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Stem Cell Therapy for Thalassemia: A Review

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Abstract: In the present article the stem cell therapy of thalassemia, its advantages, disadvantages and possible complications were discussed in details .It was found that the patients who were under the treatment of stem cell therapy had a good prognosis .This therapy proved to be success among the various treatment measures, But certain disadvantages were encountered, like graft verses host rejection and liver damage.This article provides adequate information about the various aspects of stem cell therapy and helps as a guide towards proper treatment.
Keywords: Thalassemia,stem cell therapy,HLA typings.

Introduction:

Thalassemia are forms of inherited autosomal recessive blood disorders that originated. In thalassemia, the disease is caused by the weakening and destruction of red blood cells. Thalassemia is caused by variant or missing genes that affect how the body makes hemoglobin. Hemoglobin is the protein in red blood cells that carries oxygen. People with thalassemia make less hemoglobin and fewer circulating red bloodcells than normal, which results in mild or severe anemia.[1] Thalassemia will present as microcytic anemia which may be differentiated from iron deficiency anemia using the mentzer index calculation. One of the treatments for thalassemia is stem cell transplantation. Stem cell therapy is an intervention strategy that introduces new adult stem cells into damaged tissue in order to treat disease or injury. Stem cells are biological cells found in all multicellular organisms, which can divide (through mitosis) and differentiate into diverse specialized cell types and can self-renew to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues.

Sources of stem cells:

Stem cells are of two types: embryonic and adult. Stem cells can be totipotent, pluripotent, multipotent, oligopotent or unipotent. Stem cells can be derived from adults which includes Adult stem cells Cord blood, umbilical cord blood, Bone marrow, Blood, peripheral blood stem cells,Skin, Placental tissue. Embryonic stem (ES) cell lines are cultures of cells derived from the epiblast tissue of the inner cell mass (ICM) of a blastocyst or earlier morula stage embryos. The primitive stem cells located in the organs of featuses are referred to as fetal stem cells. Multipotent stem cells are also found in amniotic fluid. A certain kind of cord blood stem cell (CB-SC) is multipotent and displays embryonic and haematopoetic characteristics.[2]

HLA typing:

Stem cells are transplanted only if the human leukocyte antigen of the donor matches with the recipient. HLAs are proteins found on the surface of white blood cells. Our immune system uses HLAs to tell which cells belong to you and which don't. Because HLA markers are inherited, an identical twin is the best donor match. Brothers or sisters also can be good matches. However, many people don't have a good match in their families.

The largest number of transplants for thalassemia performed to date have been from HLA matched related donors. Major hurdles encountered have been graft rejection, acute graft-versus-host disease (GVHD), chronic GVHD, and late sequelae from conditioning regimens and transfusion support [3].

Transplantation:

Bone marrow transplant:

The main cure available today for Thalassamia is Bone Marrow Transplantation (BMT) from compatible donor (a matchingsibling),invented in the 1980′s,Prof. Guido Lucarelli (Cure Thalassemia scientific advisor). Prof. Lucarelli and his team have done morethan 1,500BMTs for thalassemia (about 50% of all the BMTs done in the world) in the last 30 years, and are the worldwide authorities in this field. In low risk young patients, the thalassemia free survival rate is 89%,with no more need of blood transfusions; the mortality risk is 3%. The patient has to stay in the hospital for about 40-45 days, and he has to come back every week for 3-6 months. In Asia the cost of a BMT is about $25-30,000, in western countries it is up to 6 times higher. Hematopoietic stem cell transplantation is a life-saving procedure for thalassemia. However, wide application of this procedure is limited by availability of suitably HLA-matched adult donors. Umbilical cord blood (UCB) has being increasingly used as hematopoietic stem cell source for these patients. To date, over 6000 UCB transplant procedures in children and adults have been performed worldwide using UCB donors. Broader use of UCB for adult patients is however limited by the available infused cell dose. This has prompted intensive research on ex vivo expansion of UCB stem cells and UCB graft-engineering including accessory cells able to improve UCB engraftment and reconstitution and for tissue regenerative potential. Recently, two large European and North American retrospective studies demonstrated that UCB is an acceptable alternative source of hematopoietic stem cells for adult recipients who lack HLA matched adult donors. UCB is anticipated to address needs in both transplantation and regenerative medicine fields. It has advantages ofeasy procurement, no risk to donors, low risk of transmitting infections, immediate availability and immune tolerance allowing successful transplantation despite HLA disparity [3,6].

Complications:

Graft-versus-host disease (GVHD) is a common complication following a allogenic tissue transplant. It is commonly associated with stem cell orbone marrow transplant but the term also applies to other forms of tissuegraft. Immune cells (white blood cells) in the tissue (the graft) recognizethe recipient (the host) as "foreign". The transplanted immune cells then attack the host's body cells. GVHD can also occur after a bloodtransfusion if the blood products used have not been irradiated. It isassociated with higher mortality (80-90%) due to involvement of bone marrow lymphoid tissue, however the clinical manifestations are similar to GVHD resulting from bone marrow transplantation. Transfusion associated GVHD is rare in modern medicine. It is almost entirely preventable by controlled irradiation of blood products to inactivate the white blood cells (including lymphocytes) within. Treatment of GVHD: Intravenously administered glucocorticosteroids such as prednisone arethe standard of care in acute GVHD and chronic GVHD. The use of these glucocorticoids is designed to suppress the T-cell-mediated immune response on the host tissues; however, in high doses, this immune suppression raises the risk of infections and cancer relapse. Therefore, it is desirable to taper off the post-transplant high-level steroid doses to lower levels, at which point the appearance of mild GVHD may bewel come, especially in HLA mis-matched patients, as it is typically associated with a graft-versus tumor effect [5 4]

Discussion:

A blood and marrow stem cell transplant replaces faulty stem cells with healthy ones from another person (a donor). Stem cells are the cells insidebone marrow that make red blood cells and other types of blood cells. A stem cell transplant is the only treatment that can cure thalassemia. But only a small number of people who have severe thalassemias are able to find a good donor match and have the risky procedure [8.]

Conclusion:

The beneficial results of stem cell transplantation from HLA identical members for patients with severe thalassemia are clear. patients have a very high probability of cure with a very low early and late morbidity and mortality. Delay of transplantation until the patient is in a risk category reduces the probability of transplant success and jeopardizes the reversibility of liver and cardiac damage. It is reasonable to suggest that patients

with thalassemia who have HLA identical donors should be transplanted as soon as possible. Umbilical cord blood (UCB) has been shown to be capable of reconstituting the bone marrow of the patient with thalassemia after myeloablated pre-conditioning treatment. The major advantage of UCB over other sources of stem cells is the ability to cross HLA barriers, and there is evidence of less GVHD. The use of related –donor UCB stem cells with HLA mismatches at one to three antigens needs to be considered. It would be worthwhile to do a prospective study to evaluate the role of UCB stem cell transplantation in the treatment of the thalassemias and hemoglobinopathies.[8]

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