia episode.

Results: Five AML patients underwent allogeneic transplantation. Three of them transplanted from match sibling donors, one from unrelated donor, and one from (7/10) mismatch mother (haploidentic transplant). They had febrile neutropenia after transplantation, before engraftment. They were given antibiotics. Before the granulocyte transfusion, on the 13th – 18th days of transplantation, their neutrophil counts were 0.03-0.08 x 10^3/dl. We started Granulocyte transfusion for three days. Granulocyte was collected from unrelated and same blood groups donors. Mean infused granulocyte counts were 3.6 x 10^10 (1.3 - 4.6x10^10) /day. Twenty-four hours after granulocyte transfusion, mean neutrophil counts were 0.6x10^3/dl (0.4-0.8 x 10^3/dl). Neutrophil counts were 2.6 x 10^3/dl, (1.7-2.6 x 10^3/dl), after 48 hour. After 72 hours, neutrophil counts were 3.4 x 10^3/dl. (2.1- 4.5 x 10^3/dl). After 4th days of granulocyte transfusion, neutrophil counts were normal levels (> 0.5 x 10^3/dl.)

Conclusion: Granulocyte transfusions during the febrile neutropenia, helped to better-overcome febrile neutropenia periods in allogeneic transplant patients before engraftment. In addition, granulocytes transfusion also may help early neutrophil engraftments.

Autologous Cord Blood Transplantation in Children with Acquired Severe Aplastic Anemia

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Background and Aim: Introduction Autologous cord blood transplantation for acquired aplastic anemia has been reported only rarely. But there is a growing number of children with SAA may have had their stem cells harvested through cord blood collection. Objective To investigate the efficacy of autologous umbilical cord blood transplantation in the treatment of aplastic anemia in children. We were analyzed 4 cases during the period of 2010 to 2016 in our center.
Methods: Methods 1) The 4 patients with 3 girls and 1 boy were diagnosed with acquired severe aplastic anemia. The age of the 4 cases was 5 years old, 3 years old, 1 years and 8 months old and 3 years and 8 months old respectively. 2) The regimen was with mainly immune regulation treatment: ATG+CTX+FLU. 3) In 01 days autologous cord blood were transfusion after the third human umbilical cord mesenchymal stem cells infusion. The total number of umbilical cord blood cells were 2.054 ×107.kg-1, 1.64×107.kg-1, 6.73×107kg-1, 5.5×107. kg-1 respectively and CD34+ cell counts were 0.634×105kg-1, 0.57×105 kg-1, 4.56×105. kg-1, 1.2×105 kg-1, respectively. 4) The first and the second patient were not treated with immunosuppressive agents after transplantation. The third and the fourth received cyclosporine A orally for half a year after transplantation, and then gradually stopped.
Results: Results 1) Durable hematopoietic reconstitution was seen in all the 4 patients. The time of leukocyte engraftment was +21 days, +23 days, 19 days and 23 days respectively. The platelet engraftment time was +23 days, +25 days, 28 days and 26 days respectively. 2) The recurrence of the disease occurred in half of the first case after transplantation, the other three cases remained normal after the transplantation, and the quality of life was good.
Conclusion: Conclusions 1) There is no rejection in the autologous umbilical cord blood transplantation, so there is no implant failure. And there is no requirement for autologous umbilical cord blood cell count. 2) autologous umbilical cord blood transplantation without GVHD occurred in children with fewer transplants events and higher quality of life. 3) It is suggested that cyclosporine be maintained for six months after transplantation in order to avoid recurrence. 4) Autologous umbilical cord blood transplantation is the first choice for the treatment of acquired aplastic anemia.

Expansion of Umbilical Cord Blood Hematopoietic Stem Cells on Biocompatible nanofiber Scaffold as co-culture with Bone Marrow derived Mesenchymal Stem Cells

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is one of the treatment approaches for malignant and non-malignant hematologic diseases. The most important disadvantage of UCB in HSCT is low number of cells that can be collected. So, different systems for ex vivo expansion of HSCs were designed to overcome this limitation. The goal of this study was to examine different conditions of ex vivo expansion of HSCs.
Methods: In this study, HSCs were cultured in four conditions: 1- In two-dimensional culture (2D), 2- Co-culture with mesenchymal stem cells (MSCs) in 2-D (2D-Co), 3- In three-dimensional culture (constructed with poly eter sulfon nanofibers) (3D), and 4- Co - culture with MSCs in 3-D (3D-Co).
Results: The comparison of these groups showed that 3D-Co group had more expansion levels and expression of CD34 marker than other groups. Moreover, the clonogenic capacity in this group was increased in comparison to other groups
Conclusion: The results of our study showed the possibility of usage of this system for expansion with lowest levels of differentiation in CD34+ HSCs. Further studies are needed to evaluate expanded cells with this system to use in clinical practice.

Hepatogenic Differentiation of IPS Cells on an Aligned Polyethersulfone Copared to Random Nanofibers

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Background and Aim: Combination of induced Pluripotent Stem Cells (iPSCs) and nanofibrous scaffolds has potential treatment for liver tissue engineering. Recently Polyethersulfone (PES) is introduced as a biocompatible biomaterial for artificial liver system. Due to the importance of hepatocyte cells functionality in vitro, in this study Hepatocyte like cells differentiation of iPSCs was investigated on aligned PES versus random nanofibers scaffolds.

Methods: Aligned and random PES/COL nanofibrous scaffolds were fabricated by electrospining and their surface modified through plasma treatment and collagen coating. The scaffolds were characterized using scanning electron microscopy (SEM) and ATR-FTIR. Morphology and biochemical activities of the differentiated hepatocyte-like cells (HLCs) were examined after 5 and 20 days of differentiation. Real-Time RT-PCR and ICC showed no significant difference in the mRNA and protein levels of two important definitive endoderm specific markers, including Sox17 and Foxa2 between two scaffolds.

Results: However, Real-Time RT-PCR analysis indicated an increase in the expression of Cyp7A1 gene over the period of the differentiation procedure on the aligned nanofibers but there was no difference in other genes such as Albumin and CK19. Moreover, comparison of hepatogenic differentiation evaluated by Albumin production in conditioned media of HLCs differentiated on aligned PES/COL, showed increase expression of these markers after 20 days compared to that of the random nanofibers.

Conclusion: Taken together, the results of this study may indicate that aligned PES/COL nanofibrous scaffolds can improve terminal differentiation of HLCs from iPSCs.

Mild Hypoxia and Bone Marrow Mesenchymal Stem Cell Enhances Expansion and Homing of Human Cord Blood CD34+ Stem Cells

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Background and Aim: Cord blood (CB) is a rich source of Hematopoietic stem cells (HSCs) that has been used successfully to treat a variety of hematologic and non-hematological disorders. Beside the advantage of CB, the main disadvantages of CB are the limited number of stem cells available for transplantation and delayed engraftment. Identifying strategies to enhance expansion, engraftment and homing of HSCs can improve transplant efficiency. The goal of this study was to examine different culture conditions on ex vivo expansion and homing capacity of CB-HSCs.

Methods: In this study, human cord blood CD34+ HSC isolated by MACS ,Cultured in the serum-free medium (Stem line II) supplemented with cytokines(TPO,FLT3L,SCF) with/without Bone marrow Mesenchymal stem cell feeder layer in normoxia (21% O2) and mild hypoxia (5% O2) for 7 days . Before and after of this period, Total nucleated cell count (TNC), CD34+ cells count, CFC assay, migration assay and CXCR4 expression by Real time PCR were evaluated. The data analyzed using the paired t-test. Value < 0.05 were considered statistically significant.

Results: At the end of 7 days of culture, highest number of total nucleated cell (TNC) , CD34+ cells, Colony forming units (CFUs), migration percent and CXCR4 mRNA level were seen in coculture of HSC with bone marrow Mesenchymal stem cell (MSC) feeder layer at 5% O2 . Our findings demonstrated statistically significant (1.7-3.2 fold) increase of CXCR4 gene expression in hypoxia versus normoxia.

Conclusion: Bone Marrow (BM)-MSC and mild hypoxia (5% O2) combination not only improves HSC expansion but also enhanced homing capacity of HSC and better mimicked the niche microenvironment conditions.

Co-Transplantation of Mesenchymal Stem and Hematopoitic Stem Cell in ß-thalassemia Patients

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Background and Aim: Mesenchymal stromal cells (MSCs) possess immunomodulatory properties and may play important roles in graft- versus- host disease (GvHD) and engraftment. This study examined co-transplantation of MSCs and HSCs (Hematopoietic Stem Cells).

Methods: We investigated co-administration of ex vivo expanded MSCs along with HLA-identical sibling-matched HSCs in β thalassemia major patients. We recruited 70 patients from January 2010 to January 2015 in our study. All participants received Cyclophosphamide-based or Fludarabine–based conditioning regimens and short-course Methotrexate and Cyclosporine as GVHD prophylaxis. MSCs were administered intravenously (1.0–2.0* 106/kg) into patients (n=41) four hours before infusion of HSCs. The outcomes were then compared to those of 29 patients transplanted with HSCs alone

Results: The median follow-up in the MSC and non-MSC group was 2.98 and 2.62 years, respectively. Median time to WBC engraftment >0.5 _ 109/L was 17.7 days (range: 15–20 days) in both groups (p-value =0.83) and median time to platelet engraftment >20_109/L was 27.2 days (range: 22-31 days) in the MSC group, while it was 36.6 days (range: 22–50 days) in the non-MSC group (p-value=0.26). Fifty-six percent of patients had acute GvHD in the MSC group compared to the non-MSC group where 65.5% developed acute GvHD (p-value=0.42). Meanwhile, chronic GvHD was 21% in the MSC group and 37% in the non-MSC group (p-value=0.14). Three-year overall survival rates were 70% and 61% in the MSC and non-MSC group, respectively (p-value=0.78). Three-year thalassemia-free survival rate was 54% in the MSC group and 61% in the non-MSCs group, showing no statistically significant difference (p-value=0.35). The 3-year rejection incidence in the MSC and non-MSC group was 19% and 3 %, respectively (p-value=0.07). There was no statistically significant difference between the two groups in terms of 3-year transplant-related mortality (p-value=0.79).

Conclusion: This study indicates that co-transplantation of HLA-identical sibling HSCs with MSCs does not inflict harm on bone marrow transplantation procedure and seems to be safe and secure. On the other hand, differences between the two groups in

acute and chronic GvHD, engraftment, overall survival, thalassemia- free survival and rejection incidence did not reach any statistical significance. Therefore, despite the immunomodulatory activity of MSCs and their role in GvHD amelioration and engraftment improvement resulted from in vitro studies, their efficacy in the clinical setting has not been conclusively proven which indicates further multicenter randomized clinical trials are required.

Evaluation of HLA-Identical sibling Allogenic Peripheral Blood Stem cell Transplantation for Acute Myelogenous Leukemia at BTH, Vietnam

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Background and Aim: Peripheral blood hematopoietic stem cell transplantation could improve the prognosis of AML. The purposes of this study was to assess the efficacy of HLA-identical sibling allogenic peripheral blood stem cell transplantation in the treatment of acute myelogenous leukemia (AML) at Blood transfusion and hematology hospital at Ho Chi Minh City.

Methods: retrospective study, case series

Results: from June 2005 to September 2016, there were 47 AML patients included 24 males and 23 females, with median age of 36 years old. Engraftment was achieved in 47 patients (100%). The median number of transfused CD34+ cells was 7.5 x 106/kg. The median time for neutrophil and platelet engraftment were 11 ± 2.8 days and 12.5 ± 10.1 days respectively. Oral mucositis occurred in 38 patients (80.9%), febrile neutropenia in 42 patients (89.4%), acute graft-versus-host disease (aGvHD) in 14 patients (29.8%), chronic graft-versus-host disease (cGvHD) in 10 patients (21.3%), and VOD in 6 patients (12.8%). Transplant-related mortality (TRM) was 4 patients (8.5%). Median follow-up time was 52.26 months. Patients remained alive were 27 (57.4%). The 5-year overall survival (OS) and disease-free survival (DFS) were 55% and 54% respectively.

Conclusion: HLA-identical sibling allogeneic blood stem cell transplantation can reconstruct hematopoiesis quickly and is a favorable therapeutic method for AML patients. Further development and improvement of hematopoietic stem cell transplantation techniques along with graduated and individualized therapy are expected to provide better outcomes and improved quality of life for AML patients.

ABSTRACT
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Haploidentical Back-Up Donor in the Allogeneic Hematopoietic Stem Cell (HPC) Transplantation

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Background and Aim: Haploidentical stem cell transplant is an attractive form of transplantation because of the immediate donor availability, ease of stem cell procurement, and the possibility to further collect donor cells for cellular therapy.
Methods: In the allogeneic hematopoietic stem cell (HPC) transplant, when a patient found a primary suitable unrelated stem cell donor, the needs of back-up donor will be considered seriously by alternative medical committee. According to 148 work-up procedures that have been performed for 158 patients by Iranian Stem Cell donor program(ISCDP); for about 85% of these work-ups, a haploidentical donor has been selected by alternative medical committee and about 15% of back-up donors were non-haploidentical based on patient's diagnosis.
Results: Fortunately, all transplantations have been performed by the primary selected donor and no back-up donors were used for this reason.
Conclusion: The selected haploidentical back-up donor is always considered as an important issue beforehand even though we never used them during patient's transplant process. And selecting a haploidentical donor is also considered as fastest and easiest way for patient saving time.

Comparison of Survival Rate between Autologous and Allogeneic Bone Marrow Transplantation In The Treatment of Patients With Leukemia: Adjusted Analysis With Semiparametric Model

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Background and Aim: Autologous and allogeneic bone marrow transplantation (BMT) or stem cell transplantation (SCT) are increasingly considered for treatment of patients with acute lymphoblastic leukemia (ALL) and acute myelocytic leukemia (AML). The purpose of this study is to compare survival rate after autologous and allogeneic BMT in patients with ALL and AML.

Methods : In a retrospective study, total of 93 patients with ALL and AML who had received autologous and allogeneic BMT, registered in Hematopoietic Stem Cell Research Center (from 2007 to 2016), Taleghani hospital, Tehran, Iran entered to this study. Kaplan-Meyer and ordinal logarithm methods were used to compare the survival rate between autologous and allogeneic BMT. Also age, sex, blood group, types of leukemia, white blood cell (WBC) count at the time of diagnosis, CD34+ and total mononuclear cells (MNC) were analyzed. Modeling of data was carried out using STATA, version11, and Cox regression method.

Results: The mean age of the patients at diagnosis was 32.11 ± 10.32 years (range, 2-61 years) and 47 patients (50.5%) were male. The average follow-up period was about 20.29±22.58 months (range: 0.33-87.37). Out of 93 patients, %36.6 had ALL and %63.4 had AML. Allogeneic transplantation was performed in 72 (77.4%) patients while autologous transplantation was given to 21 (22.6%) patients. The mean (± standard deviation) survival time for allogeneic transplantation was 48.22±5.04 months while for autologous transplantation was 64.02±8.6 months. The multivariate Cox model showed that there was a significant relationship between age, logWBC and total MNC with leukemia survival rate.

Conclusion: According to our data survival rates of patients with leukemia who was received autologous transplantation was greater than patients who was given allogeneic transplantation.

Evaluation of CD34 and MNC Cell In Improving The Time of Engraftment In Patients Undergoing Peripheral Blood Stem Cell Transplantation

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Background and Aim: Hematopoietic stem cells consist of 0.1%-1% bone marrow and CD 34+ is popularly used as the cell marker to identify these subsets from other blood cells. The rate of CD34+ cells is 0.01%-0.1% in peripheral blood mononuclear cells (MNC). To satisfy the effective fringe inferred by undifferentiated hematopoietic cell transplantation, requires the administration of the compelling mobilizer to expand the rate of CD34+ cells in the fringe blood. Joining chemotherapy and G-CSF is at present being viewed as the best program for HSC mobilization. The aim of this paper is to evaluate the accomplishment of PBSCT in both of autologous and allogeneic transplantation, furthermore this sort of transplantation needs a durable and quick procedure. This study was a descriptive and cross-sectional article which have been carried out in Imam-Reza Hospital Transplantation Center in Kermanshah province during 2 years ago on 43 patients who have been diagnosed with malignancy and need peripheral blood stem cell transplantation.

Methods: In this study we analyzed and compared the effects of CD34 and MNC (mono nuclear cell) to CD3 in engraftment time in patients who have been referred to Imam-Reza Hospital Transplantation Center with malignancy diagnosis as follows: 7 Patients with diagnosis of Acute myeloid Leukemia, Multiple myeloma 21 patients, Hodgkin lymphoma 9, non-Hodgkin lymphoma 3, primary myelofibrosis 1 and acute lymphoblastic leukemia 2. Regarding the conditions of patients and their type of malignancy, from 43 patients 9 of them were transplanted with allogeneic and 34 patients underwent autologous transplantation. The patients received granulocyte-colony stimulating factors (G-CSF) after chemotherapy. The average mononuclear cells (MNC) collected from each patient were 7.15 * 10^8 MNC/kg and mean CD34 and CD3 in these patients were 35.73 and 64.66 cell/µl, respectively. Also the mean

age in the patients was 45.4 years and we have evaluated the data by analytical software: SPSS and Pearson correlation.

Results: In this study, by performing a statistical analysis, we found that the relationship between a number of important markers in transplantation and improving the timing of engraftment was as follows. The mean engraftment time in the patients was 9.41 days. The most important relationship was found between CD34 and MNC markers and reduced engraftment time (p=0.021, p=0.00 respectively). Also there was a direct relationship between CD3 and engraftment time (p=0.04), which led to a significant reduction in the time of engraftment by decreasing the cell marker in collected cells.

Conclusion: Peripheral blood stem cell transplantation (PBSCT) is an effective treatment for hematological malignancies. Also According to extracted statistical data, we concluded that there is a special correlation between these markers and the shortening of the engraftment time. As in this study, patients who had a large number of CD34 in the stem cells derived from mobilization had decreased their time of engraftment. Consequently, these markers can be utilized to anticipate an opportunity to enhance transplantation.

Results of an Alternative Method for Custom Prime: A Case Series of Successful Peripheral Blood Stem Cell Harvesting from Twenty Five Low-Weight Child donors

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Background and Aim: In different hematological malignancies and disorders as well as and non-hematological malignancies stem cell transplantation is a key to the cure after remission. Peripheral blood stem cell apheresis (PBSCA) is one the most common methods to the collection of stem cells for transplantation. Although in low weighted donors this method is accompanied with different complications.

Methods: This study evaluated results of PBSCA in less than 20Kg donors during Jan 2014 to Jan 2017 in Shariati Hospital (Tehran, Iran). Donors and receivers were assessed for demographical information as well as diagnosis, success rate and details of the procedure, cell counts, and occurrence of graft versus host disease (GVHD).

Results: The receivers were categorized into the allogeneic (N: 25 and the same number of donors) and autologous (N: 12). In allogeneic group, the average of CD34 positive cells was 4x106 and CD3 positive cells counted as 300x106. For autologous group CD34 positive cells counted 10x106. The most common diseases were shown as thalassemia (44%), acute lymphoblastic leukemia (16%), and acute myeloid leukemia (12%). The success rate was 100% which after a mean of 41 months follow-up 76% of receivers were alive. The incidence of both acute and chronic GVHD was 56%.

Conclusion: Authors hope that current information may help clinicians to have a better insight for less than 20Kg weighted donors.

Prognostic Effect of Pre-Treatment Cytogenetic Abnormalities In Iranian Adults Acute Myeloid Leukemia After Allogeneic Hematopoietic Stem Cell Transplantation

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Background and Aim: Several studies have revealed the significance of pre-treatment cytogenetic findings in tumor cells as a strong clinical predictor. We aimed to evaluate the effect of pre-treatment cytogenetic abnormality on treatment outcomes in Iranian adults with acute myeloid leukemia (AML) after allogeneic hematopoietic stem cell transplantation (HSCT).
Methods: A total of 323 adult patients with non-M3 AML underwent allogeneic HSCT from March 2011 to March 2015 in Shariati General Hospital, from which 206 patients with pre-treatment cytogenetic data were included in our study with median follow-up time of 47 months. Overall survival (OS) and Disease-free-survival (DFS) rate of different cytogenetic abnormalities were compared with normal karyotype.
Results: Five-year OS rate for all patients were 58.54 %. OS and DFS rates were significantly lower in abn(3q), inv(3)(q21;q26),t(3;3)(q21;q26),del(5q)/add(5q), t(6;9)(p23;q34), -7, abn(7q), +8, 11q23 and abn(11q) (excluding (11;19))(p21;q23) and (11;19)(q23;p13)), abn(17p), complex karyotype (more than 3 unrelated abnormalities) and monosomal karyotype. None of the cytogenetic abnormalities were associated with favorable outcomes.
Conclusion: Our study suggested that age and pre-treatment cytogenetic abnormalities are independent predictors of treatment outcome after HSCT in AML patients. Unlike previous studies, in our study t (8; 21) and Inversion (16) were not associated with favorable outcomes and were classified as intermediate risk groups.

Application and Assessment of Allogeneic Fibroblasts for Cell Therapy

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Background and Aim: In the recent years, due to increasing number of patients with non-healing skin ulcers, skin substitutes have been used. Skin substitutes contain living cells causing faster and better wound healing. Therefore, research on the use of autologous and allogeneic cells such as fibroblasts in skin substitutes has begun. But there are discrepancies in the immune responses to allogeneic fibroblasts. Therefore, the authors decided to review the immune responses to allogeneic fibroblasts.

Methods: Donor fibroblasts were isolated from skin of three rats. Nine recipient rats that were subcutaneously injected with three different regimens, were divided into three groups: Group 1, Phosphate buffered saline (PBS) without cells (control); group 2, allogeneic fibroblasts of one animal source suspended in Phosphate buffered saline; and group 3, Phosphate buffered saline containing mixed allogeneic fibroblasts of the three animal sources. Skin samples were biopsied at 1, 3 and 7 days after injection and were studied histopathologically.

Results: In the injection site, no signs of redness and edema were observed. In pathology, changes such as vasculitis, eosinophils and lymphocytes accumulation around fibroblasts, fibroblast apoptosis and transplant rejection at the injection site were not observed in the groups.

Conclusion: Subcutaneous injection of allogeneic fibroblasts in rats does not stimulate the immune system and it seems that these cells can be used for wound healing.

Body Mass Index as a Pre-Transplantation Prognostic Factor In Patients With Allogeneic and Autologous Hematopoietic Stem Cell Transplantation

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Background and Aim: A number of studies have identified a variety of risk factors such as disease stage, stem cell source, HLA mismatch and age that negatively influence the outcome of hematopoietic stem cell transplantation (HSCT). Obesity has been considered as a risk-factor for increased relapse/non-relapse mortality in bone marrow transplant patients and is associated with overall mortality. Obesity may also represent an independent risk factor for autologous bone marrow transplantation. The purpose of this article is to assess the association of body mass index with survival in patients with allogeneic and autologous hematopoietic stem cell transplantation (HSCT).

Methods: In this retrospective study, the data were collected from patient's files between 2008-2015 in Taleghani hematopoietic stem cell transplantation center. The comparison of BMI with one-year survival of 307 patients with allogeneic HSCT (AML, ALL, MDS, CML) and 86 autologous HSCT (MM, PNET, Hodgkin's and non-Hodgkin's lymphoma) was done. Kaplan-Meier and Cox Regression tests were used to investigate the differences between variables.

Results: From total 393 patients, 47.9% were normal and underweight, 34.6% were overweight and 17.4% were in obesity state. There was a significant difference between BMI in overweight patients and survival in allogeneic and autologous transplanted patients ($P<0.05$). But there was not a significant difference between BMI in underweight, normal patients and survival ($P>0.05$).

Conclusion: High BMI has been reported with better survival and lower relapse in leukemic patients in some studies. BMI is a good prognostic factor in leukemic patients before allogeneic and autologous transplantation and investigation of the association between BMI and other related survival factors can be useful for the patients follow up before and after transplantation.

Induction of Hematopoietic Stem Cells by Plerixafor and G-CSF In Patients With Autologous Hematopoietic Stem Cell Transplantation

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is an effective way for treatment of leukemia patients. Mobilization and collection of peripheral blood stem cell is the essential part of stem cell transplantation. Isolation of CD34+ cells from peripheral blood is essential for either autologous or allogeneic transplantation and also remains one of the challenges of using this treatment strategy. About 5-30 percent of patients do not have more than 2.0 x 106 CD34+ cells/kg. In this study, the use of plerixafor and G-CSF in patients with previous mobilization failure in order to mobilize hematopoietic stem cells was done

Methods : Patients with poor mobilized CD34+ stem cells that were treated with G-CSF additionally received the plerixafor were involved in this study. After treatment, CD34+ stem cells were collected from 15 plerixafor-induced autologous patients (MM, PNET, hodgkin's and non- hodgkin's lymphoma) and was compared with 20 autologous patients that were traditionally received G-CSF. CD34+ stem cells were evaluated using flowcytometry.

Results: The CD34+ stem cells were increased in the patients that simultaneously received Plerixafor (3.6 × 103 / kg) and G-CSF (1.3 × 103 / kg) compared with the patients that received G-CSF only ($p< .05$). The MNC in the patients that simultaneously received Plerixafor (5.5 × 106 / kg) and G-CSF (4.6 × 106 / kg) compared with the patients that only received G-CSF was not significantly different between two groups ($p>0.05$) .

Conclusion: HSCs mobilization with simultaneously use of plerixafor and G-CSF improve autologous hematopoietic stem cell transplantation in patients with mobilization failure.

Association of Hemoglobin Levels with Clinical Outcome In Patients Undergoing Hematopoietic Stem Cell Transplantation

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is an effective way for treatment of leukemia patients. The time for discharging a transplanted patient is different and depends on blood counts and immune system recovery of the patient. During the hospitalization, the risk of infection and bleeding are high and the physician should be confident of patients' general condition. One of the key survival predictive factors in bone marrow transplanted patients is assessing their hemoglobin (Hb) level. The purpose of this article is to assess the post-transplant Hb level in hematopoietic stem cell transplanted patients.

Methods: In this retrospective study, the data were collected from patient's files between 2008-2015 in Taleghani hematopoietic stem cell transplantation center. The comparison of Hb and one-year survival of 392 patients with allogeneic (AML, ALL, MDS) and 100 patients with autologous (MM, PNET, hodgkin's and non- hodgkin's lymphoma) HSCT were done. Kaplan-Meier and Cox Regression tests were used to investigate the differences between variables.

Results: There was a significant difference between Hb and survival in allogeneic (AML, ALL, MDS) and autologous (MM, PNET, hodgkin's and non- hodgkin's lymphoma) patients with HSCT ($P<0.05$). There was a significant difference between Hb and duration of hospitalization in allogeneic (AML, ALL, MDS) and autologous (MM, PNET, hodgkin's and non- hodgkin's lymphoma) patients with HSCT ($P<0.05$).

Conclusion: Our results confirm an association between Hb level and one-year survival and hospitalization in patients with autologous and allogeneic transplantation. Hb level as a survival factor after HSCT can be helpful to predict the discharging time of patients and management of disease to improve a better treatment for the patients.

Can Platelet Count Predict The Results of CD34+ Stem Cell Mobilization?

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Background and Aim: Hematopoietic stem cell transplantation is considered as a lifesaving solution for many hematological malignancies. Granulocyte-colony stimulating factor (G-CSF) is used to mobilize HSCs to peripheral blood for HSCT. The collection of stem cells from the peripheral blood is highly depends on the activity of the bone marrow and Blood platelet counting before mobilization and can be considered as an indicator of bone marrow activity. In this study we assessed the pre-transplant platelet count with mobilization yield to see if platelet count can be a predictive factor for patients with poor mobilization or not.

Methods: In this retrospective study, the data of 316 patients who underwent autologous transplantation at Taleghani BMT center from 2010 to 2016 were gathered. A comparison was made between platelet counts (as a selective marker, 250,000×103/µl) before G-CSF administration and MNC count of apheresis product. Spearman's rho test was used to assess the difference between variables. We evaluated the correlation between pre GCSF treatment platelet and mononuclear cell count.

Results: The results showed that there was no significant correlation between platelet counts before G-CSF administration and mobilization results (MNC: r= 0.0, p=0.9 and CD34+: r = 0.1, p=0.2).

Conclusion: According to the results, it is possible to obtain significant results by considering larger samples and changes in cutoff range (< or >250,000×103/µl). And also, type of disease, the history of previous chemotherapy regimens and the severity of bone marrow involvement during transplantation be effective for the prediction.

The Effect of Blood Group on Mobilized MNC Counts In Normal Donors For Allogeneic Stem Cell Transplantation

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Background and Aim: The donor's mobilization response to granulocyte-colony stimulating factor (G-CSF) and subsequent apheresis yields may exert a significant effect on transplant outcomes. Although the discovery of CD34 has revolutionized the assessment of progenitor cells in the peripheral blood stem cell graft, however many physicians still consider mononuclear cells (MNC) and CD34+ cells counts together. The purpose of this study was to assess the association between donor blood group and MNC count.

Methods: 145 donors between 2010 and 2016 were enrolled. The donors were normalized based on their age (median 37), type and administration schedule of G-CSF (Filgrastim) and all subjects were healthy related donors undergoing their first PBSC mobilization.

Results: There was a significant association between blood group and MNC count (p value<0.05). Among 8 blood groups, AB-and A- donors showed the highest MNC counts (mean: 12.1 and 11.25 respectively) and B- donors showed the lowest (mean: 5.6).

Conclusion: Our retrospective study confirms the presence of associations of donor blood group with MNC count. It can be beneficial in donor selection in case of the presence of more than one HLA-matched donors and also for optimizing the dosage of G-CSF for other treatments and every donation based on the blood group. However in order to generalize these results, greater subjects are required to have adequate number of all kinds of blood groups. Overall, our findings shed lights on the importance of investigating new donor factors for predicting a successful harvest.

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Comparison of Myeloid Engraftment In ABO-Matched and Mismatched Allogeneic HSCTS

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Background and Aim: Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative option for a variety of disease. Due to the fact that the human leukocyte antigen system is inherited independently of the blood group system, approximately 40–50%of all HSCTs are performed across the ABO blood group barrier .In this study we aim to see if there is any difference in myeloid engraftment between ABO matched and mismatched HSCTs, and also between three subcategories of ABO mismatch.

Methods: In this retrospective study we categorized 109 patients (both genders of male and female with average age of 34) who had allogeneic HSCT between 2010 and 2017 in two categories of ABO blood group matched and mismatched. Also we categorized mismatched transplantations in three subcategories as following; minor, major and bidirectional mismatched transplantations.

Results: There is a significant correlation between myeloid engraftment and ABO matched or mismatched HSCTs (p value<0.05). Although we found no significant correlation between myeloid engraftment and different types of ABO mismatches (p value >0.05)

Conclusion: Since finding a HLA-matched donor is not easy, we suggest optimizing RBC depletion and plasma reduction methods to have a better outcome. Also we suggest another study with much more patients to have a better conclusion of effects of different types of ABO mismatch on myeloid engraftment.

Assessment of Changes in White Blood Cells In Patients Underwent Hematopoietic Stem Cell Transplantation: Random Effects Model

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Background and Aim: Hematopoietic cell transplantation is a standard care procedure, frequently curative where no other treatment is an option. In this process, the WBC counts change for various reasons, including the conditioning regimen, and different factors that may affect these changes. The aim of this study was assessment of changes in WBC count in patients who underwent HSCT using a random effects model.

Methods: In this retrospective study, data were collected from 100 allo/auto- patients (50 women and 50 men, mean age: 42.6± 13.39 and 35.5 ±15.29 years, respectively) admitted in the HSCT ward of Taleghani hospital from 2007 to 2014. The comparison of WBC count with the type of disease and timeline of transplantation was done. The analysis was performed using a random effects model and SAS software. $P<0.05$ was considered as significance level.

Results: The result of this study indicated that type of disease ($P<0.001$) and a timeline of transplantation ($P<0.001$) had a significant effect on changes in the WBC count.

Conclusion: We found out that the WBC count in patients who underwent HSCT was associated with the type of the disease and time trend. The effect of the timeline on WBC count represents the fluctuation of blood cells following conditioning regimen and this can be affected by disease type, as some disease influence bone marrow and impair it so it can affect recovery of bone marrow and thereby WBC count after HSCT.

Comparison of G-CSF Administration In +1 and +5 Day In Patients With Allogeneic and Autologous Hematopoietic Stem Cell Transplantation

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Background and Aim: Granulocyte colony-stimulating factor (G-CSF) has widely used for stem cell mobilization, treatment of therapy-induced neutropenia and to accelerate the engraftment after hematopoietic stem cell transplantation (HSCT). Utilizing G-CSF is common in autologous and allogeneic transplantation because it can raise the count of hematopoietic stem cells in donors before transplantation and recipient post transplantation. The purpose of this article is to assess of G-CSF efficacy in patients with allogeneic and autologous hematopoietic stem cell transplantation from 2008-2016.

Methods: In this retrospective study, the data were collected from patient's files between 2008-2016 in Taleghani hematopoietic stem cell transplantation center. The comparison of the first day and fifth day G-CSF administration with WBC, PLT, and duration of hospitalization in 350 patients with allogeneic (AML, ALL, MDS, CML) and 96 patients with autologous (MM, PNET, hodgkin's and non- hodgkin's lymphoma) HSCT were done. Mann-Whitney test was used to investigate the differences between variables.

Results: The difference between G-CSF administration in two groups was not significant (P>0.05). WBC and PLT counts in two groups were not significantly different (P>0.05), as well as duration of hospitalization (P>0.05). Also, engraftment and hospitalization were not different between two groups (P>0.05).

Conclusion: Although the G-CSF administration is appropriate to increase the patient stem cells and shorten the engraftment and hospitalization, but our results indicate that there is no difference in G-CSF administration in +1 and +5 day after HSCT. Therefore, use of G-CSF can be started in +5 day in allogeneic and autologous patients to achieve a better and cost-effective treatment.

CXCL12-A Allele, an Independent Molecular Biomarker To Predict The Yield of CD34+ Progenitor Cells

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Background and Aim: The interaction between CXCL12/CXCR4 has a pivotal role in homing et al. The CXCL12 G801A polymorphism has dual amazing negative and positive roles. One effect of this SNIP is its association with an increased jeopardy of various types of cancers and another one is its association with the count of CD34+ progenitor cells in allogeneic transplant donors who were administered by G-CSF. Since the putative prediction and notification of CD34+ cells yield can be helpful for adopting appropriate strategies such as continuing of G-CSF administration especially in elder donors, we decided to investigate this SNIP in 57 donors.

Methods : in this pilot study, PCR-RFLP technique and flowcytometry were used to detect the CXCL12 G801A polymorphism and the count of CD34+ progenitor cells respectively in 57 allogeneic transplant donors (female/male=25/32; age range 9-65 years). The analysis of results was performed using the unpaired t-test or the Fisher's exact test for nonparametric distribution using Microsoft Excel and Statistical 12.5.192.7 Enterprise for Windows software.

Results: Results showed that the count of CD34+ progenitor cells in the first leukapheresis yield was significantly higher ($PV<0.05$) in CXCL12-A allele donors, particularly in AA homozygous genotype in comparison to GG homozygotes.

Conclusion: Our findings reinforce this notion that CXCL12-A allele can be considered as an independent molecular biomarker to predict the yield of CD34+ progenitor cells in the allogeneic transplant donors who induced by G-CSF solely for choosing appropriate strategies in special conditions.

Can G-CSF Eliminate Circadian Oscillation of Hematopoietic Stem Cells to Peripheral Blood

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Background and Aim: hematopoietic stem cells are usually separated from the bone marrow but the small amount of these cells are present in peripheral blood. The preferred method for increasing the number of these cells in PB is G-CSF therapy. In steady state HSC trafficking is regulated by oscillation of biological rhythms. But whether G-CSF can alter endogenous progenitor rhythms or not is unclear. So in the present study we investigated the impact of G-CSF therapy on circadian oscillation of HSCs in peripheral blood.

Methods: 15 healthy donors were selected. Samples from peripheral blood were taken at 9 am and 9 pm before injection of G-CSF and at 9 am and 9 pm in the fourth day of the G-CSF injection. The total count of leukocytes and CD34 stem cells were assessed by flowcytometry. Plasma levels of adrenaline and noradrenaline were also measured by ELISA.

Results : It was determined that the total WBC and CD34 stem cells count , as well as plasma levels of adrenaline and noradrenaline were increased in the morning. Additionally, after G-CSF therapy, the levels of adrenaline and noradrenaline and the amount of CD34 cells in the morning remained higher similar to control samples.

Conclusion: As the count of stem cells and total WBC were higher in the morning, this pattern is also preserved after injection of G-CSF. It is suggested that the mobilization, as well as other biological processes of the body, is affected by circadian oscillation. In fact, G-CSF also utilizes natural factors along with other functional mechanisms to increase the egress of stem cells to the PB.

Association of Body Mass Index With Stem Cell Mobilization In patients With Autologous Hematopoietic Stem Cell Transplantation

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is an effective way for treatment of leukemia patients. Mobilization and collection of peripheral blood stem cells is the essential part of autologous stem cell transplant. Factors such as the type of G-CSF, the administration dosage, apheresis device settings, age of patients, chemotherapy drugs, the protocol which were utilized and how many times they went on chemotherapy regimens are associated with the count of mobilized stem cells. The purpose of this article is to assess the association of body mass index with stem cell mobilization in patients with autologous HSCT.

Methods: In this retrospective study, the data were collected from patient's files between 2008-2015 in Taleghani hematopoietic stem cell transplantation center. The comparison of BMI with CD34 and mononuclear cells (MNCs) of 307 patients with autologous HSCT (MM, PNET, hodgkin's and non- hodgkin's lymphoma) were done. Spearman's Rho test was used to investigate the differences between variables.

Results: From total 393 patients, 47.9% were normal and underweight, 34.6% were overweight and 17.4% were in obesity state. There was no significant difference between BMI in overweight, underweight, normal patients and CD34 ($P>0.05$). A significant difference between BMI in overweight patients and MNCs in leukemic patients was seen ($P<0.05$).

Conclusion: Higher BMI is a good factor for a successful stem cell mobilization. Our results indicate that higher BMI is associated with higher MNCs and mobilization in patients with autologous HSCT. The impact of BMI on CD34 stem cells should be confirmed with further studies.

ABSTRACT Medical Poster

Comparison of The Efficacy of Neupogen, Pdgrastim and Zarzio With Stem Cell Mobilization In Patients With Autologous Hematopoietic Stem Cell Transplantation

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is an effective way for treatment of leukemia patients. Mobilization of hematopoietic peripheral stem cell is the most common approach in stem cell transplantation. Stem cell mobilization is done after chemotherapy followed by granulocyte colony-stimulating factor (G-CSF). Recombinant forms of G-CSF have been an important part of therapy in leukemia and lymphoma. The purpose of this article is to assess the comparison the efficacy of Neupogen, PDgrastim, and Zarzio on stem cell mobilization in autologous HSCT.

Methods: In this study, the data were collected from multiple myeloma (MM), Hodgkin and non-Hodgkin patients in Taleghani hematopoietic stem cell transplantation center. The comparison of CD34+ stem cells and mononuclear cells (MNCs) with Neupogen, PDgrastim and zarzio in 96 autologous patients were done. Kolmogorov–Smirnov test was used to investigate the differences between parametric and Mann–Whitney test for non-parametric variables.

Results: There was a significant difference between CD34+ stem cells with Zarzio and Neupogen. Neupogen mobilized stem cells more than other forms of G-CSF ($P<0.05$). Neupogen mobilized higher CD34 compare with Zarzio, but MNC mobilization was not different between them ($P>0.05$).

Conclusion: According to get better efficacy for G-CSF agents in autologous and allogeneic patients, the use of these agents can help to prevent neutropenia in leukemic patients. Our results indicate that Neupogen mobilized higher CD34+ stem cells in comparison with other agents after HSCT. But the study should be done on a larger scale to confirm this result.

Effects of Non-Pharmacological Interventions on Reducing Fatigue after Hematopoietic Stem Cell Transplantation

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Background and Aim: Fatigue is one of the main complaints of patients undergoing allogeneic and autologous hematopoietic stem cell transplantation (HSCT). Since nonpharmacological interventions are cost effective and causes fewer complications, this study aimed to review the studies performed on the effects of nonpharmacological interventions on fatigue in patients undergoing HSCT during September 2016.

Methods: MEDLINE, CINAHL, Scientific Information Database, IranMedex, PubMed, ScienceDirect, Scopus, Magiran, and IRANDOC databases were searched using Persian and English keywords. A total of 1217 articles were retrieved, 21 of which were used in this study.

Results: There is ample evidence on the effects of exercising on the reducing fatigue in patients undergoing stem cell transplantation. There is a multitude of studies on some of the complementary and alternative therapy methods such as music therapy, yoga, relaxation, and therapeutic massage. These studies demonstrated the positive effects of the aforementioned therapies on reduction or elimination of fatigue in patients undergoing stem cell transplantation. All the investigated methods in this study were non-aggressive, safe, and cost-effective; they could be used along with common treatments or even as an alternative for pharmacological treatments for the reduction or elimination of fatigue in patients undergoing stem cell transplantation.

Conclusion: Given the advantages of complementary and alternative medicine, conducting further studies on this issue is recommended in order to reduce fatigue in patients after stem cell transplantation.

Necrotizing Fasciitis Is a Rare Complication After Bone Marrow Transplantation: a Case Report

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Background and Aim: Necrotizing fasciitis is an uncommon disease and a soft tissue infection that spreads along fascial planes with associated inflammation and necrosis. Herein, this study reported necrotizing fasciitis as a rare complication after bone marrow transplantation (BMT) in an Iranian patient and the efficacy of early treatment in improving it. A 28-year-old lady who was known case of first relapse of Hodgkin's lymphoma and had admitted for auto-BMT in 2016.
Methods: Five years ago due to abdominal-pelvic massive lymphadenopathy, she was treated with six courses of ABVD regimen combined with involved field irradiation. Due to Hodgkin's relapse, the patient was treated with six courses of ICE regimen and after complete remission was selected for auto-BMT.
Results: Necrotizing fasciitis was reported by MRI and the patients was treated with combination of a number of antibiotics after fasciectomy.
Conclusion: Necrotizing fasciitis is a rare complication of BMT, especially autologous type that drug selection and rapid surgical fasciectomy are important decisions for prevention of mortality and morbidity of this complication.

Successful Osseo Integration of Dental Implants In a Patient With GVHD Treating With Photopheresis

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Introduction: Despite of advantages of Bone Marrow Transplantation (BMT), the most important concern is post transplantation complications such as rejection, infection and graft versus host disease (GVHD). The 5-years survival is 25% and 5% for grade III and IV, respectively. So, GVHD is a major cause of death following BMT. Case Report: In a 28-year-old male following spontaneous gingival and subcutaneous bleeding the diagnosis of AML was confirmed. Unfortunately, he developed GVHD 2 years following BMT, so he was underwent photopheresis. He also received 6-unit implant in mandible. Three years following GVHD and photopheresis, he is in good general and oral health with adequate osteointegration.

Conclusion: Thus, there appears to be a reduced risk of infections with the use of extracorporeal photopheresis (ECP) as compared with the use of other immunosuppressive agents. Early diagnosis and control of treatment related complications can significantly reduce mortality rate.

Evaluation of Allo and Autoantibody Prevalence In Transfusion-Dependent Beta Thalassemia of Ardabil province of The North West of Iran

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Background and aim: Lifelong regular red cell transfusion has remained the mainstay treatment of patients with thalassemia major that may be accompanied with alloimmunization. This study was carried out to determine the rate of RBC alloantibody and autoantibody in patients with major and intermediate β- thalassemia of Ardabil province.

Methods: A total of 90 transfusion-dependent β-thalassemia patients were included in this study. Demographic information was collected from the patients. Laboratory analysis was performed for detection of auto- and allo antibody. All the data was analyzed by SPSS software.

Results: the patients including 66 (73.3%) and 24 (26.7%) cases of major and intermediate β thalassemia, respectively. Out of patients, 53(58.89%) and 37(41.11%) cases were male and female, respectively, with average age of the 23.24 ±8.78 years. 12 (13.33%) patients had alloantibody including anti-Kell, anti-C, anti-Fyb and anti-JKa, but autoantibody wasn't detected. The most frequent antibody is anti-Kell (12.22%) and the incidence of Anti-C, Anti-Fyb and Anti-JKa were (1.11%). There are no significant correlation between the rates of alloimmunization and either sex or age ($p>0.05$), also no significant association between the age of transfusion start or splenectomy with development of alloantibody.

A Survey of Infection In Allogeneic Hematopoietic Stem Cell Transplantation In Patients With Acute Myeloid Leukemia

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Background and Aim: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) is a potentially curative treatment for acute myeloid leukemia (AML). Patients undergoing HSCT are at risk for infection due to impairment of immunity. The aim of this study is to evaluate the rate of bacterial, viral and fungal infections and their effect on 2-year overall survival of AML patients who have undergone allogeneic SCT.
Methods: It is a Cross sectional retrospective study, on 49 patients who underwent allogeneic BMT from full-matched donors during 2006- 2013 at BMT center in Tehran Imam Khomeini hospital complex. All Autologous transplantations and PML patients were excluded. All data was analyzed by SPSS VER 18. P-values less than 0.05 were considered as statistically significant. Survival rate was estimated using the Kaplan Meier method and the Log-rank test.
Results: All patients (except one) had fever in an average of 7 days after transplantation and received broad spectrum antibiotic. The rate of severe sepsis was 6.1%. None of the patients had fungal infection during admission. The rate of admission due to sepsis after discharge was 27% in living group (mean onset: 54 days) and 73% in dead group (mean onset: 52 days) which was significantly different between two groups. The most common site of infection was lung (70%). CMV antigenemia (positive PP65) rate was 20.4% during 2years after HSCT.
Conclusion: We have reported our experience in post BMT infection in AML (non PML) patients. The rate of infection is a negative prognostic factor for 2-year OS. The rate of CMV antigenemia was less than similar studies (51%); which could be due to full-matched donor-recipients, requiring less immunosuppression.

ABSTRACT Medical Poster

Efficacy of Azithromycin in Prophylaxis of Acute GVHD Following Allo-SCT IN Hematology-Oncology Research Center of Shariati Hospital

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Background and Aim: GVHD remains one of the main obstacles to broader application of allogeneic HSCT. GVHD Is Initiated By Donor T Lymphocytes. To Date, Most Therapeutic Approaches Designed To Attenuate GVHD Have Focused On Suppressing Donor T-Cell. However, These Strategies May Increase The Risk Of Relapse And Opportunistic Infections. Azithromycin reduced alloreactive T cell expansion with down-regulation of MHC II on dendritic cells. These results demonstrate that preventive administration of azithromycin can reduce the severity of GVHD after allo-HCT.

Methods: We performed a double-blind, randomized, placebo-controlled study from October 2013 to August 2014 in the Hematology–Oncology and SCT-RC of Shariati Hospital. In this study we evaluated the efficacy of Azithromycin in prophylaxis of acute GvHD and mucositis in 94 patients with acute leukemia after allogeneic HSCT. The trial was registered at IRCT/ n: IRCT201403281030N16. Patients were randomly assigned to receive either oral Azithromycin at a daily dose of 500 mg or placebo. Azithromycin and placebo was administered as a capsule in similar forms. Medication started six days before BMT and was continued until day +12.

Results : acute GVHD Grades 0- II, developed in 43 patients (91.5%) on the azithromycin arm compared with 37 patients (82.2%) on the placebo arm and grades III-IV, developed in 4 patients (8.5%) receiving azithromycin and 8 patients (17.8%) receiving placebo. Although the severity of acute GvHD was higher in the placebo group but it failed to reach statistical level of significance (PV: 0.281). chronic GVHD, grades 0-1, developed in 25 (61%) and 16 (41%) patients receiving azithromycin and placebo, respectively. Grades II- III, developed in 16 patients (39%) receiving azithromycin and 23 patients (59%) receiving placebo (PV: 0.074). In azithromycin arm oral mucositis, Grade 1 developed in 17 patients (36.2%) Grade 2 in 20 (42.6%) and Grade 3 in 1 patient (2.1%) compared with OM in placebo arm that Grade 1 developed in 21 (44.7%), Grade 2 in 17 (36.2%) and Grade 3 in 7 patients (14.9 %) (PV=0.022). Survival estimates at 1 year were 76.1% and 79.1% for azithromycin and

placebo groups, respectively (PV=0.67). One-year relapse-free survival estimates for the two groups are 88.5% and 81.2%, respectively (PV=0.37).

Conclusion: There was a statistically insignificant trend to a higher rate of relapse in placebo group compared to azithromycin group. But there was no difference in the overall survival and RFS between the two groups. Within the limitations of the sample size, this study failed to show a significant effect of prophylactic treatment with oral azithromycin in preventing acute GvHD and in improvement of outcome. In summary, our study showed that azithromycin given prophylactically before or early after transplantation significantly decreased Oral mucositis and marginally significant prevented chronic GVHD in allo HCT recipients.

Lower Serum Levels of Epinephrine and Norepinephrine Is Associated With Higher Risk of Acute Graft-Versus-Host Disease

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Background and Aim: Graft versus host disease (GvHD) is the major impediment of curing hematologic diseases by allogeneic hematopoietic stem cell transplantation (AHSCT). Epinephrine (E) and norepinephrine (NE) are stress hormones recently found to have immunomodulatory properties and can decrease the probability of GvHD through interaction with adrenergic receptors. In this study, we have compared the serum levels of epinephrine and norepinephrine in patients who develop acute GvHD (aGvHD) with recipients without aGvHD.

Methods: We have studied 15 candidates for AHSCT with median age of 38 years old (range: 25-45). Blood samples were taken from patients 5 days before transplantation and serum levels of epinephrine and norepinephrine were measured using Enzyme-linked Immunosorbent Assay (ELISA). The occurrence of aGVHD were measured according patient's clinical manifestations. T-test was used to analyze data of the study.

Results: Our results showed that 5 patients out of 15 patients presented aGVHD during 100 days after AHSCT. The mean serum levels of E and NE in patients who presented aGvHD were significantly lower than recipients without aGVHD (P-value <0.05).

Conclusion : According to the lower levels of serum E and NE in patients with aGVHD in comparison with recipients without this complication, we concluded that the lower serum levels of these nervous hormones is associated with lower immunomodulation and consequently might have a role in developing aGVHD. Hence, serum levels of E and NE could be a target for prediction and management of aGVHD and be considered as a predictive biomarker.

Evaluation of Effective Factors for Relapse In Patients Under Hematopoietic Stem Cell Transplantation Using Logistic Regression Model

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Background and Aim: Currently, hematopoietic stem cell transplantation is still an essential treatment approach for leukemia. It is shown that the type of malignancy is a critical factor affecting outcome of the patients who underwent hematopoietic stem cell transplantation (HSCT). The aim of this study was to evaluate the correlation of diseases type and type of transplantation with relapse after HSCT.

Methods: In this retrospective study, data were collected from patients' files who underwent allogeneic (AML, ALL, MDS) and autologous (MM, NHL, HD) HSCT in Taleghani hospital from 2008 to 2016. Analysis was performed using Logistic Regression model.

Results: According to these data and based on the Logistic Regression model, we found out that type of disease significantly is associated with relapse after HSCT. (P-value=0.048). The estimated odds of relapse occurrence after HSCT for MM vs HD was 1.71-fold with 95% confidence interval (0.92, 3.13), and for NHL vs. HD was 1.67-fold with 95% confidence interval (0.7, 3.71). Correlation of type of transplantation and relapse after HSCT was not significant (p-value > 0.05).

Conclusion: This study showed that patients with MM had the highest chance of relapse after HSCT. Evaluation of relapse in patients with HSCT, can lead to better management of these patients.

Assessment of Survival and Prognostic Factors after Bone Marrow Transplantation In Adults With Hematologic Cancer From IRAN, Between 2007 and 2016

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Background and Aim: Hematologic cancers are cancers of the blood, bone marrow, and lymph nodes that include leukemia, lymphoma, and myeloma. A bone marrow transplant (stem cell transplant) is a treatment for hematologic cancers. Also relapse rates in treatment of hematologic cancers with bone marrow transplantation is less than treatment of hematologic cancers with conventional chemotherapy. Determining the survival rate of patients with hematologic cancers after bone marrow transplantation is important. The aim of this study is to determine survival rate and the factors influencing predicted survival of patients with hematologic cancers.

Methods: In a retrospective study, total of 453 patients 16 to 67 years of with hematologic cancers who had received bone marrow transplantation, registered in Bone Marrow Transplantation Research Center (from 2007 to 2016), Taleghani hospital, Tehran, Iran entered this study. In this study, all of the diagnosed patients with Multiple Myeloma (MM), Non-Hodgkin's lymphoma (NHL), Hodgkin's disease (HD), acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) were entered into analysis. Also, demographic and clinical features including age, sex, blood group, white blood cell (WBC) count at the time of diagnosis, CD34+, body surface, and the final status (alive or dead) were collected. Survival analysis was performed using parametric log-normal model. The analysis was carried out using STATA, version11, and P-value less than 0.05 considered as significance level.

Results: The result indicated that, the mean age of the patients at diagnosis was 39.30 ± 13.35 years (range, 16-67 years) and 213 patients (44.7%) were male. Blood group for 136 (30%) patients was A, 99 (21.9%), 38 (8.4%), and 161 (35.5%) were B, AB and O, respectively. Also, 155(34.2%) was MM, 53(11.7%), 56(12.4%) and 34(7.5%) were NHL, AML and ALL, respectively. The mean (± standard deviation) survival time after Bone marrow transplantation was 78.42±2.59 months. NHL, AML, ALL and age were independent prognostic factors, according to log-normal model.

Conclusion : According to these data and based on parametric log-normal model, we found out that only age and the three morphology for hematologic cancer which include NHL, AML, ALL have a significant effect on patients' survival after transplantation of bone marrow.

Hematopoietic Stem Cell Transplantation In The Developing World: Experience From a Center In Western IRAN

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is a well-established therapeutic procedure for a variety of malignant and non-malignant diseases in children and adults. Before transplantation, patients receive intensive myeloablative chemoradiotherapy followed by stem cell "rescue.

Methods: We describe our experience of first 33 consecutive hematopoietic stem-cell transplants (HSCT) done between 2014 and 2016 at the Imam Reza Hospital, Kermanshah.

Results: 24 autologous HSCT and 9 allogeneic HSCT were performed. Autologous HSCTs (auto-HSCT) represented the majority (72.73%) in both years. The main Indications for autologous transplant were 50% multiple myeloma, 6.82% non-Hodgkin lymphoma, 20.45% Hodgkin lymphoma, and 15.91% acute myeloid leukemia. Main indications for allogeneic transplants were 4.55% acute lymphoblastic leukemia and 2.27% Myelofibrosis. The median age of autologous and allogeneic patients' cohort was 41- 50 years. Median follow-up period for all patients was 39 months.

Conclusion: About 96.97% of the patients remained alive between one to 12 months after stem cell transplantation. Nearly, 3.03% of our patients died after stem cell transplantation and the main cause of death was infection. Our results are comparable to many national and international published reports.

Curability of Hematopoietic Stem Cell Transplant (HSCT) For Malignant and Non-Malignant patients In Amirkola Bone Marrow Transplant Center

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Background and Aim: Hematopoietic stem cell transplant is the main and definitive treatment for thalassemia major and some malignancies. For this purpose we tried to treat some of our thalassemia major patients who had suitable completely match donors with HSCT. We also treated different malignancies with allogeneic and autologous HSCT in Amirkola B.M.T ward.
Methods: From 121 cases who underwent to HSCT from August 2010 to August 2017 in Amirkola B.M.T ward 39 of them were suffered from thalassemia major. 18 Patients were female and 21 male, age distribution was between 3-26 years. The patients were divided in two groups on the basis of Lucarreli classification (on the basis of portal fibrosis, hepatosplenomegaly and serum ferritin level). Group I were patients in class I and II and group 2 were patients in class III. Age distribution in group I was between 3 to 17 year and age distribution in group II was from 18 to 26 year. For Malignant Patients, 15 cases with acute lymphoblastic leukemia (ALL) treated with allogeneic HSCT. 5 out of 6 patients with acute myeloblastic leukemia (AML) had allogeneic HSCT and 1 patient had autologous HSCT. 15 patients with Hodgkin disease had autologous HSCT. 1 patient with Non- Hodgkin lymphoma was treated with autologous HSCT and 6 patients had autologous HSCT. 1 patient with myelodysplastic syndrome was treated with allogeneic HSCT. From cases of multiple myeloma 2 patients had allogeneic and 37 cases had autologous HSCT. We collected all information about engraftment and B.M.T failure, rejection, survival and event free survival, also mortality and some side effects such as GVHD. All information was collected and analyzed.
Results: Event free survival in major thalassemia group I was 75% and in group II was 40%. 3 out 23 patients in class I died and 6 patients in class III died. Severe GVHD happened in 6 cases, but only in two cases in group I. For Malignant Patients 2 leukemia cases relapsed for ALL and 2 for AML and 13 in Multiple Myeloma cases. 5 of Multiple Myeloma cases died 1-3 years post HSCT.

Conclusion: HSCT is the way of choice to relieve thalassemia major patients from their problems especially in class I and II cases. Also it is effective in relapsed malignancy cases with different results.

Safety and Efficacy of Autologous Bone Marrow Mesenchymal Stem Cell Transplantation In Autism Spectrum Disorder: Case Series

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Background and Aim: Stem cell therapy is increasingly used in the treatment of most disorders such as Autism Spectrum Disorder (ASD). In addition to uncertainties related to clinical response, there are concerns over the side effects of using this therapy. The present study, which is the pilot phase of a bigger clinical trial, investigates the possible side effects of autologous mesenchymal stem cell therapy in 5 children with ASD.

Methods : The plan of treatment includes obtaining the bone marrow samples from the iliac crest of the children and then injecting of processed cells in two stages (BMC 6-8 hours and MSC approximately one month after BMA). The side effects were continuously assessed within 72 hours, and then weekly until 1 month after the second injection

Results: The present study showed that despite some short-term side effects such as fever, nausea, pain in the injection sites, and allergic reactions that were well controlled by supportive therapy, there was no serious and dangerous complication.

Conclusion: According to the results of this study, stem cell therapy in children with autism is a safe procedure and not only side effects were at their lowest, but also helped reduce the intensity of the symptoms of autism.

The activity of Cord Blood Banking During 6 Years in Iran National Cord Blood Bank

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Background and Aim : Nowadays, Umbilical Cord blood (UCB) as hematopoietic stem cells has been used in treatment of malignant and non-malignant hematopoietic diseases and many cord blood banks have been established around the world for collection and cryopreservation of cord blood units. In this study, we summarized 6-year experiences in CB processing and storage in Iran National Cord Blood Bank (INCBB).

Methods: During November 2010 to 2017, 13081 donors registered in INCBB network and within them 8605 units were collected from 4 maternity hospitals in Tehran. All donors signed consent forms and screened based on medical history and laboratory tests. Selected units which were about 38% of collected units were processed according to the Netcord standards and 3150 units passed the INCBB banking and storage criteria.

Results : The mean±SD volume of units was 116.2±31.9 ml and after volume reduction, the mean±SD of TNC, CD34 absolute count , CFU assay and viability were 12.75×108 ±5.5×108 , 2.6×106±0.9×106, 4.2×105 ±1.2×105 and 91.1±7% respectively. Further, 14 units were transplanted to the children with different hematopoietic disorders.

Conclusion: Now, the main side activity of this center focused on the strategies for improving the engraftment of cord blood, expansion of CB units, co-culture and expansion of CB units with mesenchymal stem cells and optimization ways to use Haplo-Cord Transplants.

Hematopoietic Stem Cell Transplantation In Taleghani Hospital

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Background and Aim: This report summarizes current transplantation activity of the Taleghani bone marrow transplantation center (Tehran-Iran) as the second center of marrow transplants in Iran. Clinical use of bone marrow transplantation was first developed at Taleghani Hospital more than 6 years ago (established at 2007). Allogeneic HSCT was mainly applied for leukemia, lymphoproliferative disorders, and non-malignant disease. Significant indications for autologous HSCT were lymphoproliferative disorders, solid tumors, and leukemias. The main sources of stem cells are peripheral blood for autologous, peripheral blood and bone marrow for allogeneic HSCT. We are also advancing the use of transplants for other cancers, bone marrow deficiencies, inborn errors of metabolism, and immune disorders. In this study, hematopoietic stem cell transplantation in Taleghani Hospital is reported from 2007-2017.

Methods: In this retrospective study, the data were collected from patient's files between 2007-2017 in Taleghani hematopoietic stem cell transplantation center. The number of hematological and non-hematological malignancies, sex of patients and type of transplantation were analyzed. Frequency and mean tests were used to investigate the differences between variables. The SPSS software was used to analyze the variables

Results: In the Taleghani bone marrow transplantation center, from 2007 to 2017, 870 patients in 24 types of hematological and non-hematological malignancies were admitted form which 384 (41.8%) were female and 506 (58.2%) were male. From these patients, 670 (77%) were subjected to autologous transplantation, in which 268 (40%) were female and 402 (60%) were male. Among the patients, 200 (33%) were subjected to allogeneic transplantation of which, 96 (48%) were female and 104 (52%) were male. The MM group received the highest number of patients, 314 (36.1%) of which, 116 (36.9%) were female and 198 (63.1%) were male.

Conclusion: Overall, our results show that in the past 4 years, the overall number of transplants has been increased by 3-fold per year and includes 3.6-fold and 2.1-fold changes in allogeneic and autologous HSCT respectively.

Optimizing Donor Recruitment and Selection For Allogeneic Transplantation In Qatar: Challenges and Opportunities

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Background and Aim: In Qatar the National Centre for Cancer Care and Research (NCCCR), is the provider of Stem Cell Transplant (SCT) services for the State. The SCT program was established in 2015. To enable allogeneic SCT we established and customized the new stem cell donor service and recruitment pathways to the needs of our unique local patient population. Prompt confirmation and availability of suitable HLA-compatible donor are major determinants of clinical outcome in allogeneic SCT. This process is generally supported by accessibility to family members and to international donor registries allowing for high probability searches for HLA-compatible donors. In Qatar however, the identification of SCT donors poses unique challenges, due to: (a) the origin of the local residents, 85% of whom are single male immigrants; (b) the geographical remoteness of the majority of their immediate family members, typically residing in developing countries with limited availability/high cost immunogenic services; (c) the ethnic heterogeneity of the country's residents d) the consistency of the population mainly of individuals with ethnic origin and therefore HLA types generally underrepresented in the international stem cell donor registries resulting in low probability unrelated donor searches.
Methods: To overcome these challenges, from the outset of our donor program we developed a set of measures expected to enhance the likelihood of HLA-compatible family member and unrelated donor identification for our patient population. Our process for donor identification consists of pathways for internal and external donors. For Qatari nationals and expatriates of certain ethnic background the allogeneic donor approach includes screening of donors within the family, including extended family members, based on possible consanguinity. (Fig.1)
Results: For external SCT donors we developed a system based on collaborations with internal and external organizations to systematically obtain DNA samples from siblings residing in developing countries, with HLA testing based on long-distance retrieval of DNA using free-of-charge shipment and return of high-yield DNA collection kits ensuring prolonged sample stability. HLA-compatible siblings are subsequently invited at no cost to our Center for stem cell collection. To increase likelihood of successful identification of donors with HLA types underrepresented in major international registries but common in Qatar-based ethnicities, we are setting

up a national stem cell registry representing population diversity of the country. Further, we have established partnerships and a robust multidisciplinary process for donor identification and recruitment, supported by SCT infrastructure, Qatari academic and charitable organizations.

Conclusion: In conclusion, our experience indicates that HLA-compatible donor identification and recruitment in Qatar requires the efficient use of newly developed services and diverse existing resources under a novel approach and operational model. Our approach may be of interest for healthcare providers and SCT programmers operating in similar context.

ABSTRACT Medical Poster

Survival Analysis in Patients Underwent Hematopoietic Stem Cell Transplantation In Taleghani Hospital

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Background and Aim: Allogeneic hematopoietic cell transplantation (HCT) is an increasingly used curative modality for hematological malignancies and other benign conditions. Different factors can affect the survival rate of these patients. When interested in discovering the factors influencing the life expectancy of patients with Leukemia, survival analysis can be used. In this study, we analyzed the survival of patients with hematopoietic stem cell transplantation in Taleghani hospital from 2007-2016 to identify effective factors on survival by statistical models

Methods: In this descriptive-analytic study, data were collected from allo/auto-patients admitted in the HSCT ward of Taleghani hospital from 2007 to 2016. Comparison of age, sex, type of disease, type of HSCT, number of relapses of the disease before hematopoietic stem cell transplantation, the number of relapses after transplantation with survival was done. The Cox proportional hazards model and Kaplan-Meier curve have been used to evaluate the factors affecting the patients' survival.

Results: Cox proportional hazards model showed a significant correlation between survival and number of relapses before transplantation (p-value=0.0012) as well as the type of transplantation. (P-value=0.05)

Conclusion: Cox proportional hazards model revealed a significant correlation between the survival of patients with types of transplantation and the number of relapse before HSCT. Patients with allogeneic HSCT have less survival rate because of severe complications after this type of transplantation. Furthermore, more frequent relapses before HSCT could reduce the performance of patients and therefore can cause less survival.

Evaluation of Survival Rate of Patients Undergoing Hematopoietic Stem Cell Transplantation Using a Frailty Model

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Background and Aim: Allogeneic hematopoietic stem cell transplantation (HSCT) is an excellent therapeutic option for a variety of serious malignant and benign diseases. The aim of this study was evaluation of the survival rate in patients who underwent HSCT using a frailty model.
Methods: In this retrospective study, data were collected from 493 patients with leukemia who admitted in Taleghani Hospital (Tehran, Iran) from 2007 to 2016. Age, sex, time between diagnosis until the transplantation, type of disease, number of relapses prior to transplantation, type of transplantation and the time of transplantation to death were investigated in the study. Analysis was performed using a frailty model. Software used for data analysis was R, and $p<0.05$ was regarded as significant.
Results: The result indicated heterogeneous fraction of the population at the end of follow-up. In this model, there was a significant difference between all the variables, including age, sex, time interval between diagnosis and HSCT, type of disease, number of relapses prior to HSCT, type of transplantation and the time interval between HSCT and death and frailty ($p<0.05$).
Conclusion: Based on the frailty model, there are heterogeneities in the population of patients in this study and covariate could not take into account this heterogeneity.

Adipose-Derived Stem Cells As a Feeder Layer Increase C-MYC Oncogene Expression of Human Expanded Hematopoietic Stem Cells Derived From Cord Blood

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Background and Aim: the number of hematopoietic stem cells (HSCs) per cord blood unit is limited and this can result in delayed engraftment or graft failure. Therefore Scientists suggest the use of cytokines to enhance proliferation of HSCs. Along with cytokines. Feeder layers are used to maximize the proliferation and survival of these cells

Methods : ⟦CD34⟧^+ cells were cultured for7 days in three groups with mentioned cytokines including : (a) directly in contact with ADSCs feeder layer (b) separated by a transwell insert membrane (c) without a feeder layer . Gene expression was evaluated by real-time reverse transcriptase-PCR

Results: Expression level of c-Myc in co-culture system with cytokines was higher than the other groups. Also our data showed that direct culture of ⟦CD34⟧^+ cells on feeder layer was important for HSCs expansion

Conclusion: The high expression of c-Myc indicates to increase in self-renewal of HSCs. Therefore the proliferation of HSCs in co-culture system was higher than the other groups Also the results showed that direct culture of ⟦CD34⟧^+ cells on feeder layer was important for HSCs expansion

Bone Marrow Mesenchymal Stem Cells: For Cutaneous Wound Healing

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Background and Aim: Wound healing is a process that occurs after skin injury .One of the medical science objectives is attempting to heal a wound in a shorter time span, with fewer side effects. Clinicians have been searching for ways to obtain "super normal" wound healing. MSC populations in cells derived from Bone Marrow tissue has been studied as an alternative source of MSCs, providing multipotent differentiation. We aimed to evaluate the wound contraction and stem cell properties on managing full-thickness wounds in vivo.

Methods: This experimental study was carried out on 54 adult male Wistar rats weighing 200-250 gr, and ages of 3-4 months. A square 1.5*1.5 wound was made on the back of the neck. The rats were divided into control and two experimental groups. Additionally, the control and experimental groups were separated into three subgroups corresponding to 4, 7, and 14 days of study. Mesenchymal stem cells isolated from BONE MARROW, Cell collected and cultured. The control group did not receive any treatment. In first experimental group, MSCS was used once on the wound. The second experimental group received 1% phenytoin cream on the wound. For histological studies, samples were taken from the wound and adjacent skin. This tissue was examined using histological staining (H&E). Wound surface and wound healing were evaluated. Data were analyzed by using one-way ANOVA with post hoc Turkey test and ($P<0.05$) was significant.

Results: The results of microscopic study showed histological parameters in wound's bed (the number of fibroblasts, blood vessels, neutrophils and macrophages) in the experimental group were significantly different than the control group. The macroscopic and microscopic evaluations showed that the percentage of wound healing on different days in the control and experimental group were significant ($P< 0.05$).

Conclusion: The beneficial activity of MSCs in wound healing is complemented by the effects of growth factors and ECM produced by the native placenta tissue cells. Using Mesenchymal stem cells on open wounds will accelerate the healing process.

A Study To Investigate The Effect of An Autologous Platelet-Released Growth Factor (APRFG) Injection On The Improvement of Sexual Dysfunction After Pelvic Irradiation

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Background and Aim: Sexual dysfunction is a common sequel of cancer treatment, affecting the quality of life (QOL) in women treated with pelvic radiotherapy. In this study we aimed for the first time to identify, describe, and evaluate the safety, symptom resolution, and objective improvement the injection of autologous platelet released growth factor (APRGF) for treatment of sexual dysfunction in patients after pelvic irradiation.

Methods: This prospective case series study enrolled 10 cancer patients with Sexual Dysfunction who underwent pelvic radiotherapy at least 3 years ago. Each patient received 1-2 cc PRFG within three-week (3 times injection) period. All ten patients were re-evaluated at eight weeks and six months.

Results: The mean age of participants was 46.90± 7.90 years. 70% of women were multiparous and 30% were multigravida. In 50 % of cases, sexual activity was inactive and frequency of sexual relations were less than 6 times in year, the type of cancer in participants included: rectum 20%, cervix 40%, bladder 20% and endometrial cancer 20%. Radiation type was containing brachytherapy in 40% of case and external radiotherapy in 60% of case. 40 % of patients had history of hormone replacement therapy. The result of this study showed that PRFG injection was effective and symptoms disappeared in all patients with significant objective improvements in vaginal diameter (mean transvaginal length before PRFG injection was 6.5 cm and 7.1 cm after PRFG injection (p-value = 0.001). In addition vaginal flexibility improved. Mean flexibility before treatment was 0.72 cm and it was increased to 1.85 cm after PRGF injection (P-value = 0.026). Characteristics of discharge before the injection in 60% of patients included dry vagina and 40% had mild discharge and after PRFG injection 40% of patients had moderate and 60% had mild and sufficient discharge (P-value= 0.190). Sexual satisfaction after the injection of PRFG was clinically difference and all patients had sexual satisfaction that was related to TVL, vaginal flexibility and discharge. In the follow-up visit of patients, any patient needs to repeat the treatment.

Conclusion: Taken together, the results of this study showed that PRFG injection had positive effects on increased transvaginal length (TVL), vaginal flexibility and genital hiatus with speculum, vaginal discharge and Sexual satisfaction.

Evaluation of Survival Rate of Patients with Leukemia Using Mixture Cure Model

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Background and Objective: One of the main reasons of death around the world is cancer. Leukemia is a cancer which usually starts in the bone marrow and causes the formation of abnormal white blood cells. In 2012, 352 thousand people around the world have been diagnosed with blood cancer, and this caused the death of 265 thousand people. The aim of this study was to evaluate the survival rate in Iranian leukemia patients using mixture cure model.

Materials and Methods: Data was recorded from 490 patients with leukemia who registered in Taleghani Hospital (Tehran, Iran) from 2007 to 2016 in a retrospective study. Analysis was performed using mixture cure model. Software used for data analysis was R, and significance level was regarded as 0.05.

Results: The result indicated that, at the end of follow-up, 48 percent of people did not experience this event which represents a cure fraction in the population. Variables were age, sex, time between diagnosis until the transplantation, disease type, number of relapses prior to transplantation and type of Bone Marrow Transplant (BMT). The final variable was the time from transplantation to death. Using Wald statistic cure ratio was significant.

Conclusion: Based on mixture cure model a significant proportion of the population has been cured and regardless of the results is wrong conclusion.

The Possibility of Co-Culturing Cells to Repair Damaged Cells

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Background and Aim: In various diseases, including diabetes, cells are damaged for defective causes. Cell damage causes the cell to not work normally. When a cell such as a beta cell is damaged the body will try to repair or replace the cell to continue normal functions. Therefore, one of the strategies for treating diseases is repair cell damage. The purpose of this research is to repair cellular damage by beta cells through the use of progenitor cells.
Methods: First, beta cells were damaged by the use of Alloxan or Streptozotocin. After that, the damaged cells were cultured in the vicinity of the progenitor cells. The rate of damage and recovery was confirmed by evaluation of biochemical and physiological factors. Standard methods were used to measure biochemical factors. All values were expressed as the mean ± standard deviation of the mean. Statistical analysis was performed using SPSS 18. The p-value less than 0.05 was considered as significant level. The sample size was based on the outcome of previous studies. When data were normally distributed and the variance was homogeneous, the differences between treatment groups were analyzed using ANOVA.
Results: The results of the present study showed that the co-culture the damaged cells and progenitor cells improves the damaged cell function. The amount of insulin synthesis increased. Glucose levels also decreased.
Conclusion: Co-culture treatments show promising early results in the treatment of damaged cells .The progenitor cells seem to release factors and signals which is involved in the repair of damaged cells. Understanding these factors and their use in the treatment of diseases, including diabetes, will help in the future. Co-culturing cell research may aid quest to repair damaged cells.

Evaluation of Homing Gene Expression In Fucosylated Umbilical Cord Blood Hematopoietic Stem Cell Expanded On Laminin Coated Electrospun Scaffolds

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Background and Aim: Due to self-renewing and undifferentiating capability of umbilical cord blood (UCB) hematopoietic stem cells (HSCs), they can be differentiated into most blood cells. HSCs are easily accessed in UCB and their higher level of immune tolerance of human leucocyte antigen (HLA) mismatches with a potentially decreased risk of graft versus host disease (GvHD). As a result, HSCs have been thought-out for therapeutic aims, as compared to other sources. (Bone marrow and peripheral blood). Low progenitor cells content in one unit of UCB limits its application. Furthermore, defect in the bone marrow (BM) homing ability of UCB cells appears to be related to defect in binding to selectin. It is noteworthy to mention that HSCs homing and engraftment is presumably a polyphase method that shares some common aspects with the migration of leukocytes to inflammatory positions and homing of lymphocytes into lymph nodes. In other words, HSCs intercommunicate with neighboring cells, matrix ingredients and supportive factors in extracellular matrix (ECM), which describe a "niche". Ex vivo expansion of fucosyltransferase VI (FT-VI) treated CD133+ cells on niche like environment, as a laminin coated poly L-lactic acid (PLLA) scaffold has been done to increase the cell dose available for transplants.

Methods: Evaluation of MACS isolated CD133+ cells purity and measurement of CD133+ cells fucosylation by flowcytometry showed that they were suitable for next experiments. For mimicking cell-cell interactions between CD133+ cells, 3D culture systems as electrospun scaffolds were widely used in this study. The viability of cells seeded on scaffolds was proven using MTT assay. The cells attachment and proliferation were observed by SEM micrographs of the cells, and clonogenic potency of the cells was observed by colony assays of the cells seeded on the scaffolds after 7 days. Moreover, the CD133+ cells homing was analyzed by real time PCR of homing gene for the C-X-C chemokines receptor-4 (CXCR4), very late activation antigen–4 (VLA4), very late activation antigen–5 (VLA5), lymphocyte function associated antigen–1(LFA-1) and E-cadherin(E-cad).

Results : Our data showed the best homing of cells on the selectin laminin coated scaffold in comparison laminin PLLA scaffold, PLLA scaffold, and 2D culture system according to above mentioned gene expression. Although flowcytometry analysis of CXCR4 marker on CD133+ cells expanded on laminin coated scaffold for 7 day, showed 73% purity and confirmed real time data. High number of GEMM colony count in this group after 14 day, showed its more clogenicity potential.

Conclusion: Thus, we concluded that the FT-VI treated CD133+ cells expansion and homing on the selectin laminin coated PLLA scaffold were optimal and could overcome UCB stem cells limitation for clinical applications.

CRISPAR/CAS9 System For Cell Therapy of Mesenchymal Stem Cell of SLE Patients

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Background and Aim: Systemic lupus Erythematosus (SLE) is a chronic autoimmune disease that involves the skin, joints and kidney. These patients have very painful joints that cause some limitation. More than 90% of cases of SLE occur in women, frequently starting at childbearing age. So genetic and heredity play an important role in SLE pathogenesis. Stem cells are undifferentiated biological cells that can differentiate into specialized cells so they have an important role in disease pathogenesis when they have some genetic mutations. Also, they can be used for disease treatment because of their regenerative ability. Therefore, genome editing techniques such as CRISPR/Cas9 systems can edit genetic mutation in stem cells to solve disorders like SLE.

Methods: Expression profile of mesenchymal stem cells of SLE patients was extracted from Geo datasets. Then genes were compared with logic into two groups of SLE patients and healthy individuals, and divided into hyper expression and hypo expression genes. Next the genes related to cartilage problems in SLE patients were chosen from the group of hypo expression genes. Then the best guide RNA for CRISPR system were selected by CHOPCHOP.
Results: COMP or Cartilage Oligomeric Matrix Protein had hypo expression in the mesenchymal stem cell of SLE patients that plays an important role in the structural integrity of cartilage via its interaction with other extracellular matrix proteins. Therefore, identification of the best gRNAs of COMP in CRISPR/Cas9 system which were located within promoter, can help us to regulate its expression.
Conclusion: Genome editing techniques such as CRISPR can be used to edit some changes in the genome of any kind of cells like stem cells. Because of stem cell proliferation ability, these edits will pass to daughter cells and can help solving these disorders.

The Effect of DBM Scaffold On Expansion of Umbilical Cord Blood Mononuclear Cells In Hypoxia Culture Condition

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Background and Aim: The main purpose of tissue engineering is constructing of functional tissues for transplantation and repairing of damaged tissues. Approaching this goal requires making suitable environment for proliferation and differentiation of stem cells that can control them as same as body. Recently, many groups have examined the effect of dissolved oxygen concentration and different scaffolds in maintenance, proliferation and differentiation of hematopoietic stem cells (HSCs), through in vitro culture. This study aimed to determine the effect of DBM scaffold on expansion of umbilical cord blood mononuclear cells contains hematopoietic stem cells in hypoxia culture condition

Methods: Three-dimensional culture context which is made of DBM scaffolds were prepared and placed in one culture plate and the other culture plate was without DBM scaffold. 10,000 mesenchymal stem cells were cultured in each plate for five days in Hypoxia incubator. Then 1 million mononuclear cells were (MNC) isolated from umbilical cord blood and co-cultured with MSCs for seven days in each plate. After completion of the culture period, cells were isolated from the scaffold and plate without scaffold, and the expression of the CD34 surface marker and CD38 surface marker were studied by flowcytometry techniques.

Results: In flowcytometry study, the expression of the CD34 surface marker on day 0 and 7 for cells cultured in DBM scaffold on average, reported 47% and 63% respectively, and expression of the CD38 surface marker on day 0 and 7, on average, reported 29% and 21% respectively. The expression of CD34 surface marker on day 0 and 7 for cells cultured in culture plate without DBM scaffold on average, reported 47% and 45% respectively, and expression of the CD38 surface marker on day 0 and 7, on average, reported 29% and 58% respectively.

Conclusion: Considering that the CD34 surface marker is hematopoietic stem cell surface marker, so high expression of this marker in cells that were cultured in DBM Scaffold indicates the positive impact of 3D condition on the expansion of HSCs.

A Favorable Tool for Gene Editing By Using of CRISPAR/CAS9

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Background and Aim: The socioeconomic burden in uncommon genetic disorders is developing. Using various methods, novel approaches to treat genetic diseases have been created. The recent approaches to targeted genome modification, such as Zinc Finger Nucleases, TALENS and CRISPR-Cas9, is revolutionizing the way that molecular biologists interrogate the functionality of the eukaryotic genome. Technology of CRISPR emerges as a promising tool to correct genetic abnormalities.
Methods: CRISPR-Cas9 genome editing is based on the type II CRISPR adaptive immune pathway that is utilized by Streptococcus pyogenes, to defend against bacteriophage infection. This simple two-part system comprise of a designing guide RNA that leads the Cas9 endonuclease to a genomic locus, causing double stranded DNA breaks (DSB), When DSBs are introduced, the lesion may be corrected by one of two major repair pathways: homology-directed repair (HDR) or nonhomologous end joining (NHEJ). HDR allows the exchange of genetic information between DNA molecules with similar sequences, whereas NHEJ creates short insertions or deletions (indels) in the target sequence. NHEJ does not need a repair template, but the consequent indels can cause frame shift mutations that conduct to the production of incomplete, nonfunctional proteins or to micro-RNA degradation by nonsense-mediated decay. From the other point of view, the HDR machinery can repair DNA using by exogenous single or double-stranded DNA templates with sequence similarity to the DSB site.
Results: Therefore, utilization of HDR has permitted researchers to insert new genetic information at a target site, or to execute direct substitution of a mutated gene. CRISPR-Cas9 genome editing allows the production of insertion or deletion (indel) mutations, the deletion of large genomic loci and the introduction of specific small DNA changes, such as SNPs.
Conclusion: The relatively high competence and extensive applicability of this technology has opened the door to experiments that were thus far not possible. These contain genetic engineering in non-model organisms and correcting disease mutations in vivo. These acquisition of knowledge have and will go on to provide perception into prevent or cure disease regarding to how genome is structured, regulated and can be modified.

Role of CRISPAR/CAS9 For Gene Editing On Induced Pluripotent Stem Cells

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Background and Aim: Recent advances in genome editing with programmable nucleases have opened up new avenues for multiple applications, from basic research to clinical therapy. The ease of use of this technology and particularly clustered regularly interspaced short palindromic repeats (CRISPR) will allow us to improve our understanding of genomic variation in disease processes via cellular and animal models. CRISPR-Cas9 is a revolutionary genome editing technique that allows for efficient and directed alterations of the eukaryotic genome. IPSCs, which are very similar to embryonic stem cells, are pluripotent cells with a high self-renewal rate that can differentiate into almost all cell types; however, their utilization is associated with significantly less ethical controversy than that of their embryonic counter-parts. Recent advances in stem cell technology are likely to provide great benefits to the clinical use of iPSCs in clinical applications. As mentioned, iPSCs have a major advantage for personalized medicine because they can be derived from the patients themselves, and can therefore avoid immune rejection when transplanted.
Methods: In gene therapy, genes in diseased cells and tissues can be corrected by two approaches: ex vivo and in vivo editing. In ex vivo therapy, the target cell population is removed from the body, modified using a programmable nuclease, and then transplanted back into the original host; thereby, preventing complications due to immunological rejection. By contrast, in vivo editing therapy involves direct transfer of genome-editing reagents, such as a programmable nuclease and donor templates, into the human body. Ex vivo therapy includes correction of patient-derived iPSCs through gene editing, as well as differentiation into nonrenewable cell types such as neurons and cardiomyocytes.
Results: The CRISPR-Cas9 system enables simultaneous knock out of multiple genes, as well as knock-in of specific alleles in iPSCs, distinguishing it from earlier gene editing technologies such as ZFNs and TALENs
Conclusion: In the future, the use of CRISPR-Cas9 with iPSCs will lead to novel combinations of gene and cell therapies

Bone Marrow Mesenchymal Stem Cells Improves Expansion and Better Maintain HOXB4 Gene Expression of Human Cord Blood CD34+ Stem Cells

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Background and Aim: Umbilical cord blood (CB) has been found to be a rich source of hematopoietic Stem Cells (HSC). One factor limiting the therapeutic efficacy of CB transplantation is the low cell dose of the graft. Cell dose can be increased by ex vivo expansion. Identifying strategies to enhance expansion and maintain self-renewal of HSCs can improve engraftment. Regulation of self-renewal for sustained maintenance of HSC pool, is controlled by specific interactions with the microenvironment in the bone marrow (BM). The goal of this study was to examine BM-Mesenchymal stem cell (MSC) on ex vivo expansion and HOXB4 gene expression, as a self-renewal marker, in cord blood CD34+ stem cells.

Methods: In this study, human cord blood CD34+ HSC isolated by MACS, Cultured in the serum-free medium (Stem line II) supplemented with cytokines (TPO, FLT3L, SCF) with/without BM-MSC for 7 days. Before and after of this period, Total nucleated cell count (TNC), CD34+ cells count, CFC assay and HOXB4 expression by Real time PCR were evaluated. The data analyzed using the paired t-test. P-Value < 0.05 were considered statistically significant.

Results: At the end of 7 days of culture, in the presence of BM- MSC, CD34+ cells gave rise to higher nucleated cell (TNC), produced more CFUs and maintain a higher HOXB4 mRNA level compared to control culture.

Conclusion: BM-MSC through cell-to-cell interactions, as well as through secretion of hematopoietic cytokines not only improves ex vivo expansion of human HSC but also contributes to the regulation of HSC self-renewal and provide a "niche-like" milieu for hematopoietic stem cells.

Successful In Utero Transplantation of Human Hematopoietic Stem Cells Into Wild Type Mice

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Background and Aim: In-utero transplantation (IUT) of stem cells has tremendous potential for treating human congenital disorders such as severe combined immunodeficiency. Moreover, recent observations support use of IUT as an in vivo method to further understand the self-tolerance mechanism. Here, to study factors affecting successful engraftment of hematopoietic stem cells, we produced a chimeric human/mouse model through in-utero transplantation of human umbilical cord blood mononuclear cells (hUCB-MNCs) into NMRI mouse fetuses.

Methods: Pregnant mice were anesthetized with isoflurane on E11.5-E13.5. The uterine horns were exteriorized and each fetal peritoneum was injected by 3-5×106 MNCs isolated freshly hUCB-MNCs. The uterine horns were replaced, followed by abdominal closure. The mothers were allowed to continue gestation. Newborn mice were treated with subcutaneous injections of human IL3, SCF and G-CSF, 3 times a week beginning at 2 weeks of age. Homing of injected cells was analyzed by tracking the PKH-positive cells in frozen section prepared from the liver and spleen of newborn mice. Also, live-born mice were analyzed for evidence of peripheral blood chimerism using human CD45 marker. Finally, 4 months after birth, bone marrow (BM) smears were subjected for human nuclear antigen (HNA) staining.

Results: Totally, 4 out of 17 mothers died due to surgical complications such as bleeding and prolonged anesthesia. Cell transplantation to 79 fetuses resulted in 39 (49.3%) live-born mice. Postoperative fetal losses were anticipated due to the technical difficulty and invasiveness of the transplant procedures. Notably, all of the newborn mice were normal, with no signs of malformations. 48 hours after transplantation, tracking the PKH-positive cells in frozen section prepared from the liver and spleen of newborn mice showed that the human cells were present in these tissues. Furthermore, human CD45+ cells detected in 55% of infants (range: 1%-3% gated events over controls). In addition, the human origin and functionality of the transplanted cells were confirmed by the presence of anti-human nuclear antigen in the bone marrow of 4-months-old mice.

Conclusion: The successful engraftment of human cord blood cells in the mouse fetuses was supported by identification of circulating human cells in PB and BM of live born mice.

Apoptin Lentiviral Transduction, A Novel Method To Improve Bone Marrow Transplantation For Multiple Myeloma

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Background and Aim: Although bone marrow transplantation is considered as a common and effective method for multiple myeloma treatment, still a proportion of patients experience disease relapse as result of residual cancer cells. The advent of novel therapeutic approaches and conflation of two newly developed methods, gene therapy and purging method, have altered the landscape of cancer treatment protocols and brought hope for cancer patients. It has been investigated that the delivery of some genes like apoptin into malignant cells using a lentiviral vector could decrease the survival rate of several cancer cells, while had no cytotoxic effect for normal cells. In this study we aimed to examine the anti-tumor activity of a designed lentiviral vector-apoptin on cell survival and proliferative capacity of multiple myeloma-derived KMM-1 cells.

Methods: To explore the cytotoxic and anti-proliferative effects of Apoptin, KMM-1 cells were cultured with lentiviral vector-Apoptin and subsequently the transduction efficiency, cell proliferative rate and metabolic activity were assessed using flow cytometry, trypan blue and MTT assays, respectively. The genes expression of Apoptin and anti-apoptotic target genes of Bcl-2 family were further examined by qRT- PCR analysis.

Results: Our study showed the high transduction efficiency of lentiviral vector-apoptin in myeloma cells. Moreover, we found that Apoptin inhibited both growth kinetics and survival rate of KMM-1 cells through down-regulating the mRNA expression level of anti-apoptotic target genes of Bcl-2 family, such as Bcl-2 and MCL-1.

Conclusion: Overall, the results of the present study suggests that lentiviral vector-apoptin could be a promising method for eliminating the contaminated clonogenic myeloma cells for bone marrow transplantation. However, further investigations in clinical trials are needed to be done to establish the effectiveness of Apoptin in bone marrow transplantation.

ABSTRACT Medical Poster

Evaluation of Antibacterial Activity of Rat Blood-Derived Products Against Several Different Bacterial Strains

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Background and Aim: Blood-derived products involve bioactive factors with special capacities and abilities, such that there is a potential use for them in the field of medicine. These products have a large number of platelets, and release a wide range of growth factors, along with biologically active substances. One critical feature of these products is their antibacterial ability. This study examines their antibacterial activity, derived from blood in rats, and their effect on the growth of several bacterial strains.
Methods: For preparing plasma rich in growth factors (PRGF), 0.9% cc of 3.8% sodium citrate was used for every 8.1 cc of the rat blood sample. The centrifugal speed was 580 g for 8 min. And for preparing platelet-rich plasma (PRP), the centrifugal speed was 1800 rpm for 10 min and 3600 rpm for 10 min, respectively. Platelet-rich fibrin (PRF) was obtained with a centrifugation method (3000 rpm for 10 min) and no chemicals were used. Bacterial strains were grown in blood-agar medium and were separately treated with rat blood-derived products for 24 h at 37°C.
Results: In this study, PRP stopped the growth of Staphylococcus saprophyticus bacteria, with a clear aura around the PRP. This blood-derived product also stopped the growth of Escherichia coli, while the PRF blood derivative prevented the growth of three bacteria: Klebsiella pneumoniae, Streptococcus pneumoniae, and Pseudomonas aeruginosa. PRGF showed no antibacterial activity against these bacterial strains.
Conclusion : PRP and PRF can create antimicrobial conditions in vitro due to their release of growth factors such as platelet factor 4 (PF4), fibrinopeptide A, and fibrinopeptide B. They can similarly be used as treatment options to improve microbial infections, although pre-clinical and clinical trials are necessary to better understand their characteristics.

EX Vivo Expansion of Cord Blood-Derived CD34 Positive HSCS with Neuropeptide Y: The Strategy for Clinically Utilization of Cord Blood-HSCT In Cell Therapy

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Background and Aim: NPY has been recognized as a potent growth factor, causing cell proliferation in human embryonic stem cells and in mature lymphoid cells; however, its possible proliferative effects in hematopoietic stem cells (HSCs) remains unknown. The aim of this study was to evaluate the proliferative effect of NPY on the umbilical cord blood HSCs in ex vivo condition.
Methods: CD34+ cells were isolated from mononuclear cells (MNC) of each cord blood (CB). Expression of NPY receptor on cord blood (CB) CD34+ cells was studied by PCR. Ex vivo culture of CB-HSCs were performed in two conditions: One with cytokines as a control group and the other with 1.0 µm NPY treatment in addition to cytokines. Proliferation responses following NPY treatment were studied by flowcytometry and with MNC and CD34+ cell number calculation. The ability of expanded cells in formation of colonies during short term and long term culture were examined via CFU assay and LTC-IC.
Results: Ex vivo expansion of CB-HSCs after 7 days resulted in significant increase in the number of total nucleated cells and CD34+ cells in NPY-treated groups in comparison to control group. NPY-treated CD34+ hematopoietic cells after 7 days of culture retained their ability to differentiate into various blood cells and formulate colonies in long term culture.
Conclusion: This study highlights the supportive role of neuropeptide Y on expansion of CD34+ hematopoietic stem cells with retaining their potential of differentiate into various cell lineage after 7-day culture period with cytokine supplementation.

HLA Typing For The Purpose of Bone Marrow Transplantation and Pre Implantation Genetic Diagnosis For Monogenic Disease

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Background and Aim: Preimplantation genetic diagnosis (PGD) in combination with HLA STR haplotyping, has been a valid, reliable method for couples at risk of transmitting a genetic disease to simultaneously select unaffected embryos and HLA matched with his/her affected sibling. This study aimed to develop a novel panel containing 16 polymorphic STR (Short tandem repeat) markers linked to the HLA gene clusters for use in HLA typing for BMT and in PGD for monogenic diseases.

Methods: Polymorphic STR markers linked to the HLA gene cluster were selected from Tandem Repeats Finder and Sequence-based Estimation of Repeat Variability databases. Genotyping of HLA markers were performed using multiplex-PCR. Haplotypes were drawn for each family. Haplotype analysis was performed. Statistical analyses were done using GenAlEx6.03.To assess allele frequencies and heterozygosity of the markers, 50 unrelated individuals were genotyped.

Results: Our results showed that the heterozygosity of selected markers were between38%-89%. Totally 140 different alleles were observed for 16 loci, with the frequency of 0.012-0.413. The most number of alleles were seen in 3S320 and the lowest was found in CS366.3 loci. Also the other loci had acceptable polymorphism information content.

Conclusion: All studied markers were in Hardy-Weinberg equilibrium. The panel provides a powerful and reliable molecular HLA typing method applicable in PGD and for PGD in combination with HLA typing. This method can help families to have a healthy child who can donate stem cells for the treatment of his/her affected siblings. The method is very sensitive and specific in diagnostic settings.

Effect of Mesenchymal Stem Cells-Derived Microvesicles (MSC-MVS) On Hematopoietic Stem Cells (CD34+ Cells) From Umbilical Cord Blood Toward Megakaryocytic Lineage

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Background and Aim: Mesenchymal stem cells (MSCs) release hematopoietic cytokines, growth factors and Microvesicles (MVs) which, support the hematopoietic stem and progenitor cells (HSPCs) in the bone marrow (BM) hematopoietic microenvironment. MVs are extracellular vesicles that are released from a various cells, and have important inter cellular communications and play a crucial role in the biological functions of their parent cells such as MSC-derived MVs (MSC-MVs). MSC-MVs contain microRNAs and proteins that are rolled in the regulation of hematopoiesis. BM transplantation is useful procedure in hematologic disorders. Cord blood (CB) is used as a suitable source for transplantation but long time recovery of platelet (PLT) after transplantation is a main problem. Therefore, we would show that, MSC-MVs could improve the differentiation of CB -CD34+ cells to MK lineage ex vivo, maybe this method could reduce thrombocytopenia period.
Methods: In this descriptive study, MSCs were cultured in DMEM for gathering supernatant. The supernatant was ultracentrifuged for isolation of MVs. HSCs were isolated from the CB source by MACS method. HSCs were cultured in an IMDM supplemented with cytokines and MVs in three conditions. The MK differentiation was evaluated by specific markers and specific genes expression after 72 hours. Finally, the data was analyzed by non-parametric t-student test ($P<0.05$).
Results: The specific markers expression of the MK lineage (CD41/CD61) in the presence of different concentrations of MSC-MVs did not show significant difference in comparison with the control group. Also, the specific genes expression of the MK lineage (GATA1, GATA2, FLI1, and c-Mpl), were normalized with GAPDH, as an internal control, then compared with control group. GATA2 and c-Mpl genes expression were significantly increased, GATA1 gene expression was not significantly decreased and FLI1 gene expression was significantly decreased. The results did not show any significant improvement of the MK differentiation in response to synergism effect of MSC-MVs and cytokines.
Conclusion: The results showed that MSC-MVs cannot improve the specific gene expression of the MK and cannot improve differentiation towards the MK lineage. However, further studies, such as evaluation of the late stages of the MK differentiation in the culture medium, are required to evaluate platelet production and shedding.

Stable Beta Globin Expression BY Lentiviral Vector For Beta Thalassemia Gene Therapy

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Background and Aim: Beta thalassemia is a common monogenic disorder caused by partial or complete reduction of beta globin chains synthesis. It is estimated that 1.5% of the global population (80 to 90 million people) are carriers worldwide. Common management consists of regular lifelong blood transfusion plus iron chelation therapy. The transfusion has its complications. In the recent years, allogeneic bone marrow transplantation (BMT) has proved to be the successful cure for over 2000 patients with thalassemia major, however this is restricted due to limited matched-related donor. Therefore, a molecular approach, such as gene therapy for direct healthy beta globin gene transmission, seems quite promising to cure thalassemia. The goal of beta thalassemia gene therapy is to restore normal RBC production capacity in patients by suitable vector and correct inherited anemia. Autologous Hematopoietic Stem Cells (HSCs), which Self-renew and generate all hematopoietic linage including the erythroid lineage, are the cellular target of ex-vivo globin gene transfer. So our purpose of this study is to gene therapy by a lentiviral vector.

Methods: For this purpose, we designed the DEST Lentiviral vector carried normal beta globin gene and its promoter and packaged levtivirus in LentiX cell line. Then targeted cells (K562 cells) was transduced by packaged lentivirus containing β-globin cassette. After transduction, the β-globin mRNA level was determined by quantitative Real-Time PCR and beta globin protein expression was analyzed by flowcytometry

Results: Our results showed that we have successfully packaged and generated letivirus in LentiX cell line and Real-Time PCR and flowcytometric analysis showed that beta globin expression in treated cells was more than untreated cells.

Conclusion: These data indicated that vector used in this study can be useful in gene therapy in patient's hematopoietic stem cell. The final goal of this study is to examine designed vector in hematopoietic stem cells promising therapeutic strategy for genetic diseases like beta thalassemia.

Assessment of Adhesion and Homing Molecules Alteration In EX VIVO Expansion of Umbilical Cord Blood CD34+ Hematopoietic Stem Cells

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Introduction: In order to overcome the main limitation of UCB HSCs in transplantation, the cells were expanded in different conditions. HSCs expansion requires saving stemness and functional capacity of the cells. Microenvironment and cell-cell interaction of HSCs recovery after UCB transplant greatly depends on homing and adhesion of HSCs to BM niche, in this study, we investigated the surface expression alteration of these molecules during ex vivo expansion of human UCB HSCs.

Methods: This investigation was performed to compare the expression of three adhesion molecules (N-cadherin, CD117, CaR) affecting homing before and after expansion in various culture conditions. CD34+ HSCs and MSCs were isolated characterized. The expression level of CD34+ HSCs surface adhesion molecules were evaluated by flowcytometry (partec, Germany) before and after expansion as MFI of anti-molecules antibodies reactions.

Results: there was no significant change in expression level of CaR adhesion molecule in all culture conditions (P>0.05). But expression level of CD117 adhesion molecule in culture conditions with cytokines alone was increased (P 0.05).

Conclusion: Ex vivo expansion of HSCs in these culture conditions did not reduce homing and adhesion molecules expression. Cultured cells with cytokines and mesenchymal cells as feeder layer can provide the best culture conditions for successful transplantation.

Transfection of Human Beta-Globin Gene into the AAVS1 Locus of K562 Cell Line Using CRISPR/CAS9 Technology

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Background and Aim : Beta thalassemia is a kind of hereditary illness ,which is due to an impairment in production of globin chain .There is a need to find a suitable treatment for this disease _ in respect to the both high prevalence of the disease in Iran and the lack of proper remedies until now . CRISPR-Cas9 is a new promising genome editing technology having high efficiency in gene correction .In this study , we inserted the human beta-globin gene site specifically into the AAVS1 locus using AAVS1 Transgene knock-in vector kit (Origen) .
Methods: At first, we amplified the health beta globin gene from human blood sample with PCR . At the next step, the beta-globin amplicon was cloned in the pTG19-T vector. The fragment was then sub cloned into the pAAVS1-puro-DNR vector using NotI restriction enzyme and sequenced. Second part of our study was transfection of K562 cells with the kit vectors.
Results: For this purpose, the K562 cells were cultured in RPMI 1640, FBS 10% and 1% penicillin-streptomycin and incubated at 37°C, 5% CO2 and 95% humidity. Transfection was optimized using pEGFP-C1 plasmid in electroporation by examine different electrical pulses and concentration of vectors. In addition, for minimal fatal concentration of puromycin, the K562 cells were exposed with different dose of the antibiotic. Now, we are evaluating the locus-specific integration of the transgene using PCR and specific primers and also the ability to express of beta-globin transgene.
Conclusion : We produced the engineered vector , having the health Beta-thalassemia gene,and confirmed it by sequencing .we could optimized the fatal dose of puromycin of this cells and transfect them by PE-GFP vector .Now , we are transfecting this cell with both vectors , pAAVS1-puro-DNR including our target gene and Pcas- guide - AAVS1 .

A Study to Evaluate Prevalence of Wilm's Tumor-1 (WT1) Gene Mutation in Acute Myeloid Leukemia Patients

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Background and Aim: WT1 was identified as tumor suppressor gene, located at chromosome 11p13, encodes transcriptional regulatory protein for genes involved in cellular growth and metabolism [1] and its mutation was reported in both syndrome-associated and sporadic cases of renal malignancy. Many studies have indicated that WT1 gene is over expressed in acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), and other leukemia disease, and this gene is highly expressed in more than 80% of AML patients in bone marrow (BM) and PB in comparison with normal control [2]. WT1 mutations have been found in about 10%- 15% of cases of AML. WT1 mutations cluster mainly in exons 7 & 9 and less in exons 1, 2, 3, & 8 [3]. Therefore, WT1 gene mutation and related significant in AML need to be studied to emphasize its potential role as a marker of disease progression.

Methods: All patient of AML which were diagnosed on basis of morphology, cyto-chemistry and immunophenotyping, were collected for this study, a total of 100 consecutive cases of AML and 10 healthy controls. In all case and control, genomic DNA were extracted from blood/bone marrow sample using Qiagen® DNA extraction kit. However, DNA were amplified with standard PCR master mix and primer pair designed to flank intronic regions for all cases of AML and controls. Primer pair used for both exon 7 and exon 9 was standardized manually for optimal annealing temperature. PCR products were then analyzed by Sanger Sequencing using capillary electrophoresis on an ABI Genetic analyser. A total 100 case and 10 controls, amplified product of both exons 7 and 9 were taken for direct Sanger sequencing. The mutation analysis of coding region as well as intron-exon boundaries of the WT1 exon 7 and exon 9 was carried out in all cases and controls.

Results: We analyzed 100 cases of AML and 10 healthy controls for WT1 mutation in exon 7 and exon 9. In total, WT1 gene mutation were detected in 17/100 patients, (exon 7: n=10, exon 9: n=7); in which 8 silent mutation (8%), 2 missense mutation

(2%) and 7 intronic variant (7%), leading to frequency of 17%. A total 10 patient out of 100 had WT1 sequence variation affecting exon 7 (10%) whereas 7 out of 100 in exon 9 (7%). In healthy normal control, no variants were found. In overall cases of AML, 7 intronic sequence variations were detected in both exon 7 and exon 9. Therefore, total mutational frequency of WT1 gene variation in both exons is 17% (17/100).

Conclusion: This study showed significant frequency of WT1 gene mutation in sample size. Missense mutation which was detected as novel mutation in 2 case of exon 9 may interrupt DNA binding capacity through amino acid residues or zinc finger motif structure. So, study needs more number of cases to reach possible correlation of WT1 gene mutation and its RNA expression with disease outcome for prognostic and risk stratification.

Investigation of Telomerase Inhibition Effect on Apoptosis of Myeloma Cell Line U266

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Background and Aim: Telomerase-targeted therapy for cancer has received great attention because telomerase is expressed in almost all cancer cells but is inactive in most normal somatic cells. This study aimed to investigate the effects of telomerase inhibitor MST-312, a chemically modified derivative of epigallocatechin gallate (EGCG), on apoptosis of myeloma cell line U266.

Methods: In an Experimental study, U266 cells were treated with different concentrations of MST-312 at different times; then, cell viability by trypan blue exclusion assay, cell metabolic activity by MTT assay, and cell apoptosis by Annexin V Apoptosis Detection Kit were measured. To further investigate apoptosis, BAX and BCL2 gene expression of the treated cells was investigated by the quantitative Real-Time PCR.

Results: MST-312 exerted a dose-dependent short-term cytotoxic effect on myeloma cells. Over 50% decrease in the viability of treated cells was seen in 8? M concentration of MST-312 within 48 h. The cytotoxic effect of MST-312 was concentration-dependent, with approximately 25, 46, and 62% reduction in metabolic activity after 48 h exposure to 2, 4, and 8 ?M of MST-312, respectively. Gene expression analysis showed downregulation of antiapoptotic gene Bcl-2 and upregulation of apoptopic gene BAX.

Conclusion: Inhibition of telomerase activity by MST-312 represents a novel treatment strategy for Multiple Myeloma cancer.

Cyclosporin Drug Delivery by Innovative PEGylated Single Walled Carbon Nanotubes: Comparative LTT Test with Sandimmune®

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Background and Aim: Single-walled carbon nanotubes have been found to be a new family of nanovectors for the delivery of therapeutic molecules. The ability of these nanostructures to load large amounts of drug molecules on their outer surface has been considered as the main advantage by many investigators. Here, we report the development of a PEGylated SWCNT-mediated delivery system for cyclosporin A (CsA) as a potent immunosuppressive agent through the formation of an amide bond with the free amine group of PEGylated SWCNTs.
Methods: DSPE-PEG loading was optimized on single walled carbon nanotubes through non covalent functionalization method and d-optimal design. The cyclosporin was first succinylated and then conjugated via amide bond. Cyclosporin loading, in vitro release and stability studies were performed. The cyclosporin efficacy in immune suppression was then evaluated by ELISA IL II kit in LTT test in comparison to Sandimmune.
Results: Drug loading, stability of the PEGylated SWCNT–CsA complex, and in vitro release of the drug were evaluated. Loading efficiencies of almost 72% and 68% were achieved by UV spectrophotometry and elemental analysis methods, respectively. It was observed that 57.3% of cyclosporin was released from CsA–Pl–PEG5000–SWCNTs after 3 days.
Conclusion : In this investigation, we conjugated CsA to an amine-terminated phospholipid–polyethylene glycol chain attached on SWCNTs viaa cleavable ester bond and demonstrated the possible potential of PEGylated SWCNT-based systems for CsA delivery with improved immune suppression effect in comparison to conventional drug delivery as it is with Sandimmune.

Stabilization of Lactoperoxidase with Ectoine

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Background and Aim: enzymes have a widespread usage in hygiene and different industry. The enzymes processes' stabilization is necessary Because of their high valence to increase the half-life and features like sensitivity, instability toward environmental condition, the existed stress and high cost. Ectoine is one of compatible composites which does not have effect on enzymes' chemical constructions and causes the enzymes stabilization toward environmental stress such as temperature, PH, time ,different salt concentrations also protects enzyme even in its low concentrations.

Methods : The 75 microliter amount of lactoperoxidase enzyme with 1 cc of ectoine solution 0.8 molar prepared by potassium phosphate buffer 6.4 ph. is stabled for 48 hours; then the stabled lactoperoxidase enzyme and free lactoperoxidase enzyme as a control sample were exposed to heat the 25, 40, 60, 70 degree. Finally, the stabled and free Lacto peroxidase enzymes' function and stability were measured by spectroscopy UV-VIS 2600.

Results: after the examinations and measurement the function results have shown that the stabled and free Lactoperoxidase enzymes' remainder in 25, 40, 60 and 70 degree. The stabled enzyme with ectoine's remainder function are as 83% ، 68% ، 68% and 89 % respectively; whiles, the free enzyme stabled its remainder function in mentioned degrees which are as 44% ، 34% ، 17% and 20% respectively.

Conclusion: the examination showed that the stabilization with compatible samples like ectoine caused the enzyme's stability in tough condition and increasing its remainder activity.

Prognostic Effect of Cytogenetic Abnormality in Acute Lymphoblastic Leukemia

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Background and Aim: Several studies have shown the significance of pre-treatment cytogenetic findings in tumor cells as a strong clinical predictor. We evaluated the effect of pre-treatment cytogenetic abnormality on treatment outcomes in a sample of Iranian adults with acute lymphoblastic leukemia (ALL) after allogenic hematopoietic stem cell transplantation (HSCT) or chemotherapy.
Methods: 321 adult patients underwent allogenic HSCT or chemotherapy from March 2012 to October 2016 in Shariati General Hospital, Tehran, Iran. 135 patients with pre-treatment cytogenetic data were included in our study with median follow-up time of 36 months. The overall survival (OS) of different cytogenetic abnormalities was compared with normal karyotype. Patient were divided into 9 groups cytogenetically: Normal, complex, t(9,22), hyperdiploidy, del(6q), t(14,11), del(9p), t(1,19) and others (miscellaneous).
Results: Three-year OS rate for all patients were 22.96%. Hyper diploid had a positive effect in prognosis of patient and this effect was more pronounced in the HSCT group. t (1 ; 19) had a negative effect in the prognosis of patients. No significant effect on prognosis of patients was observed for the other cytogenetic abnormalities.
Conclusion: Due to the rarity of these cytogenetic abnormalities, further studies with larger samples are needed to investigate the OS in these patients.

Hospital Lighting and Its Association with Sleep, Mood and Pain Related To Cancer

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Background and Aim: The hospital environment may contribute to patient discomfort by providing a lighting structure that interferes with circadian rhythmicity, sleep, mood and cancer pain. The aim of this research was to describe the light exposure, sleep and wake patterns, mood, pain related cancer in the hospital.
Methods: A descriptive correlational design was used in this preliminary study. Between May 2016–April 2017, data were collected from a convenience sample of 23 women and 17 men with blood cancer admitted to a large academically affiliated hospital in Tehran (Shohadaye Tajrish Hospital). Over 72 hours, light exposure and sleep and wake patterns were continuously measured with wrist actigraph/light meters for each participant. The mood was measured daily using the Profile of Mood States Brief™ Form. Subjective pain scores were abstracted from medical records.
Results: Light exposure levels were low: mean daytime light intensity was 104·80 lux. Sleep time was fragmented and low: mean 236·35 minutes of sleep/night. Intra-daily stability scores indicated little sleep-wake synchronization with light. Fatigue and total mood disturbance scores were high and inversely associated with light. Pain levels were also high and positively associated with fatigue, but not directly with light exposure. Low light exposure significantly predicted fatigue and total mood disturbance.
Conclusion: Patients with blood cancer were exposed to light levels insufficient for circadian entrainment. Nevertheless, higher light exposure was associated with less fatigue and lower total mood disturbance in participants.

Evaluation of Autophagy-Related MicroRNA-101 AS a Prognostic Marker in Acute Myeloid Leukemia

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Background and Aim: Epigenetically regulation cellular processes have constructed new approaches in the evaluation of cancer prognosis and engraftment of tissues in transplanted patients. In recent years, autophagy, as a physiological mechanism which is also involved in cancer drug resistance, has been considered as one of the factors contributing to the successful hematopoietic stem cell transplantation. This process could be activated in response to stressful circumstances (i.e., chemotherapeutic agents, nutrient deprivation, etc…), and leads to degradation of damaged organelles and misfolded proteins causing enhanced cell survival in these conditions. In this regard, autophagy inhibitor chloroquine has been shown to alleviate the progression of acute and chronic GVHD. Recent studies demonstrate micro RNAs have powerful functions in regulating cellular processes. MiR-101 is one of the miRNAs which has an inhibitory role on autophagic flux. On the other hand, miR-101 also seems to have a significant role in engraftment and prevents rejection some of the organ transplantation.

Methods : In this study, we decided to use Cytarabine (ara-C), as the most common chemotherapeutic agent which is utilizing in treatment AML patients, along with autophagy inhibitor (chloroquine) and autophagy inducer (Rapamycin) on the Expression level of miR-101 in HL-60 cell line (an acute myeloid leukemia in-vitro model).

Results: Our gained results demonstrate that expression level miR-101 increased when we used ara-C in combination with autophagy inhibitor chloroquine. Likewise, enhanced apoptosis, reduced proliferation rate and decreased in some autophagy-related genes (ATG4 and ATG7) in ara-C plus CQ experimental group were seen, which all of these are under significant role autophagy in maintaining neoplastic cells in stressful situations.

Conclusion: Overall, due to the importance of autophagy and miR-101 in the improvement of organ transplantation procedures, it seems to be a bona fide prognostic marker in acute myeloid leukemia and may also be useful in hematopoietic stem cell transplantation.

ABSTRACT

Oral Nursing

22nd International Congress of Asia – Pacific
Blood and Marrow Transplantation

The Preparatory Establishment of Hematopoietic Stem Cell Transplantation Nursing Follow-up Platform in Peking University Hematology Institute

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Background and Aim: To design a nurse-leading, patient-centered and multi-discipline long-term follow-up system, and to set up an intellective corporation platform which based on the rule of follow-up in Peking University Hematology Institute.
Methods: 1. Collaborating with Yiducloud Inc., Peking University Hematology Institute set up a network collaboration platform which contains multi-center data collection module and CRF setting and follow-up task management module. 2. The 18~65 years old patients who received HSCT in Peking University Hematology Institute from Jan 2017 to Jun 2017 were elected into this program with inform consent. This is a prospective study. Baseline information was collected before hematopoietic stem cell transplantation. And the patients were going to be followed up at 1 months, 3 months, 6 months, and 1 years after hematopoietic stem cell transplantation by telephone, and the following data was going to be collected: (1) Demographic sociological data; (2) KPS score; (3) Anthropometric data; (4) Complications; (4)FACT-BMT scores; (5) EORTC QLQ-C30 scores; (6)FACT-fatigue scores; (7) HAD scores; (8)APGAR scores; (9) Laboratory data; (10) Image examination results. 3. The variables above were translated into CRF items and written into the CRF module. The follow-up task according to the rule was written into the follow-up task management module. And the task would be sent to nurses at the right time, with the questionnaires sent to patients by their smart phone.
Results: The follow-up system has received 119 patients' data. In term of family function assessment, 2%of the patients are 7 points, 4% of the patients are 8 points, and 18% of the patients are nine points. What else, the patients think the improper communication style is the main reason in family function. In the KPS function status assessment, 83.7% of the patients are greater than 60 points. After pretreatment with chemotherapy, 53 patients thought their fatigue score was greater than or equal to 2 points.
Conclusion: The follow-up system dominated by the nurse follow-up system, the nursing of prevention for complication, remind the date of reexamination, treatment recommendations and psychological support. According to the follow-up system, patients can be provided with corresponding health education. Through the study is

to establish Chinese system of long-term follow-up after hematopoietic stem cell transplantation, to promote the development of domestic different transplantation center, so that provide the best nursing care for hematopoietic stem cell transplantation patients . At the same time, it also can help reduce the occurrence of complications and improve the life quality.

Keywords: Nursing Follow-up Platform, Hematopoietic Stem Cell Transplantation, Yiducloud Inc., Nursing.

Comprehensive Use of Multiple Strategies to Prevent Perianal Infection after Hematopoietic Stem Cell Transplantation

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Background and Aim: The nursing team of the hematopoietic stem cell transplantation (HSCT) unit in the Department of Hematology of Peking University People's Hospital took the comprehensive nursing care to prevent patients who have undergone HSCT treatment from perianal infection.
Methods: From January 1, 2012 to December 31, 2013, there were 840 patients who underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT) in the Department of Hematology of Peking University People's Hospital, including 444 cases of male (52.76%) and 396 cases of female patients (47.24%). the average age was 29.8 years. Identical Sibling Donor haploidentical hematopoietic stem cell transplantation (ISD-HSCT) was performed in 245 cases (29.17%); unrelated donor hematopoietic stem cell transplantation in 31 cases (3.69%); umbilical cord blood hematopoietic stem cell transplantation in 8 cases (0.95%) and haploidentical Donor hematopoietic stem cell transplantation (haplo-HSCT) in 556 cases (66.19%). In the hematopoietic stem cell transplantation ward of Peking University People's Hospital, the nursing team manage comprehensive use of various means of prevention strategies after hematopoietic stem cell transplantation for neutropenic period perianal infection. The strategies include patient assessment, Dian Fushui after washing, bath and conventional iodoform ointment perianal and special perianal symptomatic treatment.
Results: 840 cases of patients with hematopoietic stem cell transplantation in the absence of granulocyte infection occurred in all the patients with perianal infection, the incidence was 6.2%, and the specific situation is shown in Table 1. The average value of WBC was 0.069 * 109/L during perianal infection, the highest body temperature was an average of 38.8 DEG C, the average number of days of fever was about 6.5 days, and the average number of diarrhea days was about 5 days. 118 cases (14.05%) with primary perianal problem patients. Compared with the reported incidence of perianal infection in patients with hematopoietic stem cell transplantation in the literature, the incidence rate of the center was 6.2%, which was lower than that reported in the literature.
Conclusion : We use a variety of effective prevention and nursing measures of assessment, effectively reduce neutropenia in patients with perianal incidence, reduces the risk of systemic infection, shorten the hospitalization days, reduce hospitalization costs and improve patients' safety of transplantation.
Keywords: Multiple strategies, Perianal infection, Hematopoietic stem cell transplantation

Liver Function Tests

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Background and Aim: Liver function tests are blood tests used to help diagnose and monitor liver disease or damage. The tests measure the levels of certain enzymes and proteins in blood. Some of these tests measure how well the liver is performing its normal functions of producing protein and clearing bilirubin, a blood waste product. Other liver function tests measure enzymes that liver cells release in response to damage or disease. Abnormal liver function test results don't always indicate liver diseases. Liver function tests can be used to: Screen for liver infections, such as hepatitis, Monitor the progression of a disease, such as viral or alcoholic hepatitis, and determine how well a treatment is working, Measure the severity of a disease, particularly scarring of the liver (cirrhosis) and Monitor possible side effects of medications. Liver function tests check the levels of certain enzymes and proteins in your blood. Levels that are higher or lower than normal can indicate liver problems. Some common liver function tests include: In patients with malignancy control of liver function test is very important. Before and after bone marrow transplant .liver function test important .VOD is one of the complications after transplant.
Methods: systematic review
Results: liver one of organs in body special in BMT
Conclusion: monitoring liver tests is very important in patients
Keywords: liver tests, VOD

Complications of Multiple Myeloma

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Background and Aim: Multiple myeloma (MM) is a blood cancer, in which malignant plasma cells accumulate in the bone marrow. Hematopoietic cell transplantation (HCT) has been performed as a treatment method for multiple myeloma. The aim of this paper is describing the complications of MM and the nursing care that is necessary to reduce them.
Methods: The evidence around the complications and nursing care in MM was reviewed. Ten studies were selected from searched studies and were reviewed.
Results: Bone pain/loss, hypercalcemia, infection and anemia are the complications related to MM. But kidney dysfunction is one of the important issues in these patients because the kidneys are hurt by hypercalcemia, abnormal proteins of MM, treatment and other disease which can affect the kidneys more. This situation can lead to renal insufficiency and renal failure which can finally progress to end-stage renal disease. Dietary counseling, physical activity, monitoring the blood chemistry especially serum calcium and creatinine and myeloma parameters is recommended for MM patients. Nurses should educate patients about hydration and management of hypercalcemia, avoiding use of non - steroidal anti-inflammatory drugs, injection the pneumococcal and influenza vaccines according to physician order, and erythropoietin for anemia especially in patients who receive the hemodialysis. Alongside to these the patient education about HCT complications is needed.
Conclusion: The complications of MM should be considered because some of them are life-threatening. Nurses can reduce these by patient education, monitoring and follow up the complications.
Keywords: Multiple Myeloma, patient education, Complications

Cytomegalovirus in Stem Cells Centers

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Background and Aim: Today it is known that Cytomegalovirus (CMV) is a very important pathogen in the transplant setting. CMV is a major cause of morbidity and mortality in solid organ transplant (SOT) recipients. CMV disease typically occurs during the first 3 months after SOT, without a prevention strategy. Cytomegalovirus infection is a common complication in immunocompromised patients with impaired cellular immunity, including hematologic malignancy patients and transplant recipients.
Methods: By literature review including Medline, PubMed and Google scholar from 2010 to 2017, 100 articles were reviewed.
Results: CMV infection remains a significant complication after hematopoietic stem cell transplantation (HSCT) and may have a detrimental impact on the overall outcome after transplantation. In addition to the direct effects of CMV infection, tissue-invasive CMV diseases may be associated with increased risk of graft versus host disease, myelosuppression, and invasive bacterial and fungal infections. Because of these direct and indirect adverse effects, prevention of CMV infection, mostly through primitive therapy, is one of the essential strategies that may improve outcomes of HSCT recipients.
Conclusion: There are a number of areas that are being actively explored in basic, translational and clinical research fields related to CMV disease diagnosis, prevention and treatment. Recent studies have been promising, although more confirmatory tests are needed. It is hoped that these assays will allow better risk-stratification of patients and allow more targeted prevention strategies.
Keywords: Cytomegalovirus, Stem cells centers

Transplant –Related Complications in Major Thalassemia

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Background and Aim: The thalassemias are a group of inherited hematologic disorders caused by defects in the synthesis of one or more of the hemoglobin chains. Beta thalassemia major causes hemolytic anemia, poor growth, and skeletal abnormalities during infancy. More than 60.000 children with thalassemia major are born annually worldwide. Although lifelong red blood cell transfusion and chelation have significantly improved survival of patients with thalassemia, but this remains a progressive disease with disease and treatment related complications progressing over time.
Methods: By literature review from 2010 to 2017 including Medline, PubMed and Google scholar, 110 article were reviewed.
Results: Patients with thalassemia major (TM) are severely anemic resulting from ineffective erythropoiesis and hemolysis. Hematopoietic stem cell transplantation (HSCT) is the only effective therapeutic modality for patients affected by major hemoglobinopathies such as thalassemia major. Despite improvements in transplant technology a substantial group of patients continue to have post -transplant complications which increase morbidity and mortality. Transplant-related complications continue to be a common cause of morbidity and mortality following stem cell transplantation.
Conclusion: Most post - transplant complications in patients with thalassemia are similar to those observed in malignant BMT setting. Establishing an early and correct diagnosis is crucial to prevent or minimize both morbidity and mortality. More reliable early diagnostic markers and more specific therapies are needed.
Keywords: Thalassemia, Transplantation

Helping The Patient Undergo HSCT Procedure

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Background and Aim: When a patient arrives to HSCT ward, he/she is in remission and feels well temporarily. To perform a transplantation, we have to push the patient through a challenging procedure and help him/her endure hard conditions. As a matter of fact we put the patient's life in jeopardy intentionally to save his/her life. Actually we have no choice and undesirable effects of chemotherapy impact on many systems of the body. So we have to come up with new methods to overcome the problems continuously. We should play an active role in providing comfort to the patient every moment on demand.
Methods: These methods that we are currently using in our center includes Mucosamin ,Crystallized sugar ,Distilled mint , Domperidone, loperamide, Kytril, Oral Metronidazole, oral Vancomycin, sitting in bethadin and vitamin A+D ointment.
Results: When the patient is undergoing tough situation and facing undesirable chemotherapy side effects, the patient urgently asks the nurse do something to ease and bring comfort to him/her, and the nurse thrives on the problems by using these methods.
Conclusion: We hope our experience would be useful to anyone who is struggling to solve patients' problems in HSCT centers.

Autologous Bone Marrow Transplantation

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Background and Aim: Hematopoietic stem cell transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cells derived from bone marrow, peripheral blood or umbilical cord blood. It may be Autologous (the patient's own stem cells are used) Allogenic (the stem cells come from a donor) or syngeneic (from an identical twin). Autologous transplantation is typically used as a method of returning the patient's own stem cells as a rescue therapy after high dose myeloablative therapy. This transplantation technique is generally used in chemo sensitive hematopoietic and solid tumors to eliminate malignant cells. Autologous HSCT requires the extraction (apheresis) of hematopoietic stem cells from the patient and storage of the harvested cells in a freezer. Then the patient is treated with high dose chemotherapy. The patient's own stored stem cells are transfused in to patient's blood stream, where they replace destroyed tissue and resume the patient' normal blood cell production. In this study autologous bone marrow transplantation was investigated. This research was done descriptively

Methods: This research was done descriptively

Results: 40 patients admitted in the bone marrow transplant department of Imam Reza Hospital in Kermanshah underwent autologous bone marrow transplantation.

Conclusion: Autologous transplants have the advantage of lower risk of infection during the immune-compromised portion of the treatment since the recovery of immune function is rapid. Also the incidence of patients experiencing rejection is very rare due to the donor and recipient being the same individual. These advantages have established autologous HSCT as one of the standard second –line treatments for diseases such as lymphoma and multiple myeloma. Patients undergoing autologous transplantation was discharged without side effects.

Keywords: autologous bone marrow transplantation.

The Complications of Hematopoietic Stem Cell Transplantation in Lymphoma

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Background and Aim: As a result of therapeutic advances, there is a growing population of survivors of both Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). Hematopoietic stem cell transplants (HSCT) are sometimes used to treat lymphoma patients who are in remission or who have a relapse during or after treatment. There are 2 main types of stem cell transplants: autologous and allogeneic. High dose chemotherapy followed by autologous HSCT is a common treatment of patients with HL. Allogeneic HSCT is usually offered to patients with HL as a salvage therapy following relapse or progression after autologous HSCT. For NHL both autologous and allogeneic stem cell is an effective treatment strategy but NHL is much less likely to stay in remission after an autologous transplant than after allogeneic.
Methods: This article is aimed at reviewing the literature on nursing management of complications of HSCT in lymphoma patients. A comprehensive review was conducted on databases such as Medline, Ovid and Science Direct with the following keywords: nursing, HSCT, complications, lymphoma care and oncologic emergencies. Finally, 11 English written articles published during the last 10 years were selected.
Results: Over the last decade, numbers of patients with lymphoma who have undergone allogeneic stem-cell transplantation using reduced-intensity protocols increased. This approach is associated with lower toxicity and reduced transplantation-related mortality. However, there are a wide range of complications after HSCT based on the kind of lymphoma and HSCT. Long-term complications of autologous HSCT include: treatment-related myelodysplasia/secondary leukemia, secondary solid tumors, cardiac disease, pulmonary toxicity and infection. The most common long-term complications of allogeneic HSCT include: chronic GVHD, infections, treatment-related myelodysplasia/secondary leukemia, secondary solid tumors, pulmonary toxicity and cardiac disease.
Conclusion: Nurses have critical role in management of HSCT complications. The nurse should provide education about relevant self-care strategies and encourage the patients to consider all precautions to prevent /reduce the mentioned complications.
Keywords: hematopoietic stem cell transplantation, nursing, lymphoma, complications

The Effect of Education on Self-Care Behavior in Patients with Cancer

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Background and Aim: Nursing care activities include comprehensive care of all body systems, assessment and treatment of comfort, treatment of fluid and electrolyte abnormalities, administration and management of intensive medication and early intervention and treatment of common complications/side effects of transplant including mucositis, bowel changes, myelosuppression, graft versus host disease, hemorrhagic cystitis, veno-occlusive disease, tumor lysis syndrome and sepsis. Nurses also provide ongoing education for the patients and their family and caretakers.
Methods: The study included 110 patients hospitalized in BMT wards from July 2014 to July 2016. The patients were diagnosed with AML, ALL and AA. The patients were between 17 and 60 years of age. All patients received allogeneic & autologous peripheral blood stem cell transplantation.
Results: All patients and their families cooperated with nurses and accepted their therapeutic plans. The anxiety and stress of patients were reduced and their families felt comfortable. Quality assessment was conducted and documented in the patients' medical records by using information gathered through interviews about: Side effects of treatment/Reducing side effects/How treatment works/Response to treatment/Nutritional diet during recovery/Emergency complications post-treatment/Follow up- care/Long- term side effects of treatment /Recovery time.
Conclusion: The results of the study revealed that education can help the patients and their family members understand the disease, overcome psychological problems such as stress and anxiety, reduce treatment side effects and improve outcomes.
Keywords: self-care behavior

Identifying of Back-up Donor for Unrelated Stem Cell Transplantation in Iranian Stem Cell Donor Program (ISCDP)'S Patients

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Background and Aim: Once a primary suitable unrelated stem cell donor has been found, the importance of identifying a back –up donor is often underestimated.
Methods: Transplant Centers calculated the unrelated donors to be willing, available and medically fit for donation. According to our data, which includes 158 unrelated donor work –up procedures performed for 148 Iranian patients between 2013-2017 just for ISCDP and BMDW Unrelated donors, Of all donor-related cancellation (N=10), 90 % of the procedures were deferred due to medical reasons and 10 % due to non-medical reasons.
Results: Most of the donors deferred for medical reason were female. In 50 % of the cases for whom a back–up donor was already identified, the patients were transplanted with delay of at least 5 weeks and when no back up donor was available, the median delay increased to 20 weeks. We strongly encourage implementation a search for at least one back up donor in the primary search.
Conclusion: Identifying a backup donor can save precious time and speed up the work up procedure for patients.
Keywords: Back-up donor, unrelated donor search, Stem cell Transplantation

The Effect of Self-Care Behaviors on Gastrointestinal Side Effects in Patients Undergoing Chemotherapy

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Background and Aim: Cancer is a deadly disease that humanity is involved. One of the main options is use of chemotherapy treatment. In 40 to 80 percent of the chemotherapy treatments complications such as nausea and vomiting, mouth sores and disorders of the bowel can occur. The aim of this study was to determine the effect of self-care behaviors on gastrointestinal side effects in patients undergoing chemotherapy.
Methods: This study is a randomized clinical trial on about 60 women with breast cancer who were referring to Chamran hospital as chemotherapy center. Prior to chemotherapy and after obtaining the consent for the random sampling method block, patients were divided into two groups. Patients in the intervention group received routine treatment to improve the side effects of chemotherapy, in addition they received self-care training by the researcher. Data were collected by a demographic questionnaire, a questionnaire for side effects of chemotherapy and Morrow standard questionnaires were collected. Data were analyzed using descriptive and inferential statistics by SPSS v21 software.
Results: The results showed that the use of self-care education led to reduced mouth sores and also leads to a reduction in frequency and severity of nausea and vomiting in patients. This reduction was statistically significant ($p < 0.05$).
Conclusion: The results showed that the use of self-care training alongside drug regimen reduces the side effects of chemotherapy in patients. Therefore, it is recommended that nurses use this technique as a complementary method to reduce side effects of chemotherapy
Keywords: self-care, side effects of chemotherapy, chemotherapy, nurses

Results of an Alternative Method for Custom Prime: A Case Series of Successful Peripheral Blood Stem Cell Harvesting From Twenty Five Low-Weight Child Donors

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Background and Aim: In different hematological malignancies and disorders as well as and non-hematological malignancies stem cell transplantation is a key to the cure after remission. Peripheral blood stem cell apheresis (PBSCA) is one the most common methods to the collection of stem cells for transplantation. Although in low weighted donors this method is accompanied with different complications.

Methods: This study evaluated results of PBSCA in less than 20Kg donors during Jan 2014 to Jan 2017 in Shariati Hospital (Tehran, Iran). Donors and receivers were assessed for demographical information as well as diagnosis, success rate and details of the procedure, cell counts, and occurrence of graft versus host disease (GVHD).

Results: The receivers were categorized into the allogeneic (N: 25 and the same number of donors) and autologous (N: 12). In the allogeneic group, the average of CD34 positive cells was 4x106 and CD3 positive cells counted as 300x106. For autologous group CD34 positive cells counted 10x106. The most common diseases were shown as thalassemia (44%), acute lymphoblastic leukemia (16%), and acute myeloid leukemia (12%). The success rate was 100% which after a mean of 41 months follow-up 76% of receivers were alive. The incidence of both acute and chronic GVHD was 56%.

Conclusion: Authors hope that current information may help clinicians to have a better insight for less than 20Kg weighted donors.

Keywords: Peripheral blood stem cell apheresis, Thalassemia, Acute lymphoblastic leukemia, Acute myeloid leukemia

Viral Respiratory Infections in Patients under Stem Cells

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The human body respiratory system is complex and relatively massive. It covers the nose to the lung air sacs .The leading cause of death in solid organ and hematopoietic stem cell transplant recipients is infection. Viral respiratory infections (VRIs) are frequent after hematopoietic stem cell transplantation and constitute a potential cause of mortality. Despite preventive strategies and increased awareness, a high incidence of respiratory viral infections still occur in patients with hematological malignancies (HMs) and in recipients of hematopoietic cell transplant (HCT). Progression of these viral infections to lower respiratory tract may prove fatal, especially in HCT recipients. According to the location of the infection, you can classify the infectious diseases of this System: Common Cold, Influenza, Sinusitis, Rhinitis, Acute pharyngitis, Inflammation of the tonsils and adenoids, Laryngitis, Bronchitis and Pneumonia. Several consensus guidelines outline specific recommendations for the prevention of respiratory viral infections through infection prevention and control practices. Patients with suspected respiratory viral infections (based on presence of symptoms) should take Standard precautions and droplets observed in dealing with these patients. Hand hygiene is extremely important, as most respiratory viruses are transmitted through direct contact. Symptomatic health care workers should be restricted from patient contact and symptomatic visitors should be actively excluded from visiting until symptoms are completely resolved. Enough sleep and rest for the patients, good oral health, and increased consumption of hot liquids should also be considered.

Disseminated Intravascular Coagulation (DIC)

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Disseminated intravascular coagulation (DIC) is one of the most serious conditions of patients that each nurse may face it. DIC is a systemic process with the potential for causing thrombosis and hemorrhage. The acute type of this condition can be a life-threatening emergency which requires a prompt diagnosis and intervention. DIC reflects an underlying condition and can be associated with high levels of mortality and morbidity. The key element of proper management of DIC is identifying DIC and the underlying condition responsible for it. Therefore, nurses need to be aware of how what patients are at risk for DIC and how to quickly diagnose and manage this condition. Common causes of DIC include sepsis, malignancy, and trauma, as well as obstetrical complications and acute hemolytic transfusion reaction. Diagnosis of this condition is based on both clinical and laboratory findings. Patient monitoring, as a nurse important responsibility, is a critical action to prevent DIC progression by timely detection.

Prevention of Bacterial Infections in Patients with Bone Marrow Transplantation

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Introduction: Hematopoietic cell transplant (HCT) recipients are at increased risk for a variety of infections based upon their degree of immunosuppression and exposures. Patients can develop a range of bacterial, fungal, viral, and/or parasitic infections following HCT. Infection in HCT recipients is associated with high morbidity and mortality. Thus, prevention of infection is a major goal, which involves determination of risk, careful selection of donors, prophylactic and/or preemptive antimicrobial therapy, immunization, and additional measures (e.g. infection control).
Material and method: Fluoroquinolones such as ciprofloxacin and levofloxacin are drugs that are prescribed for the prevention of bacterial infections in these patients. Carbapenems, Vancomycin and Piperacillin and tazobactam are among the most commonly used drugs used to treat bacterial infections in these patients.
Results: Antimicrobial prophylaxis should be initiated with the conditioning regimen or at the time of stem cell infusion (to avoid deleterious interactions with the conditioning regimen) and should be continued throughout the period at risk for infection. Prevention of infection in these patients has reduced the mortality rate.
Conclusion: Fluoroquinolone prophylaxis for allogeneic HCT recipients who have received myeloablative conditioning regimens is recommended. Levofloxacin (500 mg orally once daily) and ciprofloxacin (500 mg orally twice daily) have been studied most extensively.

Palliative Care in Bone Marrow Transplantation (BMT)

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This paper highlights that palliative care is necessary to be considered alongside medical treatment after the diagnosis of a life- threatening illness. Research findings have shown that it offers the most benefit, when started early during the treatment course. Early Palliative Care (EPC) can help three involved parties (patients, their families and health care providers) in a variety of ways; especially in health care setting that provides services to those clients suffering from the life threatening diseases such as leukemia, lymphoma and etc.

Palliative care is a specialized medical care for people with serious illnesses. Palliative care is provided by a team of palliative care specialists, including doctors, nurses and social workers. This team works together with other doctors to provide an extra layer of support for patients. The goal of palliative care is to improve quality of life for both the patient and their families. It does this by providing relief from the symptoms and stress of a serious illness or a serious medical treatment like bone marrow transplant. Bone marrow transplants (BMT) are typically used to treat serious blood conditions like leukemia, lymphoma and multiple myeloma. Bone marrow transplants are also used to treat other kinds of aggressive medical disorders.

Bone marrow transplants generally begin with a high dose chemotherapy, radiation or both. This treatment kills cancer cells. It also kills all remaining healthy bone marrow cells. The purpose of the bone marrow transplant is to replace all the destroyed cells with healthy ones. Some people have few or mild side-effects from a bone marrow transplant. But others may experience a wide variety of physical symptoms. These can include: Infection, Bleeding, Pain, Weakness, Fatigue, Nausea, Insomnia, Shortness of breath, Anxiety and Depression. Also after a bone marrow transplant is completed, some people may experience a condition called “Graft-versus-host Disease.” (GVHD). This is a serious condition that causes its own set of symptoms, which palliative care can also help.

So, it is never easy to go through the process of a bone marrow transplant. But palliative care is there to help patients even before their bone marrow transplant process begins. Some palliative care treatments for transplant include medicines that relieve pain, help patients sleep, manage shortness of breath and help them to be relaxed. Palliative care is appropriate at any age and at any stage in a serious illness. It works hand-in-hand with curative treatment.

Keywords: Palliative care, Bone Marrow Transplantation or SCT and symptoms management.

Antifungal Prophylaxis in Patients Undergoing Hematopoietic Stem Cell Transplantation

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Invasive fungal infections are a leading cause of morbidity and mortality in patients undergoing hematopoietic stem cell transplantation (HSCT). Therefore, antifungal prophylaxis is widely used in transplantation centers especially for allogeneic patients who receive immunosuppressant. Tri-azoles (e.g., fluconazole, voriconazole) are the most common anti-fungal agents which have been used in these patients. Due to high level of efficacy, low cost, and low toxicity, fluconazole is used widely in HSCT patients. Voriconazole as a new tri-azole is prescribed for this reason in some specific conditions. Although voriconazole causes more severe adverse effects than fluconazole, its coverage for aspergillus species is appropriate.

Extravasation of Cytotoxic Agents in HSCT

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Introduction: extravasation of cytotoxic agents is the unintentional installation or leakage of these agents in to the perivascular and subcutaneous spaces during their administration.
Materials and methods: This cross section is about skill staff. Management at extravasation .experience and skillful at prevention Knowledge in cytotoxic drug pharmacology: vesicants, non-vesicant, irritant.
Result: Training employee, variance & analysis, teaching.
Conclusion: Decrease extravasation in wards, cost effective for patient & hospital, prevention and management.

Individual Protection Equipment in Chemotherapy in HSCT

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Working with chemotherapy drugs for staff who can deliver, transport, or carry these drugs can be very dangerous.
Individual protection equipment and how to use them in the preparation of chemotherapy drugs is very important.
Individual protection equipment that can be mentioned:

-Hood class 2
-Filtered masks
-Protective glasses
-Scrubs (clothing) special for chemotherapy
-Understanding of collecting chemotherapy drugs spilled on the floor.

The purpose of this article is to introduce ways to reduce the damage that chemotherapy drugs can bring to the personnel of paramedical and medical groups, which is very important.

Key Note Lecture in Persian Medicine

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Bone marrow is a sponge-like intrabone tissue in which blood cells are made. All blood cells, including red blood cells, white blood cells and platelets, are made from a primary cell type in the bone marrow called stem cell. Bone marrow transplantation is actually an unhealthy bone marrow replacement with a healthy bone marrow. This is used to cure many diseases that involve the bone marrow
Bone marrow and stem cell transplantation (BMT) requires significant infrastructure. Patients undergoing bone marrow and stem cell transplant face various side effects. Infections and bleeding, nausea, vomiting, fatigue, loss of appetite, oral ulcers, hair loss and skin reactions include side effects of bone marrow transplantation and stem cell transplantation. In conventional medicine; several drugs have been investigated as post-transplant maintenance therapy.
In Persian Medicine(P.M), so as a medical school and the old index, Although not addressed to BMT, but there are effective ways to reduce its side effects..
Life style Modification is the first and most important factor to protecting and promoting the health in Persian Medicine and therefore is very effective in prevention, well as reduce and controlling bone marrow and stem cell transplantations side effects. Many factors in this medical school to improve life style, have in common with views of conventional medical scientists in this field. Weather modified and avoid from micro-pollutants and cigarette, using fresh and healthy, natural and Non synthetic food and beverages, regular and adequate physical activity and sleep, avoiding from enviromental stresses and good mental condition, Clearing the body of waste and harmful factors, is considered to side effects of bone marrow and stem cell transplantation. Drug treatment is also one of the key tenets of Persian Medicine. Drugs origin used in P.M, is divided in the three categories of plant, animal and mineral.
Due to predict the impact of lifestyle modification and medications referred to P.M, in control of side effects of BMT; Seems to be more experimental and clinical research to prove conclusively is required.
Keywords: Persian Medicine(P.M), BMT, life style modification

ABSTRACT
Poster Nursing

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Blood and Marrow Transplantation

Reviewing the Performance of Bone Marrow Transplantation Unit in Imam Reza Hospital

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Background and Aim: One of the best and modern achievements of medical science is transplantation of an organ that in a relatively short time in the world medical history has been accepted as a new and inimitable way for curing many diseases. The hematopoietic stem cell transplantation (HSCT) needs intravenous infusion of cells for reestablishing bone marrow function for diseases in which bone marrow is destroyed or weaken. This approach is performed as a redeemer way after high dose chemotherapy for malignant diseases. Bone marrow transplantation is the main and final therapy for many of hematological and malignant diseases such as aplastic anemia, kinds of thalassemia and leukemia and hereditary metabolic disorders.

Methods: During last 2 years in BMT ward at Imam Reza hospital of Kermanshah 44 successful cases of bone marrow transplantation was operated.

Results: From these patients 27.27% were women and 72.73% were men. 40.91% were uneducated and others were 22.73% under diploma, 13.63% diploma, 9.9 % associated, 11.37% graduated and 2.27% are doctoral respectively. The average age of the patients was 41-50 years old. 27.27% were allogeneic and 72.73% autologous transplantation respectively. From all of transplanted patients 50 % affected by multiple myeloma, 20.45% Hodgkin's lymphoma, 6.85% Non Hodgkin's Lymphoma, 15.91% AML, 4.55% ALL and 2.27 % Myelofibrosis .68.18 % of patients before transplantation had not recurred. In 92.68% of patient's cell separation was done just once. Obtained MNC average of patients was 6-8. For 75% of patient's engraftment was attained between 6 to 10 days. The average received platelet for patients was 31 to 40 bag.

Conclusion: After transplantation 92.68 % of patients did not have complications. After discharge 33.33% of patients were hospitalized again due to several causes. In pursuance of patients 95.83 % continue their life without any problem. Pearson correlation between CD3-CD34 was 76% and between CD3-MNC is 238 % and maximum correlation between CD34-MNC was 33%.

Keywords: BMT transplant – Report

Registry of Unrelated Hematopoietic Stem Cell Donors in West Iran: A Population Based Cross-Sectional Study

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Background and Aim: Hematopoietic Stem Cell Transplantation (HSCT) is a curative method for both health-threatening malignant and nonmalignant conditions such as lymphoma, leukemia, immuno deficiencies, congenital metabolic disorders, hemoglobinopathies, and Myelodysplastic and Myeloproliferative Syndromes. Nowadays, Donation of hematopoietic stem cells by an unrelated donor may be the only opportunity for 70% of those in need of hematopoietic stem cell transplantation, although HSCT with a Human Leukocyte Antigens (HLA) _matched donor like sibling is the first choice. Hence, individual donor registries are established across the world to facilitate finding the best available donor. We sought to find (HLA)-matched donor for all patients with different racial/ethnic characteristics and also assess social contribution rates in donation of Hematopoietic Stem Cells (HSCs) in Kermanshah, west of Iran 2016-2017.

Methods : This population based cross-sectional study have been constructed to estimate social contribution rates in donation of HSCs among those attending Health Care Centers, hospital etc. and also using mobile teams, in western Iran (2016-2017). Participants were excluded from the study if they had chronic diseases and/or aged less than 18 years or more than 55 years and/or those who did not sign consent form to participate in the study. A validated questionnaire was used to gather data related to the objectives of study. Under safety medical strategies, peripheral blood samples were collected in EDTA tubes and kept at -18 º C. All of tubes were labeled with the people's name and identification number. All data analysis was performed using statistical package for social sciences (SPSS) statistical software (Version 23; IBM Corporation, Chicago, USA). The categorical variables were summarized as frequency and percentages and also normally distributed continuous variables were reported as means and standard deviations. Using Chi-square, the relationships between outcome variable and predicting variables were assessed.

Results: Overall, 3669 unrelated stem cell donors contributed in the stem cell donation campaign. Participants' age was (31.36±10.40 years) (μ±SD) and most of them (59.6%) were men. There was no difference in nationality and religious status among donors. Mainly (39.7%) they had completed academic education and most of them (60.6%, 2224/3669) were employee or student (academic level). Educational status was significantly associated with contribution rates.

Conclusion: Hematopoietic stem cell Donors registries are structured based on positive and altruistic feelings to save patients. Furthermore, continued recruitment of unrelated hematopoietic stem cell donors can increase the probability of finding an HLA-matched donor; although majority of patients of all racial/ethnic population still leave without a match. In conclusion, social contribution rates could be improved by educating people and providing encouragement strategies.

The Effect of Chamomile Mouthwash on the Prevention of Oral Mucositis Caused by Chemotherapy in Children with Acute Lymphoblastic Leukemia

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Background and Aim: Mucositis is a complex inflammatory response of the digestive system mucous membrane and it is also one of the most common painful side effects following chemotherapy in children with carcinoma. Developing mucositis affects the patient's life severely and can lead to long – term hospitalization. Therefore, this study was conducted to evaluate the effect of chamomile mouthwash on the prevention of oral mucositis in children with acute lymphoblastic leukemia.
Methods : This double-blinded clinical trial study was done on 31 children with acute lymphoblastic aged 6-15 who were admitted to 17 Shahrivar hospital, Rasht, Iran between 16 July and 8December 2015. Patients and their parents were instructed to dilute 15 drops of chamomile mouthwash in 10cc of water, rinse around the mouth for one minute, outpour it, and avoid eating for one hour. After three times tooth brushing a day, the mouth cavity of patients was evaluated one day before chemotherapy, on the seventh day and fourteenth day of chemotherapy according to the world health organization criteria. SPSS (version 11) was used in order to analyze the data and random statistical index and independent t test were run.
Results: The severity of oral mucositis on the seventh and fourteenth day after chemotherapy had no significant difference with the first day (P = 0.59). The incidence and severity of oral mucositis didn't increase 14 days after chemotherapy in comparison with the seventh day.
Conclusion: Chamomile mouthwash can be effective in preventing the incidence and severity of oral mucositis and it can be used as a suitable mouthwash in children undergoing chemotherapy.
Keywords: Acute Lymphoblastic Leukemia, Chemotherapy, Mouthwashes, Oral Mucositis

Nursing Informatics: A New Idea for Addressing Challenges in E-Health

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Background and Aim: Nowadays, Nursing Informatics (NI) is defined as a technology that integrates computer Science, Nursing, Cognitive Science, and Information and Communication technology to manage data, information, knowledge and wisdom in nursing practice. It also supports decision making in nursing practice, improves e-learning in nursing care, and accelerates e-health. This support is accomplished through the use of information structures, information processes, and information technology. This paper presents an overview of nursing informatics describing their characteristics, effects on quality factors, main building blocks. It then proposes a new nursing autonomous informatics model using autonomous properties and discusses on main challenges such as learning, the autonomic elements life cycle, and the element competency.
Methods: This is a novel idea
Results: Autonomic Elements (AEs) are the basic building blocks of autonomous systems and their interactions produce self-managing behavior. Each AE has two parts: Managed Element (ME) and Autonomic Manager (AM). An ANI system is established from Managed Elements whose behaviors are controlled by Autonomic Managers. Autonomic Managers execute according to the administrator policies and implement self-managing. An ME is a component from system. It can be hardware, application software, patient electronic record or an entire system. Sensors retrieve information about the current state of that managed element and compare it with expectations that are held in knowledge base by the AE
Conclusion: Due to the increased implementation of technology such as the electronic medical record (EMR), NI has gained world attention. Nursing informatics improves e-learning in nursing care, and accelerates e-health and nursing care. This paper proposes an autonomous nursing informatics model. The proposed model improves performance factors such as scalability, reliability, response time, functionality, and portability. It also facilitates management and control of the entire nursing care system.
Keywords: Nursing Care, Nursing Informatics, Self-managing Systems, E-health, Software Engineering.

The Effect of Teaching Palliative Care on the Pain Management in Cancer Patients

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Background and Aim: Pain is one of the most frequent and distressing symptoms in cancer .despite the existing guide lines about pain management, effective pain treatment is not possible yet. The purpose of this study was to evaluate effect of teaching of pain palliative care on the pain management in cancer patients.
Methods: This study performed on 98 cancer patients who referred to a hospital in arak, Iran. Participants were selected by screening pain numeric rating scale and were randomized to either intervention or control groups. Patients in intervention group were trained for pain palliative care, 6 times a week, 30 minutes each, in the hospital .pain numeric rating scale and pain experience scale (PES) were used at the beginning of the trial, 3 and 6 weeks .Data were analyzed using spss16 by fisher, chi-square, t-test, repeated measure and post-hoc tests.
Results: At the end of 6 weeks the intervention groups (n=49) had a significant improvement in severity of pain and knowledge of pain management compared to the control group. (n=49). ($p<0.001$), ($p<0.001$)
Conclusion: The results of this study showed that teaching pain palliative care is effective in reducing severity of pain and improving knowledge of pain management in cancer patients.
Keywords: cancer patients, palliative, care, pain

The Comprehensive Strategies for Oral Mucositis after Hematopoietic Stem Cell Transplantation

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Background and Aim: In the Department of Hematology of Peking University People's Hospital, the nursing team of the hematopoietic stem cell transplantation (HSCT) took the comprehensive nursing care to prevent patients who undergone HSCT treatment from oral mucositis (OM).
Methods: From January 2017 to July 2017, there are 477 patients in the Department of Hematology of Peking University People's Hospital for HSCT, including 242 male patients (50.73%), 235 female patients (49.27%), the average age of patients is 27.1 years. In our hospital, the Department of HSCT nursing team took the comprehensive strategies to prevent OM after transplantation. The strategies that is Compound Chlorhexidine Gargle (500ml gargle contains chlorhexidine gluconate 0.6g, metronidazole 0.1g, 25ml glycerin, peppermint water 5ml) and 5% sodium bicarbonate gargle are used in alternation, calcium folic acid gargle is used after transplantation. When the patient suffered OM, the strategies are ultraviolet irradiation, iodine glycerin application, the colony factor mouthwash, and so on.
Results: Among 477 patients, 90 cases of OM occurred, the incidence rate of OM was 18.86%. The highest average temperature of oral mucositis was 37.5℃, neutrophil absolute minimum average value was 0*10^9/L and the minimum average value was 0.2*10^9/L for white blood cells. The oral mucositis grades were as follows: Grade I in 47 cases (52.23%), grade II in 29 cases (32.22%), grade III in 10 cases (11.11%) and 4 patients with grade IV (4.44%). Pain grade was: 29 cases for 0 scale (32.22%), 33 cases for 1 scale (36.67%), 16 cases for 2 scale (17.78%) and 12 cases for 3 scales (13.33%).
Conclusion: We use a variety of effective prevention and nursing measures of assessment, to reduce OM incidence and to reduce the risk of patients with systemic infection, to shorten the hospitalization days and costs and to improve patient transplantation safety.
Keywords: Hematopoietic Stem Cell Transplantation, Oral Mucositis, Comprehensive Strategies

Positive Psychotherapy for Reduce Anxiety and Depression in Adolescents with Cancer after Transplantation through Virtual Social Networks (Telegram)

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Background and Aim: In the modern health services there is an ongoing development in virtual social networks and their application for patients' support, diagnosis, self-care, and education. On the other hand, applying short messages as the easiest, simplest, and cheapest way of presenting information would be helpful especially for adolescents. In this study it was paid attention to psychological interventions for adolescents with cancer after transplantation.
Methods: This is a semi-experimental pre-test-post-test with control group. The statistical population of the study consisted of all adolescents who underwent transplantation in Mahak hospital. In this study, 36 of participants were randomly selected and assigned to experimental and control groups. The Health-related quality of life inventory (HRQOL), Beck depression inventory-II & Beck anxiety inventory were completed by both groups before the intervention. Then, positive psycho-therapy as an intervention was performed on the experimental group during 14 sessions, while the control group did not receive it. Then, both groups completed questionnaires again. Data were analyzed by covariance statistical analysis.
Results: Positive psychotherapy through virtual social networks had a significant effect on reducing anxiety post test in the experimental group ($P < 0.05$).
Conclusion: Positive psychotherapy through virtual social networks can be used as one of the effective and cost effective treatments for improving the quality of life for adolescents in pediatric oncology and palliative care wards.
Keywords: pediatric oncology, adolescents, anxiety, depression, Virtual social networks.

A Review of the Determinant Factors on Quality of Life in Patients Undergoing Bone Marrow Transplantation

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Background and Aim: Haematopoietic stem cell transplantation (HSCT) is a modern therapeutic procedure used for treatment of haematological malignancies and acts as a platform for other advanced therapies such as gene therapy and immune cell therapy. Based on Maslow´s theory of needs, Quality of life (QoL) generally defined as a patient´s subjective evaluation of his life situation can be affected by HSCT. In the form of a review of the literature, we review all research studies carrying out for revealing factors affecting Quality of life in patients undergoing bone marrow transplantation.
Methods: We retrieved papers in English via searching science direct, PubMed and google scholar. QoL evaluation in the majority of studies was carried out by means of generic and specific questionnaires such as SF-36, Functional Assessment of Cancer Therapy– Bone Marrow Transplantation (FACT-BMT), World Health Organization Quality of Life Questionnaire (WHO QOL-100) and the Hospital Anxiety and Depression Scale (HAD).
Results : Being male, having higher level of education, having a good marital status, Believing in God and spending time lapse more from transplantation were associated with higher quality of life and there was a correlation among being female, being single or divorced, increasing number of associated diseases and lower QoL . There was a difference in QoL depending on the type of HSCT so that QoL was worse in patients after allogeneic than autologous HSCT due to chronic Graft Versus Host Disease (cGVHD) after allogeneic HSCT.
Conclusion: Understanding information about HSCT and its effect on quality of life helps us improve treatment methods and take steps to control the complications of the HSCT.
Keywords: HSCT, quality of life. Questionnaires

The Effect of Writing Emotional Disclosure by Mothers on Their Emotional Reactions in Pediatric Stem Cell Transplantation Unit in Shariati Hospital Affiliated to Tehran University of Medical Sciences

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Background and Aim: Among the chronic diseases of childhood, cancer has been of great interest, because of the high prevalence and much impact on lives of children and their families. Many researches indicates the incidence of depression, anxiety and chronic stress in particular, among mothers of children with cancer. The aim of this study was to evaluate the effectiveness of Writing Emotional Disclosure by mothers on their depression, anxiety, and stress.

Methods : This quasi-experimental study with pre-test and post-test on mothers of children hospitalized in pediatric stem cell transplantation unit has been done in doctor Shariati hospital in Tehran. 62 mothers were selected by convenience sampling method, study was performed from the third to the tenth day of admission to stem cell transplantation unit. Before implementation all mothers were evaluated with depression, anxiety and stress scale (DASS-21) and then complete Writing Emotional Disclosure for a week every day for 15 to 30 minutes. After a week, mothers were evaluated for Depression, Anxiety and Stress Scale (DASS-21).The results were analyzed with SPSS and using t-paired test

Results: The results showed the mean score of maternal depression before Writing Emotional Disclosure was 25/03 and after the implementation of WED dropped to 15/12 ($p<0.001$).The average anxiety score of mothers before WED was 21/58 so after the implementation of WED fell to 13/09 ($p<0.001$). In addition, the average maternal stress before WED was 27/77 and after the implementation of WED reached to 16/87($p<0.001$). The findings indicated statistically significant difference between the mean scores of depression, anxiety and stress in mothers before and after the intervention. So WED can reduce maternal depression, anxiety and stress.

Conclusion: The findings of this study showed, Writing Emotional Disclosure can act as an effective, simple and low-cost program in dealing and coping with negative life events in transplant centers to be used as a complementary therapy alongside medical treatment.

Keywords: Writing Emotional Disclosure, mothers depression, anxiety and stress, stem cell transplantation ward

Hyperbaric Oxygen Therapy for Hemorrhagic Cystitis in Allogeneic Transplant

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Background and Aim: Hemorrhagic cystitis (HC) is a significant clinical problem that occurs after allogeneic transplant and is often refractory.
Methods: The patient was a forty-year old man who suffered from HC after two months following blood-maker stem cells allogeneic transplantation. Several different treatment methods were used to cure the patient, but satisfactory results were not achieved. The doctor in charge of the patient's treatment suggested 5 sessions of ozone therapy. After finishing the sessions, clinical symptoms related to HC disappeared and were fully cured.
Results: the method ozone therapy is an effective.
Conclusion: This study shows that the treatment of HC with ozone therapy method is an effective and bearable method to cure and it can be tolerated and it does not have any special clinical side effects.
Keywords: Hyperbaric oxygen therapy, Hemorrhagic cystitis, Allogeneic stem cell transplantation

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Note :