

Umbilical Cord Blood Banking (UCB): Current Issues and Future Challenges

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Abstract

Umbilical cord blood (UCB) is collected from left out cord from placenta and contains Hematopoietic (blood) stem cells. It a source of precious primitive hematopoietic stem cells (HSC) and progenitor cells that can reconstitute the hematopoietic system in patients with malignant and non-malignant disorders treated with myeloablative therapy.

Umbilical cord blood (UCB) contains stem cells which have already successfully treated a variety of diseases, including leukaemia, lymphomas, hemoglobinopathies, immunodeficiency, and disorders of metabolism. Much ongoing research continues to find out potential treatment of additional diseases. UCB cells possess an enhanced capacity for progenitor cell proliferation and self-renewal in vitro. UCB is usually discarded, and it exists in almost limitless supply. The blood remaining in the delivered placenta is safely and easily collected and stored.

Cord blood can be stored in private banks or public banks. Private cord blood banks save cord blood for use by the family only, at a cost. Public cord blood banks accept donations and the cord blood are then used for the general public and/or research. A review of the literature finds that public banking is the preferred recommendation over private unless there is a known family member with a disease that can currently be treated with cord blood.

After more than one decade of clinical experience, it is currently accepted that UCB transplants, related and unrelated, are equivalent to or might compare favourably with bone marrow (BM) transplants, especially in children. Initial studies of long-term survival in children with both malignant and non-malignant hematologic disorders, who were transplanted with UCB from a sibling donor, demonstrated comparable or superior survival to children who received BM transplantation.

This article discusses cord blood banking options for patients as well as the information for both healthcare providers and patients when dealing with umbilical cord blood banking and some important ethical issue related to cord blood banking.

Keywords: Umbilical Cord Blood; Cord Blood Banking; Hematopoietic Stem Cells; Informed Consent.

Introduction

After a baby is born, cord blood is left in the umbilical cord and placenta. It is relatively easy to

collect, with no risk to the mother or baby. It contains Hematopoietic (blood) stem cells: rare cells normally found in the bone marrow.

Hematopoietic stem cells (HSCs) can make every type of cell in the blood – red cells, white cells and platelets. They are responsible for maintaining blood production throughout our lives. They have been used for many years in bone marrow transplants to treat blood diseases[1]. There have been several reports suggesting that cord blood may contain other

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types of stem cells which can produce specialized cells that do not belong to the blood, such as nerve cells. These findings are highly controversial among scientists and are not widely accepted.

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Many ongoing researches continue to find out potential treatment of additional diseases. Cord blood can be stored in private banks or public banks. Private cord blood banks save cord blood for use by the family only, at a cost. Public cord blood banks accept donations and the cord blood are then used for the general public and/or research. A review of the literature finds that public banking is the preferred recommendation over private unless there is a known family member with a disease that can currently be treated with cord blood [2]. This article discusses cord blood banking options for patients as well as the information for both healthcare providers and patients when dealing with cord blood banking.

Definition

A Cord Blood Bank is a facility which stores umbilical cord blood for future use. Banking cord blood in a private umbilical cord blood bank is a personal choice made by both parents. Both private and public cord blood banks have developed since the mid-to-late 1990s to treat diseases of the blood and immune systems.

In the United States, the Food and Drug Administration (FDA) regulates cord blood under the category of "Human Cells, Tissues, and Cellular and Tissue Based-Products". The Code of Federal Regulations (CFA) under which the FDA regulates public and private cord blood banks is Title 21, Section 1271[3]. Other countries also have regulations to cord blood.

Public banks accept donations to be used for anyone in need. Unlike private cord blood banking, public cord blood banking is supported by the medical community. Generally, an expectant mother interested in donation should contact the bank before the 34th week of pregnancy. The National Marrow Donor Program has a list of public cord blood banks

on their website. Once the blood is donated, it loses all identifying information after a short period of initial testing [4].

The parents have custody of the cord blood until the child is an adult. The cord blood might someday be needed by the donor baby, or it could be used by a relative who is a close enough match to receive a transplant from the donor, typically a sibling. Private Banks charges a fee of around \$1,000 to \$2,000 to preserve the harvested cord blood for family biological insurance. Private Banks have been criticized for aggressive marketing campaigns to expectant parents.

Composition of Cord Blood

Cord blood contains Hematopoietic Stem cells, progenitor cells which can form Red Blood cells, White Blood cells, and Platelets, neonatal cord blood is so physiologically valuable, it is of great benefit for the neonate to receive upon birth.

Method of Collection of Cord Blood

The predominant collection procedure currently practiced involves a relatively simple venipuncture, followed by gravity drainage into a standard sterile anti-coagulant-filled blood bag, using a closed system, similar to the one utilized on whole blood collection. After aliquots have been removed for routine testing, the units are cryopreserved and stored in liquid nitrogen. UCB banks are being established throughout the world and UCB units are collected for allogeneic unrelated and related HSC transplantation. In unrelated cord blood banks donated UCB units are collected and stored for allogeneic use in patients who do not have an identified HLA matched relative.

Steps to be Followed

Cord blood collection happens after the umbilical cord has been cut and is extracted from the foetal end of the cord, diverting up to 75 +/- 23 mL from the neonate. It is usually done within ten minutes after giving Birth. Additional stem cells may be collected from the Placenta called Placenta Cord Banking [5].

After the health care provider draws the cord blood from the Placental end of the Umbilical cord, the placenta is couriered to the stem cell laboratory, where it is processed for additional stem cells.

An adequate cord blood collection requires at least 75 ml in order to ensure that there will be enough cells to be used for transplantation.

Before the cord blood is stored for later use, it undergoes viral testing, including tests for HIV and Hepatitis B and C, and tissue typing (to determine HLA type).

It will also be examined for nucleated cell count, cell viability, blood group antigen (ABO & Rh), molecule cluster (CD34), and bacterial and fungal growth [5].

Banking Umbilical Cord Tissue

Expectant parents can now also collect and preserve stem cells from the tissue of the umbilical cord, whose medical name is Wharton's jelly. Whereas cord blood is a rich source of hematopoietic (HSC) that differentiates to form the lineage of blood cells, cord tissue is a rich source of mesenchymal (MSC). The International Society of Cellular Therapy (ISCT), which has established criteria for defining MSC. Mesenchymal stem cells differentiate to build bone, cartilage and connective tissue [7].

Method to Preserve Cord Blood- Cryopreservation

After the collection, the cord blood unit is shipped to the lab and processed, and then cryopreserved. Some processing methods separate out the red blood cells and remove them, while others keep the red blood cell. A Cryopreservant is added to the cord blood to allow the cells to survive the cryogenic process. After the unit is slowly cooled to -90°C, it can then be added to a liquid nitrogen tank which will keep the cord blood unit frozen at -196°C.

The slow freezing process is important to keep the cells alive during the freezing process. The protocols used for the cryopreservation have largely been adapted from those originally designed for the bone marrow haematopoietic stem/progenitor cells. There is no consensus yet on optimal procedures for these cord blood cells, although many cryopreservation strategies suggest using dimethyl sulfoxide (DMSO), slow or controlled rate cooling, and rapid thawing [5].

Use of Cord Blood in Human Being

Cord blood stem cells are currently used in the treatment of several life-threatening diseases & ACT as Regenerative medicine includes

- Immune system related conditions
- Genetic Diseases
- Cancers
- Type I Diabetes Mellitus

- Myocardial infarction
- Stroke
- Multiple Sclerosis, & Parkinson's disease
- Crohn's Disease.
- Leukaemia & Thalassemia

However, studies have shown that cord blood stem cells can also be used for siblings and other members of your family who have a matching tissue type. Siblings have up to a 75% chance of compatibility, and the cord blood may even be a match for parents (50%) and grandparents [6].

Issues on Cord Blood Banking

Autonomy

The principle of autonomy and informed consent is two basic concepts for contemporary bioethics. Autonomy has been defined as "the quality or state of self-governing". Following as the elements of the process leading to informed consent: (i) threshold elements (preconditions), including *competence* to understand and decide, *voluntariness* in deciding; (ii) information elements, including *disclosure* (of material information), the *recommendation* of a plan and *understanding* of the previous elements; and (iii) consent, including a *decision* in favour of a plan and *authorization* of the chosen plan [7].

The implementation of the abovementioned three steps of the consent process in the context of umbilical cord blood collection, storage and use is problematic.

Informed Consent of Donors

(i) Who has the right to give consent? Usually the mother is required to give consent, but, if we accept that the cord blood belongs to the baby, it is necessary to consider that the mother does not consent for herself, but on behalf the baby. Moreover, she shares parental authority with the father. The involvement of the father in the consent process is highly recommendable.

(ii) What is the object of the consent? It is necessary to clarify the content of the consent. It is important that it includes not only the collection and storage of the blood, but also its possible uses.

(iii) How should consent be obtained? Information is a constitutive part of informed consent. Again, it is not possible to inform the baby (the party directly concerned). The mother should be adequately informed and the consent should be obtained in a convenient form (written, not hurried, etc.).

(iv) Who is qualified to accept consent? Various responses might be possible: the nurse, the medical doctor or the hospital administration.

(v) When should consent be given? Different answers are again possible: on the occasion of a medical examination during the pregnancy, at the moment of hospitalisation, at the moment of childbirth. Since informed consent requires adequate reflection, a request of consent just before childbirth should be avoided.

Based on Above Issue Some Consent Practices are Followed for Cord Blood

Timing of getting consent-Before or within 7 days of delivery, consent should be obtained before the collection procedure.

Surrogate mother-Consent should be obtained from both the surrogate and the biological mother.

Specific elements to be included in the consent-If for an allogeneic transplant, the donor will be made available to other individuals and may not necessarily be available to the donor or donor's family at a later date.

-A review of the medical record of the mother and infant will be performed.

-A description of the cord blood collection procedure should be explained to mother.

-Maintenance of linkage for the purpose of notifying donor/family of infectious or genetic diseases-use of cord blood for research, quality control or validation studies.

-Disposal of cord blood units not meeting criteria for banking.

Beneficence

The ethical obligation to benefit the patient, while exposing him/her to the smallest possible risk, is the basis for the use of haematopoietic stem cells from the blood of the umbilical cord *in specific diseases*. This principle is ignored or not appropriately understood by private banks when, on the one hand, they offer a service based on false promises, such as that of "biological insurance," for which there is no scientific evidence; on the other hand, deceiving donors by assuring them that the tissue will remain in storage and available to be used at any moment of the life of their child [8].

Non Maleficence

The traditional moral obligation of Hippocratic

medicine is *primum non nocere*, to first do no harm. In private banks, as opposed to public banks, it is not known if the criteria for quality control are followed and no harm is done. These banks have no rigorous control over such as: cellular viability, sample volume, method of acquisition, handling and transportation. How then, could the quality of the tissue transplanted be guaranteed when the donor needs to use it [8]?

The main concern of cord blood banking, private or public is the long-term viability of cryogenically frozen cord blood, although studies have shown that the cord blood can be cryogenically frozen indefinitely. Other established treatments may be more suitable for the patient, rather than cord blood transplants, and it may become possible to obtain the needed blood or more generalized stem cells by other means, such as from the bloodstream of an adult or from tissue culture.

Likelihood for Use

Cord blood transplants require less stringent matching between the tissue types of the donor and patient, known as their HLA type's Human leukocyte antigen.

Bone marrow transplants require a complete match on six key antigens, which are measures of graft-versus-host reaction, known as a 6/6 match.

Cord blood transplants achieve the same medical success with only a 4/6 match. HLA type is inherited from both parents, so siblings are particularly likely to be a match, and people from the same ethnic heritage are more likely to match [8].

The Stem Cell Act of 2005 mandated HRSA to fund public cord blood banks to recruit more cord blood donations from ethnic minorities

The odds that two siblings will have the 6/6 match required for a bone marrow transplant are 25%. The odds that two siblings will have the 4/6 match required for a cord blood transplant are 39% [9,10].

Availability of cord blood banking options for patients

There are two types of banking facilities for storing the cord blood cells of your baby:

- public donor banks
- private banks

Reli Cord is the first to have a registered cord blood bank and repository in India as well as the entire region of South East Asia-Reli Cord has already stored over 3,500 cord blood samples at its repository. It conforms to the AABB and USFDA

guidelines and has an infrastructure to collect cord blood from any corner of the country through its collection centres. ReliCord offers public as well as private banking and is the only facility in India that offers stem cell research for current and future applications. The cord blood samples are stored at the Dhirubhai Ambani Life Sciences Centre (DALC) campus in Navi Mumbai [12].

The Tamil Nadu government has recognised cord blood banking in the State, arguably the first State to do so, by agreeing to provide a grant of Rs. 9 crore to a public cord blood bank established by Jeevan Blood Bank and Research Centre. Stem cells will now be available to the poor free of cost, while the cost of transplantation is covered under the Chief Minister's Comprehensive Health Insurance Scheme. At any given time there are several hundred patients admitted to various hospitals in the State with these condition.

Public Donor Banking Criteria

Following points to be asked before going for cord blood banking

1. Is the facility accredited by the standard Association of Blood Banks?
-This means its labs, banks, and procedures meet set standards.
2. How long has the company been in business?
-At least five years is best.
3. How many units does it store?
-Look for a bank that has thousands.
4. How many successful transplants have been performed with its stored samples?
- Having at least one demonstrates that its process works, but two or three is better.
5. Is the blood stored as a single unit or in several samples?
-Freezing in portions is preferred so the blood can be tested for potential transplant use without thawing — and wasting — the entire sample.
6. Is the company private or publicly held?
-If it's a publicly traded company, you'll have the advantage of reviewing its financials. Many banks are part of larger biotech companies.
7. Is the storage fee fixed or subject to increases?
-You want to know the total price tag up front.

Private Cord Blood Banking Criteria

If choosing a private cord blood bank, here are

some questions need to be asked before deciding on a bank [12]:

- Can you afford the collection fee and yearly storage fee for a private bank?
- Is the bank well-reputed and certified?
- What quality standards is the bank following? Private Banks may not have to adhere to the same quality standards as public banks.
- Does it have the necessary technological expertise and experience?
- Does it offer banking and stem cell therapy options? If the stem cell banking company does not provide therapy options, then the purpose of banking is defeated. If they do not invest in trials or do not take definite steps towards stem cell therapy, they are probably not providing enough for the price they charge their clients.
- Does the bank have a good network, accessibility and tie ups with hospitals? This is important to ensure that they will be able to deliver your child's stored cord blood cells soon enough when the need arises.
- Where is its storage facility situated? Ideally, you should choose a bank with its storage facility situated at a location less prone to natural disasters like floods or earthquakes.
- Does the storage facility have power back up or generators, and monitoring systems in place that ensure a controlled environment all the time?

Current Issues and Benefits for Public

Ex Vivo Expansion

Much research is focused on trying to increase the number of HSCs that can be obtained from one cord blood sample by growing and multiplying the cells in the laboratory. This is known as "ex vivo expansion". Several preliminary clinical trials using this technique are underway. The results so far are mixed: some results suggest that ex vivo expansion reduces the time taken for new blood cells to appear in the body after transplantation; however, adult patients still appear to need blood from two umbilical cords. More research is under process to understand real benefit for patients.

Some Current Issues and Benefits for Public are Discussed Below.

It could be Life-Saving

Umbilical cord blood has stem cells which used to

treat more than 80 life threatening diseases like cancer, blood disorders, immune system disorders, Multiple sclerosis, autism, spinal cord injuries, diabetes, and cerebral palsy and genetic diseases.

But...your Baby may Never Need It

The baby whom stem cell was stored may not be used immediately or directly but it could be multiplied & used by others who are in need but. By age 70, the chances are higher—about one in 200 – but this is because cancer rates increase with age.

it's not a Sure-Fire Thing

Banking your baby's cord blood isn't a total insurance policy, If your baby has leukemia, for example, using his or her own stem cells might not be the best option because "you're putting in the same immune system that permitted the leukaemia to develop in the first place," best match would be a transplant from a sibling or from an unrelated donor.

There are Other Options

Private banking is a good idea if one of your children has a disease that could be treated by a sibling's stem cells, but otherwise, experts recommend donating to public banks.

Banking is Expensive

Most banks have an initial investment of approximately Rs 50,000 to Rs 94,000, which covers collection, processing and storage for the first year, in addition to annual storage fees or monthly storage fees ranging from Rs 5000-8000 per month.

It might not be Enough

A new technology called Stem. Ex, which is currently being studied in an international clinical trial, would allow cord blood cells to be multiplied so older children and adults could be treated.

Your Doctor could be Cashing in

According to a survey conducted by the American Academy of Paediatrics, only 18 percent of paediatricians feel confident discussing the topic with their patients, while some of them are being compensated to do so.

The Future Challenges

Experts believe that umbilical cord blood is an

important source of blood stem cells and expect that its full potential for treatment of blood disorders is yet to be revealed. Other types of stem cell such as induced pluripotent stem cells may prove to be better suited to treating non-blood-related diseases, but this question can only be answered by further research [13].

Conclusion

Cord blood is the blood that remains in the newborn baby's umbilical cord after it is cut. Doctors have identified that cord blood, like bone marrow, is a rich source of stem cells, which can be used in medical treatment.

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