



Rajiv Gandhi Cancer Institute and Research Centre

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EDITORIAL

ETHICAL ISSUES IN TRANSPLANTATION

There are two types of motives propelling the donors - altruistic and non-altruistic. Most donations are purely altruistic acts. These include persons who donate organs or marrow without expecting any compensations. A sibling may expect gratitude (reward) from the recipient. It may be true but this fact does not seem to deprive the act of donation of its altruistic character. There usually exists a very strong emotional relationship between them. Donor is likely to experience very deeply the suffering of his/her sibling and especially if there is failure of the transplantation. Donor may have feeling of guilt because it is his/her tissue/cells that caused patient's death.

The matched volunteer unrelated donor (MUD) who decides to donate marrow does not know the recipient – the person whose life he/she saves. The anonymous character of the gift or donation is purely altruistic. The rule that the donor and the recipient cannot know each other is an expression of what may be called “the non-marketing approach” of transplantation. That means the organs for transplant cannot be sold or purchased. This approach does not allow donors to get money in exchange for their donations.

The donation model does well in stressing the importance of human rights. The only problem is that it does not work! It does not provide enough organs! Clearly the need for organs is great and disparity between procured and needed organs is growing rapidly and meanwhile the number of patients dying while still on the waiting list is getting out of hand. Although many will die for lack of organs, a considerable number of people willing to donate an organ never make the effort to fill out a donation card. What is needed is the implementation of a more suitable option for facilitating donation.

So can we encourage market approach for better availability of organs or marrow? The market approach creates a real danger of coerced or quasi-coerced donations from impoverished and socially disadvantaged people who are not able to make fully informed choices or where choice to donate is brought about by their critical financial situation.

Next question is – can we allow quasi - market approach? This means

allow compensation to donors by the state but prohibit individual transactions (even if mutually beneficial) between the potential donors and beneficiaries. This model needs involvement of state or any Govt. agency or NGO or eligible organization to take charge of the responsibility of payment or more properly compensating for the donor without any direct contact between donors and recipients (Iranian Model) Assuming that the donor is an adult, mentally competent who has been adequately informed about the risks and benefits of selling an organ. He might be able to take care of the loved ones in desperate needs. Why should our society prohibit such decision? This quasi market model will encourage organ and marrow availability. They may involve economic incentives to encourage actions that increase the supply of cadaveric organs. This may permit increase in supply of marrow and organs of unrelated donors. But legal system of all the states is based on non-market approach in India. We need to study further the social impact of adopting such a policy.

It seems that no religion or group actively opposes organ procurement. Every religion however holds a certain position concerning ethical norms that would determine the way the organ is procured and allocated. The goal should be to provide a moral framework for thinking about transplantation as a matter of public policy – that is when both consequences (efficiency) and just allocation (equity) are taken into account.

It is the right of a person to become a donor. If competent persons can donate organs to families, friends and even strangers as an act of charity without violating any law, then why should this not be extended to those willing to donate in return for some means of compensation (reward)?

Let me not call it “sale of organs” but a regulated ethical trade through an honest, process oriented NGO or State Govt. agency.

Dr. Dewan AK
Medical Director

BONE MARROW TRANSPLANTATION

A Bone Marrow Transplant is a procedure to replace diseased bone marrow with healthy bone marrow stem cells.

Most blood cells in the body develop from stem cells in the bone marrow.

Normally, when cells grow old or get damaged, they die, and new cells take their place. However, sometimes this natural renewal process can go wrong. Cells do not grow and divide normally, or the immune system goes haywire and attacks normal tissue.

In a person with blood cancer (leukemia, lymphoma, multiple myeloma), the bone marrow makes abnormal

white blood cells, called leukemia cells. They may crowd out normal white blood cells, red blood cells and platelets, making it difficult for normal blood cells to do their work.



Types of transplant - There are three kinds of Bone Marrow Transplants:

- **Autologous Bone Marrow Transplant:** The patient is given healthy stem cells from his / her own body, after high doses of chemo or radiation has destroyed diseased bone marrow in the point.
- **Allogeneic Bone Marrow Transplant:** Here, stem cells are taken from another person, called a donor. Most times, the donor's genes must at least partly match patient genes. HLA blood tests are done to see if a donor is a good match. A brother or sister is most likely to be a good match.
- **Umbilical cord blood transplant:** This is a type of allogeneic transplant. Stem cells are removed from a newborn baby's umbilical cord right after birth. The stem cells are frozen and stored until they are needed for a transplant. Umbilical cord blood cells are very immature so there is less of a need for matching.

Indications for Transplantation

Non-malignant diseases - Inherited red cell disorders (eg. Thalassemia), marrow failure states (eg. Aplastic Anemia) are indications for a BMT, inherited metabolic disorders, and inherited immune disorders.

Malignant / premalignant diseases that require BMT include - Acute Lymphoblastic Leukemia (ALL), Acute Myelogenous Leukemia (AML), Chronic Myelogenous Leukemia (CML), Juvenile Myelomonocytic Leukemia, Myelodysplastic Syndromes, Plasma cell disorders and Hodgkin & Non - Hodgkin Lymphoma.

Allogeneic BMT has following steps:

The Search Process

- Once a Bone Marrow Transplant is considered as a possible therapy, an appropriate donor must be identified. For allogeneic transplants, HLA histocompatibility typing is performed for immediate family members. Class I and class II HLA antigen compatibility is tested. A 6-of-6 match refers to testing of HLA-A, HLA-B, and HLA-DR, each of which has 2 alleles. Routine testing involves checking for these 6 antigens among family members.
- When only 3 of 6 mismatches, the term of haplotypic donor applies. This information helps the transplant physician to process for haplo stem cell transplant. In addition, donor age (younger is better); sex (female stem cells given to a male is less favourable), cytomegalovirus (CMV) serology, pregnancy and transfusion history, and body weight are considered.

The Transplant Process

Phase I: Conditioning

The conditioning period typically lasts 7-10 days. The purpose is to deliver chemotherapy, radiation, or both to eliminate malignancy, prevent rejection of new stem cells, and create space for the new cells. The drugs most commonly used in conditioning regimens are fludarabine, etoposide, melphalan, cytarabine, thiotepa, cyclophosphamide or busulfan. Sometimes

total body irradiation is also used in conditioning regimens.

Phase II: Stem cell processing and infusion

The stem cell infusion is usually performed over about an hour. The stem cells may be processed before infusion, if indicated. Before infusion, the patient is premedicated with acetaminophen and diphenhydramine to prevent reaction. The cells then are infused through a central venous catheter, much like a blood transfusion.

Phase III: Neutropenic phase

During this period (2 - 4 weeks), the patient essentially has no effective immune system & the patient is susceptible to infection. Supportive care and empiric antibiotic therapy are the mainstays of successful passage through this phase. Total parenteral nutrition is provided and is usually quite necessary, especially for children.

Phase IV: Engraftment phase

During this period (several weeks), the healing process begins with resolution of mucositis and other acquired lesions. In addition, fever begins to subside, and infections often begin to clear. The greatest challenges at this time include management of GVHD and prevention of viral infections (especially CMV).

GVHD generally involves the skin, GI tract, and the liver, causing a rash and blistering, diarrhea, and hyperbilirubinemia, respectively. Patients receiving allogeneic hematopoietic stem cell transplants are typically placed on one or more immunosuppressive medications to protect against the development of GVHD. The good side of GVHD is the graft versus leukemic (GVL) effect that may also be present. In addition, patients can develop an entity called venoocclusive disease (VOD). Supportive care and careful fluid management are essential.

Phase V: Postengraftment phase

This period lasts for months to years. Hallmarks of this phase include the gradual development of tolerance, weaning off of immunosuppressant, management of chronic GVHD, and documentation of immune reconstitution.

Most patients need reimmunization, usually after stopping of immunosuppressant with no evidence of GVHD.

Autologous BMT has following steps: Once patient is in complete remission the following steps are followed.

1. **Collection of patient own stem cell:** Patient is administered injection G – CSF 5 mg / kg for four (4) days and stem cell are collected on 5th day. Dose of CD 34+ stem cell are enumerated. If dose of stem cell is inadequate ($< 2.0 \times 10^6$ CD 34 + cell / kg) then the process is repeated following day. If it is still inadequate the procedure is repeated after one month with the help of another mobilizing agent.
2. **Cryopreservation:** As the viability of stem cell is maximum for 72 hours, hence it is cryopreserved with help of DMSO & Albumin & kept in cold storage at -80° C in the Blood Bank.
3. **Stem cell infusion:** After conditioning regimens the stem cell are thawed at 37°C and re – infused.
4. **Neutropenic phase:** It usually last for 7 – 10 days.
5. **Engraftment phase:** It generally takes 10 – 14 days for complete engraftment. Once patient is thermodynamically stable a fresh patient is discharged.

Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC & RC)

The institute is proud home to one of the leading transplant centres in India. The BMT team has completed close to 350 transplants and perform 100 transplants per year that include:

1. Allogeneic stem cell transplant.
2. Autologous stem cell transplant.
3. Matched unrelated stem cell transplant (MUD Transplant).
4. Haploidentical stem cell transplant (the institute holds the distinction of having performed the largest number of Haploidentical Transplants in northern India).

Dr. Bhurani Dinesh / Dr. Ahmad Rayaz / Dr. Agarwal Narender
(Team Bone Marrow Transplantation)

DOCTORS' DAY CELEBRATIONS (1st JULY 2014)



1st July 2014 was celebrated as Doctors' Day. The day is celebrated in honor of Dr Bidhan Chandra Roy, Bharat Ratna and known as the Architect of Bengal. A highly respected Physician and freedom fighter, Dr B C Roy served as the Chief Minister of West Bengal for 14 years.

On this occasion, Delhi Medical Association honored Dr. D C Doval (Senior Consultant & Director Medical Oncology) with the Chikitsa Ratn award, for his immense contribution to the field of medicine.

On the same day, Dr Sudhir Rawal (Senior Consultant & Director Surgical Oncology) delivered a scientific talk on Robotic Surgery, to the body of eminent doctors present. The talk was enthusiastically received by the audience of around 160 doctors from Delhi.

At RGCI & RC, a high tea was organized at Ashray, for all doctors of the Institute. The doctors were welcomed with a chandan tikka and flowers. RGCI Team thanked its doctors for their dedication and untiring commitment to the fight against cancer. The doctors were presented with a letter addressed to their loved ones, thanking these members of the extended RGCI family for their support.

HEALTH TALK AT BHARAT ELECTRONICS LIMITED (BEL)



RGCI & RC organized a health talk on Cancer Prevention for Senior Management of Bharat Electronics Limited (BEL), Ghaziabad, UP on 04th July 2014. Dr. A. K. Dewan delivered a talk on "Can We Prevent Oral Cancer" which was very well appreciated by the audience.

CONGRATULATIONS DR. SURENDER DABAS



Dr. Surender Dabas, Consultant - Head & Neck Surgical Oncology, was invited as an expert International speaker for a conference held on 17th - 19th May, 2014, at Sichuan Cancer Centre, Chengdu, China. Dr. Surender Dabas delivered a talk on "Robotic Surgery in Head & Neck Cancer", which was attended by 200 Head & Neck Surgeons from China, Singapore & Taiwan.

In another program Dr. Surender Dabas was invited as a trainer to train Robotic Surgeons by Apollo Health City, Hyderabad on 23rd June, 2014, to start their Robotic Surgery program in Head & Neck Cancer.

Mr. D. S. Negi (C.E.O.)
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