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Review Article

UMBILICAL CORD BLOOD BANKING: AN OVERVIEW

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ABSTRACT

Umbilical cord blood, which was once considered as a waste product and which was discarded together with placenta, is now recognized and considered to contain potentially lifesaving cells called as hematopoietic stem cells (HPSCs). Cord blood transplantation offers various distinct advantages as compared to bone marrow and peripheral stem cells such as reduced graft versus host diseases, also low vulnerability of rejection against host human leukocyte antigen (HLA), if mismatched. However the probability of a successful transplantation of a cord blood stem cell is reduced since the amount of hematopoietic stem cell isolated from the cord blood cells in an adult human are not sufficient enough. Also, Umbilical cord blood has not been included as a routine part of obstetrics care and is not medically indicated. The collection of Umbilical cord blood cells should not be compromised with neonatal or obstetrics care and also the routine practice of umbilical cord blood clamping. After discovering the clinical potential of cord blood stem cells, various private and public banks emerged to store this biological entity in various parts of the world for future purpose. While public blood banks use the stored cord blood cells for the welfare of common people, the private enterprises are set up for independent purpose. In this article we will discuss the basics of cord blood transplantation and the perspective of stem cell research in developing countries like India.

INTRODUCTION

Stem cells have the exceptional potential to develop into different cell types in our body during early life and growth period. Stem cells in many tissues have serve as an internal repair system, dividing critically without any limit to restore other cells as long as the person is still alive. Whenever a stem cell divides, each new cell posses a potential either to remain as a stem cell or become another type of cell with a more unique function, such as a brain cell, a muscle cell, or a red blood cell. [1]

Unique Properties of Stem cells

Stem cells can be Differentiated from other cell types by two Critically Important Characteristics

These cells are unspecialized cells capable of regenerating themselves through cell division. These cells can be induced to become tissue- or organ-specific cells with some unique functions, under a specific experimental condition.

In a 3 or a 5 days old embryo, called Blastocyst, the inner cell wall gives rise to an entire body of the organism, including many specialized cell and organs such as the heart, lungs, skin, sperm, eggs and other tissues.

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In adult tissues, such as bone marrow, muscle, and brain, distinct populations of adult stem cells produces replacements for cells that are lost through normal wear and tear, injury, or disease.

Types of stem cells

Stem cells can be widely classified into embryonic stem cells and adult stem cells.

Embryonic stem cells: can be derived from human embryo. These cells have the highest potential to regenerate and repair any cells of the body. Their nature is totipotent. However it is also very difficult to induce their growth and differentiation as these cells poses a risk of tumor formation.

Adult stem cells: they are found in all adult tissues. They pose excellent flexibility i.e. they have a potential to develop into any cell regardless of the origin of the parent cell from which it has been derived. Because of these cells having a great capability and ability to in co-operate into host tissues, therefore their isolation makes these cells favorable candidates for their use in cells based therapies.

Somatic stem or adult cells exist throughout the human body after embryonic development and these persist inside of various types of tissue. These stem cells have been located in tissues such as the brain, bone marrow, blood and blood vessels, skeletal muscles, skin, and the liver.

Adult stem cells

An adult stem cell is considered to be an undifferentiated cell, which is situated between differentiated cells in a tissue or an organ. These cells can renew/regenerate themselves and can be differentiated to produce some or all of the significant specialized cell types of the tissue or organ. The primary role of such stem cells in a living organism is to maintain and repair the tissues from which they are originated. Another term for Adult stem cells which is most commonly used is somatic stem cells.

Adult stem cells have been found in many organs and tissues, including bone marrow, brain, peripheral blood, blood vessels, skeletal muscle, skin, teeth, heart, gut, liver, ovarian epithelium, and testis. [2]

Embryonic Versus adult stem cells

Embryonic and adult stem cells offers several advantages over one another but one of the crucial difference between adult and embryonic stem cells is their different capability in the number and type of differentiated types of cells they can become or develop into. Embryonic stem cells can become all cell types of the body because they are pluripotent. Adult stem cells are limited to differentiating into different cell types of their tissue of origin.

Embryonic stem cells can be grown easily in culture. Adult stem cells are very rare in mature tissues, so isolating these adult stem cells from an adult tissue is challenging, and methods used to expand their numbers in cell culture have not yet been identified. [3] [4]

Umbilical cord

The Umbilical cord helps in connecting the foetus to the placenta and helps in delivering the supply of oxygen and nutrients to the developing foetus. This connecting cord is approximately 50-70 cm (20 inches) long and 2 cm in diameter, and is also known to mediate the feto-placental circulation and it originates from the same zygote which gives rise to the foetus. [5]

Umbilical cord is made of three blood vessels which are embedded deep in a gelatinous substance called as Wharton's jelly and is surrounded by a membrane called amnion . There are two umbilical arteries which carry the deoxygenated blood from foetus to the placenta whereas; an umbilical vein carries the blood rich in oxygen from the placenta to the foetus for its development and growth. As soon as the baby is delivered, the umbilical cord is clamped which was previously used to be discarded but nowadays after the discovery of cord blood transplantation and its prospective usage in therapy there is growing concern about the storage of the cord blood stem cells and hence what had been considered a biological waste so far is now playing an important role as a rescuer of human life. [6]

The Stem cells isolated from bone marrow and peripheral blood differs from those of Cord blood cells isolated from clamped umbilical cord in number, composition and properties as well. Cord blood provides a rich source of haematopoietic stem cells. These cells have the ability to differentiate into both the myeloid as well as lymphoid lineage cells and self-renewal. [7]

Isolation of Hematopoietic stem cell

The Hematopoietic Stem cells (HSCs) Isolation from Umbilical cord Blood (UCB) is Carried out Using

- Density gradient centrifugation
- CD34 immune-magnetic separation
- Fluorescence activated cell sorting (FACS).

These stem cells have been used to treat several types of malignancies like autoimmune disorders. The HSCs have long been employed in the clinical treatment/therapies and have been isolated successfully from the cord blood; UCB also carries mesenchymal stem cells which have an ability to differentiate into cells of different connective tissue lineage such as cartilage, bone and adipose tissue (Figure 1). [8]

Originally it is located in the bone marrow and the capability of differentiation of these cells decreases with age. Various public and private cord blood banks have been spread around various corners of the world to harvest and store the therapeutic prospective of these cells.

While the cord blood units stored within public banks are attainable to mass population and are not used for any profit seeking, blood at private banks are for independent use and they charge money for their storage. In India, The Cord Blood Banks are still in a stage of budding. Having the second largest population of the world India has a tremendous potential in the field of cord blood storage and for this purpose, the development of public banks has to be promoted. India has one of the biggest treasuries of UCB. [9] [10]

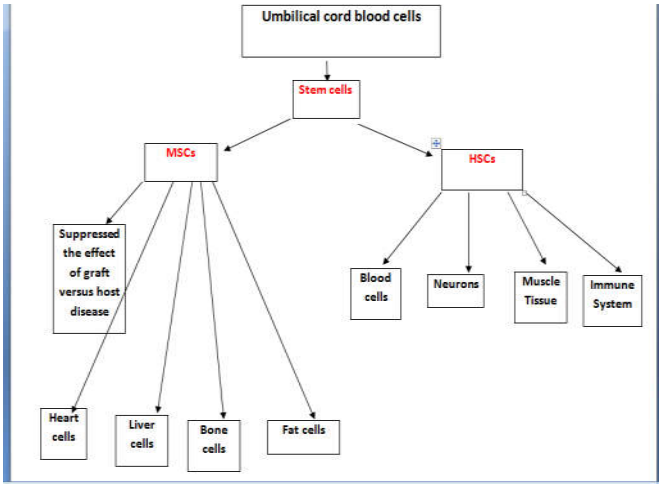

Figure 1 Differentiation potential of umbilical cord blood derived stem cells.

Cord Blood Transplantation

Umbilical cord blood (UCB), like peripheral blood and bone marrow, is a rich source for transplantation of stem cells. There are several advantages for some patients to have transplants with bone marrow or peripheral blood stem cells (PBSCs) instead of cord blood stem cell transplants.

Stem cell transplants can use patient's own stem cells (called "autologous transplants") or may use donor stem cells. The donor cells may be obtained from either a related or unrelated matched donor (called an allogenic transplant). Most of the physicians are not willing to use a baby's own cord blood (autologous transplant) to treat his or her leukaemia. This is

because of the reason that donor stem cells might fight the leukaemia better than the child's own stem cells. [11]

Umbilical cord blood transplant (UCBT) is a curative therapy for patients suffering from leukemia, lymphoma, myeloma, myelo-proliferative disorders, genetic diseases, and disorders of metabolism. The use of double cord blood transplant and reduced intensity regimens in adults has led to increased use in older patients and reduced transplant-related mortality.

In 1988 in Paris, France; the first cord blood stem cell transplantation was successfully performed. The patient was a man with Fanconi's anaemia, a genetic and potentially life-threatening type of anemia. That transplantation experiment was a huge success without any graft versus host disease and the patient is still alive. Thousands of UCB transplantations have been clinically performed since then. [12]

Sources of Stem Cells for Transplantation

The cells used in transplants can be obtained from three sources: bone marrow, peripheral blood and the blood in the umbilical cord after a baby is born.

To collect cells from bone marrow, the physician may remove marrow from a donor's hip bone in a sterile surgical procedure using anesthesia, sterile needles and syringes. In 4 to 6 weeks, the donor's body replaces the donated bone marrow.

Nowadays, the most common source of stem cells for transplantation is Peripheral blood. Peripheral blood stem cells (PBSCs) are blood-forming stem cells released from the bone marrow into circulating blood. Commonly, the bone marrow delivers only a small number of these stem cells into the blood. To obtain adequate number of stem cells from the peripheral blood for a transplant, a donor is given medication that stimulates more blood-forming stem cells to move from the bone marrow to the blood. These cells are then collected from the blood using a process called "apheresis." For apheresis, a needle is placed in the donor's vein, usually in the arm of the donor. The donor's blood passes through a machine that removes the stem cells and then returns the rest of the blood to the donor. The donor's body replaces the cells in 2 to 3 weeks. Cord blood stem cell transplantations have been given successfully to patients (mostly children) with some 70 diseases, including:

- acute lymphocytic leukemia
- acute myelogenous leukemia (AML)
- myelodysplastic syndromes (MDS)
- chronic myelogenous leukemia (CML)
- juvenile chronic myelogenous leukemia (JCML)
- chronic lymphocytic leukemia (CLL)
- Hodgkin and non-Hodgkin lymphoma
- Neuroblastoma
- Thalassemia
- severe combined immune deficiency (SCID)
- Wiskott Aldrich syndrome
- metabolic diseases such as Hurler syndrome
- Severe aplastic anemia.

Till this date, more than 5,500 cord blood stem cell transplantations worldwide have been performed from unrelated donors or several hundred from sibling donors. [13][14]

Potential Advantages

There are some advantages of using donor cord blood stem cells instead of donor peripheral blood or donor marrow stem cells in certain patients. Some of the potential advantages of cord blood stem cells are:

***Availability*:** Cord blood which is stored in a public cord blood bank is prescreened, tested and frozen and is ready to use; or it can take months to confirm and find a marrow or peripheral blood donor.

***Graft-Versus-Host Disease*:** After a cord blood stem cell's transplantation, only a few number of patients got GVHD and, amidst those patients who developed GVHD, the complications tends to be less grave than it was in patients who had bone marrow or peripheral blood transplants. GVHD is severe and sometimes fatal complication of allogenic stem cell transplantation. With GVHD, the donor's immune cells attack the patient's healthy tissues.'

***Human Leukocyte Antigen (HLA) Matching*:** HLA matching plays a vital role in successful engraftment, severity of graft-versus-host disease (GVHD) and overall survival of the patient. A close match between the patient and the cord blood unit can boost patient's aftermath after transplantation. However, although a closely matched cord blood unit is usually preferred, clinical studies have suggested that the match may not have to be as closer as the match that is essential for bone marrow or peripheral blood transplants.

***Diversity*:** Donated cord blood units have the potential to provide a source of stem cells that can be considered as racial diversity.

***Infectious Disease Transmission*:** These Cord blood stem cell transplants carry less chances of transmission of blood-borne infectious diseases as compared with stem cells from the peripheral blood or marrow of related or unrelated donors. [15]

The Collection and Storage Process

During child birth, the main focus is on the mother and baby. After the baby is born,

1. The umbilical cord is clamped; blood from the umbilical cord and placenta is then collected before or after the placenta is delivered, depending upon the procedure at the hospital.
2. The blood is then collected into a sterile bag; this bag is the cord blood unit. The collected blood is then given an identification number and stored temporarily in a sterile area.
3. The cord blood unit is transferred to a cord blood bank for freezing, testing and long-term storage.
4. Testing procedure includes HLA typing to establish the level of matching to potential recipients, cell counts and testing for any infectious agents such as the AIDS virus, CVS (cytomegalovirus) and hepatitis viruses.
5. The cord blood unit is also checked to make sure it has enough blood-forming cells for a transplant. If there are too few cells, the cord blood unit may be used for the research purpose for improving transplantation process for future patients.
6. Next, the blood is frozen and kept at a very low temperature, usually in liquid nitrogen, for future usage. When it is required for transplantation, the cord blood

unit can be shipped, within a few days, to the transplant center where it is defrosted and infused into the patient.

7. For minimizing the risk to mothers and newborn infants, normal childbirth routine should not be altered in order to collect cord blood, especially when collecting cord blood for unrelated recipients. [16][17]

Cord Blood Banking

Because of the future potential and various application of cord blood in therapy, various public and private cord blood banks had sprouted in different parts of the world. Cord blood, which is a source of the lifesaving cells, can be harvested without any considerable health risk to the mother and the new born baby from either during the third stage of labor or from the delivered placenta. [18]

The collection of cord blood is performed in sterile environment where the umbilical vein is punctured with a sterile needle attached to a sterile, collection bags containing citrate phosphate dextrose or heparin anticoagulant which is situated lower than the placenta and blood flows from the placenta through the cord and finally inside the bags. The collected units are then labeled and shipped to cord blood banks. [19]

The entire process of collection, processing, testing and cryopreservation of cord blood is rather burdensome and non-regulated and thus it leads to a loss of total 10 to 20 percent of the initially collected blood volume and cell counts. The public banks are often called as nonprofit banks since they do not ask for money for the storage and they store the cord blood so that it is always accessible to suitably matched recipients in different parts of the world.

While public cord blood banks are valued there is a distress on the hike in the number of private blood banks. These banks usually ask for high financial aid for storage of cord blood and allow it to be used only for autologous and allogenic transplants if any need arises in future.

So therefore it seems that private banks are just exploiting people out of their anxiety, concern and incognizance which are not only unethical but also deceitful. [20][21]

Regulatory Bodies in India

In India there are three major regulatory bodies, which are responsible for implementing policies regarding cord blood banking sector namely, Indian Council of Medical Research (ICMR), Department of Biotechnology (DBT) and Drug Controller General of India (DCGI).

These regulatory bodies issues guidelines on UCB banking facilities, which accelerates stem cell research via public-private partnership. They also encourage public cord blood banking to broaden affordable treatment and for the regulation of travel and tourism sector. In July 2006, the draft guidelines for stem cell research including guidelines for cord blood stem cell banking were implemented and submitted by ICMR and DBT. On July16, 2007 a joint committee of ICMR and DBT was assembled to discuss the Annexure on "Laboratory standards for cell collection and processing for clinical use". [22]

Indian Overview on Umbilical Cord Blood Stem Cells

With the birth rate of 21.8 per 1000 people; India is among one of the largest collectors of umbilical cord blood in the world. There are three public banks that have been established in India so far –

- Relicord
- Jeevan cord
- Stemcyte.

The health ministry of India has reported that there are 14 approved private umbilical cord blood banks currently employed in the country and a total of 29,993 bio-specimens have been collected from 24,533 patients in the hospitals till February 2015. [23]

According to World Bank reports, India is one of the highest ranking countries in the world as far as the number of malnourished children is concerned and according to their report of Global Hunger Index 2015, India is ranked 20th with a serious hunger scenario. So a country where people are suffering from malnutrition, poverty, hunger and illiteracy, storage of cord blood at private banks which ask for a high rate just seems to be unfeasible.

There is lack of proper training among nurses and sterile environment for the collection and storage of the blood in hospitals and hence the chance of cord blood unit getting contaminated and therefore non-viability is quite frightening. [24]

Although public banks have some potential to play a vital role in public welfare but since their number is very low they have not been much promising and this has been the major obstacle so far since most of the deliveries occur at public hospitals.
Only a few numbers of women population knew exactly what the umbilical cord blood stem cell banking is, some of them knew about private cord blood banking while only a few were aware about public cord blood banking. It has also been found that the awareness of cord blood banking depends on the level of education. [25][26]

CONCLUSION

With the high birth rate as well as genetic diversity, India has a great vision for umbilical cord blood banking. A very few number of umbilical cord blood transplantation have been performed in India so far because of the high rates and insufficient number of convenience of umbilical cord blood units. But the current existence of three public and seven private umbilical cord blood banks in India, transplantation will be enhanced in the upcoming years. Cord blood stem cells are being used in the treatment of various medical conditions with over several potential disease targets.

The clinical use of umbilical cord blood has expanded over the past few years and this has led to the blooming of the entire umbilical cord blood banking industry. Umbilical cord blood storage in India needs to raise public private partnership relation where umbilical cord blood can be stored at a feasible cost.

Various private banks keep on expanding in our country because most of the families store umbilical cord blood in private banks with hopeful advantages in degenerative disorders in the future. For increasing the number of

transplantations in India, full and active participation and extensive investment by the Government is necessary.

References

1. Armson, A., Allan, D. and Casper, R. Umbilical Cord Blood: Conselling, Collection and Banking. Journal of Obstetrics and Gynaecology Canada. 2015;37(9): 832–844.
2. Ashley, P. n. Haematopoietic stem cells: past, present and future. Cell Death Discovery , 2017;Article number: 17002.
3. Ballen, K. New trends in umbilical cord blood transplantation. Blood. 2005;3786-3792.
4. Ballen, K. Umbilical Cord Blood Transplantation: Challenges and Future Directions. PubMed. 2017;6(5):1312-1315.
5. Benirschke, K. The Umbilical Cord. NeoReviews. 2004;5(4):e134-e141.
6. Bio-Spectrum. biospectrumasia.com. October, 2009.
7. Ferguson, V. D. Bioengineering aspects of the umbilical cord. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2009;144: S108-S113.
8. Fraser, J. Cord Blood Transplantation Study (COBLT): Cord blood bank standard. J. Hemato. ther. 1998;7: 521–561.
9. Henningson, C. Embryonic and adult stem cell therapy. The journal of allergy and clinical immunology. 2003 111(2): Pages S745–S753.
10. https://www.lls.org/sites/default/files/file_assets/cordbloodstemcelltransplantation.pdf. [Visited on January 17,2019]
11. Jacqueline, S. The development, structure and blood flow within the umbilical cord with particular reference to the venous system. AJUM . 2012
12. Laughlin, M. E. Outcomes after transplantation of cord blood or bone marrow from unrelated. *New Eng. J. of Med.* 2004;351: 2265-2275.
13. Minn, T. Umbilical cord blood hematopoietic stem cell transplantation, an alternative to bone marrow. Worcester Poly. Inst. 2011.
14. Pandey, D. Banking Umbilical Cord Blood (UCB) Stem cells: Awareness, attitude and expectations of potential donors from one of the largest potential repository.(india). PLoS ONE. 2016;vol11.
15. PEDIATRICS, T. A. Cord Blood Banking for Potential Future Transplantation. Pediatrics. 1999;104(1): page166-118.
16. Percer, B. Umbilical cord blood banking: Helping parents make informed choices. Nursing for Women's Health. 2009;13: 216–223.
17. Petrini, C. Umbilical cord blood collection, storage and use: ethical issues. Blood Transfusion. 2010; 8(3): 139–148.
18. Reubinoff, B. Embryonic stem cell lines from human blastocysts: somatic differentiation in vitro. Nature Biotechnology. 2000;18, pages 399–404.
19. Sachdeva, A. e. Umbilical Cord Blood Banking: Consensus Statement of the Indian Academy of Pediatrics. Indian Pediatrics. 2018;volume 55.
20. Sullivan, M. Banking on cord blood stem cells. Nat. Rev. Cancer. 2008;8: 554–563.
21. Thomson, J. Embryonic stem cell lines derived fron human blastocyts. Science. 1998;282(5391):1145-1147.
22. Tuteja, M. Knowledge of cord blood banking in general population and doctors: A questionnaire based survey. Indian J.Pediatr. 2016;83: 238–241.
23. Verma, V. G. Cord Blood Banking: An Indian Perspective. Cellular and Molecular Biology. 2016;62(3): page 1-3.
24. Vijan, A.Unique properties of stem cells. Research & Reviews: Journal of Pharmacology and Toxicological Studies. 2016;ISSN: 2322-0120.
25. http://www.worldmarrow.org/fileadmin/WorkingGroups_Subcommittees/Cord_Blood_Working_Group/Cord_Blood_Banks_Worldwide_13042010. [Visited on January 15, 2019]
26. www.nationalcordbloodprogram.org/donation/prospective_donor_faq.html. [Visited on January 20,2019]

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