Review Article

Umbilical Cord Blood Saving - A Lifeline for a Lifetime

N YASMIN¹, N KABIR², T AFRIN³, S AHMED⁴, K KHATUN⁵

Abstract:

Introduction: Umbilical cord blood is blood left over in the placenta and in the umbilical cord after the birth of the baby. Umbilical cord blood saving consists of the collection, processing and cryopreservation of the remaining blood within the umbilicus and placenta following the birth of a child. Within this left over blood, traditionally discarded with the placenta as medical waste, lies a rich source of haematopoietic stem cells same as bone marrow. Cord blood stem cells have advantages over bone marrow in transplants and have been used in more than 30,000 transplants to regenerate healthy blood and immune systems¹. Today, stem cell therapies continue to evolve, bringing new hope to patients and their families.

Objective: To aware regarding use of stem cells of baby's umbilical cord blood in future.

Methods: A review of relevant articles and documents and some world standard stem cell banking protocol were undertaken.

Conclusion: When these cord blood stem cells are processed and stored, the cells are not only a perfect match for the baby, but it could also provide life saving benefits for siblings and other family members.

Introduction:

After a baby is born and the umbilical cord has been clamped and cut, some blood remains in the blood vessels of the placenta and the attached portion of the umbilical cord. This cord blood is rich in powerful hematopoietic (blood-forming) stem cells, such as red blood cells (RBC), white blood cells (WBC), blood platelets, and plasma similar to the ones that are found in the bone marrow^{2,3}. Hematopoietic stem cells form blood and immune cells and are responsible for the constant renewal of blood in our body. Because of this important property of hematopoietic stem cells, cord blood is used for transplantation as an alternative to bone marrow. Stem cells are immature cells have the potential to develop into any other type of body cells that form organs and tissues. They are powerful, unique cells that are the building blocks of the body. When a stem cell divides, each new cell has the

potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain celL⁴.

These stem cells in cord blood have immense potential to cure heart related disease, eighty diseases in blood, infection such as Aspergillosis ⁵ and genetic disorders⁶. Cord blood saving is a once –in-a- life time opportunity to enhance the family's future health options⁷.

Experts have found that newborn stem cells do not 'expire' if properly processed and stored⁸. In fact, research indicates that these cells can be stored indefinitely⁷. The oldest cord blood unit to the successfully thawed to date was 15 years old⁹. In addition to the remarkable potential to develop into many different cell types in many tissues stem cells

- 1. Associate Professor (OBGYN), ICMH, Matuail, Dhaka.
- 2. Professor & Head (OBGYN), ICMH, Matuail, Dhaka.
- 3. Registrar (OBGYN), ICMH, Matuail, Dhaka.
- 4. Internee Doctor, Bangladesh Medical Collage.
- 5. Assistant Professor (OBGYN), BSMMU, Shahbag, Dhaka.

serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive.

Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions⁴.

The first successful human umbilical cord blood (UCB) transplant was performed in France in 1988¹⁰. After the first sibling-donor cord blood transplant was performed in 1988, the National Institute of Health (NIH) awarded a grant to Dr. Pablo Rubinstein to develop the world's first cord blood program at the New York Blood Center (NYBC)⁷, in order to establish the inventory of non embryonal stem cell units necessary to provide unrelated, matched grafts for patients. Subsequently, over 8000 transplants have been performed worldwide¹¹. Current stem cell applications are in anaemia, leukemias, immune disorders and inherited erythrocyte abnormalities¹²⁻¹⁵.

Cord blood is stored by both public(i.e. stored and made available for use by unrelated donors) and private (i.e. the blood is stored for and the costs paid by donor families for future use to treat diseases within the family) cord blood banks. Public cord blood banks store cord blood for the benefit of the general public, and most U.S. banks coordinate matching cord blood to patients through the National Marrow Donor Program (NMDP). Majority of the private banks charge an amount of USD 2000 for preserving the cord blood. Private cord blood banks are usually for-profit organizations that store cord blood for the exclusive use of the donor or donor's relatives.

Use of cord blood is increasing day by day. In 1997, the likelihood of a child needing his or her own cord blood for transplantation was 1 in 200,000¹³. In 2001, it was estimated that the probability of a child needing to use his or her own cord blood sample was 1 in

10,000. By 2005, it was estimated that over the course of a lifetime up to age 70, the probability that a person would require a transplant of his or her own stem cells in a ratio of 1 in 450 (autologus' transplant) and the likelihood of requiring any transplant for himself or herself or a sibling would be 1 in 220 ('autologous' or 'allogeneic' transplant). In 2005, University of Toronto researcher Peter Zandstra developed a method to increase the yield of cord blood stem cells to enable their use in treating adults as well as children¹⁶.

Importance of saving Baby's cord Blood:

Collecting, processing and banking stem cells is painless, non-invasive and risk free retrieval immediately available for clinical use. It is once in a life time opportunity and potential life saving resources for children, family members with medical history of developing diseases that are potentially treatable with stem cell transplants. Cost of baby's cord blood saving is significantly lower compared to bone marrow aspiration and bone marrow transplant including treating diseases such as leukemia and immune system disorders. The highest probability for a transplant match is from a related donor. In addition, the transplant success rate of related donors is double than that of unrelated donors. The baby's cord blood stem cells guarantee a perfect match for baby and can potentially match with their siblings and parents. Here less stringent HLA (human leukocyte antigen) matching is required for use in transplantation as compared to bone marrow and there is low rejection versus low chances of life threatening graft versus host disease after transplantation¹⁷.

Diseases treatable with stem cells

For more than a decade, banked cord blood stem cells have been used to treat thousands of people worldwide with more than 80 serious diseases, such as leukemia, other cancers and blood disorders¹⁸. In addition, researchers are still learning about exciting new possibilities where cord blood stem cells may revolutionize other areas of medicine.

Current stem cell applications are in - Acute leukemias, Chronic leukemias, Myelodysplastic syndromes, Stem cell disorders, Myeloproliferative disorders, Lympho proliferative disorders, Phagocyte disorders, Liposomal storage diseases, Histiocytic disorders, Inherited Erythrocyte Abnormalities, Congenital immune system disorder, Other inherited disorders - Tay sachs Disease, Inherited platelet abnormalities, Plasma cell disorder, other malignancies such as Brain tumour, Breast cancer, Ewing sarcoma, Neuroblastoma, Ovarian cancer, Renal cell carcinoma, Small cell lung cancer, Testicular cancer. Other stem cell applications in Autoimmune Diseases like Even syndrome, Multiple sclerosis (Experimental), Rheumatoid arthritis (Experimental), Systemic Lupus Erythematosus (Experimental). Laughlin et al 4 conducted a study of 68 patients with leukemia or with other blood disorders. Most of the patients received transplants of umbilical cord cells from unrelated donors. About 90% of the patients grew new, healthy blood cells from the "mismatched" cord blood cells¹⁹.

Procedure of Cord Blood Collection

Umbilical cord blood can be collected without risk to the mother or infant donor. Cord blood can be collected from the placenta, by sterile puncturing one of the umbilical veins with a needle and allowing the cord blood to drain into a sterile bag containing an anticoagulant to prevent clotting. For long-term storage, cells undergo specialized freezing procedures and are stored in special freezers under liquid nitrogen. Maximal storage time, or expiration date, is unknown, but cells are likely to remain usable for decades. Cord blood units from public banks have been successfully transplanted after 18 years in storage⁷.

In both vaginal and caesarean deliveries, collection of placental blood is done shortly after birth. As expected, the amount of cord blood obtained in case of a caesarian delivery is relatively lesser than that of a normal delivery. The procedure of collecting cord blood is carried out by a qualified midwife or a physician, immediately after delivery of a baby, both sides of the umbilical cord are clamped and cut(Step-1). After cutting, one side of the cord is unclamped and the needle which is attached to the blood collection bag is inserted at the prepared insertion site of the disinfected umbilical cord (Step-2).

Baby's cord blood is collected into the collection (Step-3) bag- a process which normally takes 2 to 5 minutes. Besides this, placental blood is collected from the side of placenta (where the embryo is connected) and the large blood vessels that reach the fetus. Usually, the whole procedure takes less than 10 minutes and about 80- 150ml of cord blood is used for storing. The collected blood filled in bags is then sent to the cord-blood bank for future use.

Processing of cord blood

Every cord blood bag is assigned with an identification number. Some of the cord-blood banks separate out the red blood cells, whereas some prefer to retain them. In both the methods, the cord blood is processed and cryopreserved, i.e. a cryopreservant is added to the cord blood and is slowly cooled down to -90 Celsius. Then, it is transferred to a liquid nitrogen tank having temperature -196° Celsius. This way, the cells are kept alive and stored in a deepfreezing state.

A number of quality control tests are carried out to measure cell count (total cell numbers including stem cells), cell viability and sterility test (bacterial contamination) on baby's cord blood sample. The cord blood is then processed with Automated Processing Technology to achieve higher cell yield. The Automated Processing Technology separate the red blood cell and plasma to isolate stem cells without undergoing tedious manual processing procedures.

Storage of cord blood

Baby's cord blood is frozen in a specially designed freezing bag and housed in a individual metal cassette. The stem cells are then gradually frozen through a controlled rate freezer. A separate quarantine storage tank holds samples while awaiting the results of serological and microbiological testing. Finally, the sample is transferred into the permanent storage tank for long-term cyropreservation.

If the amount of cord blood is insufficient (<45ml) with Automated Processing System, one will able to obtain a higher cell yield than achievable by manual method. But the more stems cells that are available for transplantation the better because higher stem cell is often linked to improved treatment success. In multiple birth storing every baby's cord blood is recommended as it ensures perfect HLA matching of baby. In addition, the collection volume per baby in multiple birth is smaller, so collecting cord blood for all babies ensures adequate stem cells stored for future use. As their genes are different, their cord blood must be stored separately.

Stem cells from a baby are a perfect match only for the baby or for an identical twin. However it can be used for a sibling or other family member if the "matching" is acceptable. Medical research also shows that receiving stem cells from a related donor confers a greater likelihood of survival and reduced likelihood of severe transplant related complications²⁰.

Instead of throwing umbilical cord away as a waste, it can be donated for public use of cord blood. It is noteworthy that donating cord blood neither affects the mother nor the child. A healthy woman (18 years and older) who had a normal pregnancy and delivery can donate her child's umbilical cord blood in public cord-blood banks. This can be used later for saving someone with a life-threatening disease or it can be used for research studies

Conclusion:

Cord blood stem cells are a miracle of nature that are only available once in a life time. Savings a newborn's stem cells can offer significant advantages to a family. Banked stem cells can be used to treat medical conditions of newborn and other member of the family if the matching is acceptable. Receiving stem cells from a related donor can also confer a greater likelihood of survival and reduced likelihood of severe transplant related complications.

References:

- 1. Allison M, Nature Biotechnology 2012;30(4):304
- Sandhyarani N. Cord Blood Banking: Donating Umbilical Cord Blood, Buzzle.com. Last Updated: September 19, 2011
- Gluckman, E. et al. Outcome of cord-blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. 1997; 337(6): 373-815.
- 4. Kohn, D.B., Parkman, R. Stem Cell Basics:. FASEB J. 1997; 11:635-639
- 5. "Bouncing Back!". Retrieved August 16, 2011 15.
- Cairo MS, Wagner JE "Placental and/or umbilical cord blood: an alternative source of hematopoietic stem cells for transplantation.". *Blood* 90.1997 (12): 4665–4678.
- Linden, J., Preti, R., Dracker, R. New York state guidelines for cord blood banking. Journal of Hematotherapy. 1997;6:535-541

- Broxmeyer, H.E.et.al. High-efficiency recovery of functional hematopoietic progenitor and stem cells from human cord blood cryopreserved for 15 years. Proc. Natl. Acad. Sci. 2003; 100(2):645-650
- Johnson, F.L. Placental Blood Transplantation and Autologous Banking-Caveat Emptor. J. Ped.Hem.Onc.1997;19(13):183-86
- 10. Kline RM. Sci Am 2001; 284: 42-9.
- Pasquini, M.C., Logan, B.R., Verter, F., Horowitz, M.M., & Nietfeld, J.J. NEJM 1989;321:1174-8
- 12. HayaniA. et al. First Report of Autologous Cord Blood Transplantation in the Treatment of a Child with Leukemia. Official Journal of the American Academy of Pediatrics 2007; 119: 296-300.
- Gluckman, E. et.al. Outcome of cord-blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. 1997; 337(6): 373-81
- 14. Wagner J et al. Transplantation of unrelated donor umbilical cord blood in 102 patients with malignant and non malignant diseases. Blood 2002; 100: 1611-1618
- 15. Barker, J.N., Wagner, J. E. Umbilical cord blood transplantation: current state of art. Curr Opin Oncol. 2002;14:160-164
- Elizabeth R. "New strategy will boost cord blood stem cells". University of Toronto. Archived from the original on September 19, 2006. Retrieved September 20, 2006 of the Stem Cell Therapeutic and Research Act of 2005.
- 17. Moise K Jr. Umbilical cord stem cells. Obstet Gynecol. 2005;106(6):1393-1407.
- 18. Ooi J. Cord blood transplantation in adults. Bone Marrow Transplant. 2009;44:661-666.
- 19. Laughin, M.J., Barker, J., Bambach. B., et. al. Hematopoietic engraftment and survival in adult recipients of umbilical cord blood from unrelated donors. N Engl J Med. 2001;344:1815-1822
- 20. Rubinstein P., Carrier, C., Schardavou, A., et al. Outcomes among 562 recipients of placentalblood transplant from unrelated donors. N Engl J Med. 1998;339:1565-1577