



The Prominence of Remarkable Advancements in Regenerative therapy by Engaging “Golden cells” of Human Umbilical cord: General Cognizance & Expectations



G Sri Ramya Jyothi*, D Swathi, S Rajini Reddy, and M Prasada Rao

Department of Pharmacy Practice, M A M College, India

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***Corresponding author:** G Sri Ramya Jyothi, M.A.M College of pharmacy, Kesanupalli, Guntur district, Andhra Pradesh, India

Abstract

The stem cells of the Umbilical cord can be considered as “Golden cells” as they are a ray of hope. These are unique from other over 200 types of mature cells with a distinct and specialized function, like the heart muscle that beats rhythmically or RBC's that deliver oxygen to every part of the body. The Human Umbilical cord stem cells are authentic because of their self-renewal and differentiation property. In the majority of Hospitals, the umbilical cord is discarded as a biomedical waste at the time of the birth of an infant due to a lack of awareness regarding its importance. Human Umbilical cord blood can be banked in two ways: Private banking and Public Banking. Cord banks treasure all the nucleated cells from the blood for their therapeutic use. Every parent should have awareness of minimum information regarding the benefits of Umbilical cord blood constituents and their need for research to further develop its potential. The OB/GYN, Pediatricians, and any other health care professional should step forward and should take up the responsibility as a primary task to extend/ educate about cord blood donations and their prominence along with pre-natal/post-natal care. Curing the incurable, with the low impact of non-invasive therapies to create a better quality of life for patients of all ages, in providing hope. Stem cell research raises fundamentally difficult questions about the definition of human life, and it has raised deep fears about the ability to balance issues of justice and safety with the needs of critically ill patients.

Keywords: Regenerative medicine; Human Umbilical Cord; Stem cells

Introduction

Stem cells are a ray of hope. Nature has blessed each individual with stem cells that have the tremendous ability to develop into different cells, tissues, and organs. These precious cells are unique from other over 200 types of mature cells with a distinct and specialized function, like the heart muscle that beats rhythmically or RBC's that deliver oxygen to every part of the body. Especially, the Human Umbilical cord stem cells were unique because of their self-renewal and differentiation properties [1]. Owing to that, stem cells are imperative to the regeneration and healing process and thus, the important and powerful broad range of medical therapies. Stem cells can be sorted based on their origin and type of working cells they are, which can create and produce [2,3]. Haematopoietic Stem Cells (HSC) & Mesenchymal Stem Cells (MSC), which are part of the tissue-building mechanism and were also the most commonly researched adult stem cells,

that can be found in their best shape in umbilical cord tissue and cord blood have the immense and most effective ability to regenerate into different cells, tissues, cartilage, muscles, bones, etc from the precursor cells. The mesenchymal stem cells found in the cord tissue are promising in the field of cell therapy and tissue regeneration. Umbilical cord blood stem/progenitor cells are widely and easily available, and they appear to be associated with less graft-versus-host disease than other cell types, such as marrow stem cells. They have less Human Leukocyte Antigen (HLA) restriction than adult marrow stem cells and are less likely to be contaminated with herpes virus [4]. However, it is unclear how many different cell types can be generated from umbilical cord blood stem cells, and methods for differentiating these cells into non-hematopoietic phenotypes are largely lacking. The human umbilical cord measures 50-55 cm in length and

1-2 cm in breadth, although a wide range of normal lengths is recognized accordingly. The cord should be measured only if it is at one or the other extremes of length. The overall length of the umbilical cord will be decided by the fetal activity in the uterus. The cord will be longer for the more active fetuses and shorter in association with less activity.

The umbilical cord possesses two umbilical arteries and one umbilical vein. Umbilical cord stem cell growth factors, help in healing the damaged communication system in degenerative joints reset and restart. Meanwhile, in the process, healing will be initiated that helps the cells to start recovering again. Next to hematopoietic stem cells (those found in umbilical cord blood), the most widely studied stem cells in the bone marrow are marrow-derived mesenchymal stem cells, also known as marrow stromal cells. In the adult, mesenchymal stem cells are found in a higher concentration of the marrow cavity. Mesenchymal stem cell-like cells can be isolated from umbilical cord blood, placenta, per vascular areas, amniotic fluid, and the tissue surrounding the umbilical cord vessels, i.e., Wharton’s jelly [5]. In the majority of Hospitals, the umbilical cord is discarded as a biomedical waste at the time of the birth of an infant due to a lack of awareness regarding its importance. Usually, in many urbanized states and hospitals, Human umbilical cord tissue and cord blood samples are collected within the 10 minutes of birth and stored in private cord blood banks if their patients can afford to store. The collection is easy and completely harmless as well as painless to both mother and newborn in comparison with the collection of Mesenchymal stem cells from a bone marrow aspirate.

Some of the unique abilities of cord components are:

- i. Home in on-site injury & assist in the repair when injected Intravenously
- ii. Stem cells can be reconstructed into various kinds of body constituents like a group of cells/tissues/bones/cartilage etc.
- iii. Exhibit Anti-inflammatory and immune suppressant characteristics, an important application in inflammatory stages

of numerous diseases.

- iv. Stem cell treatment in recovering from brain cancer
- v. Cerebral palsy treatment with one’s cord blood stem cells
- vi. Blackfan-Diamond Anemia can be treated with cord blood stem cells from siblings.
- vii. Umbilical cord blood is an accepted source of stem cells that have already been used to treat essentially all malignant and non-malignant diseases that can be treated by bone marrow (BM) transplantation [6].
- viii. Stem cells are currently used to treat life-threatening diseases like cancers, solid tumors, inherited disorders affecting the immune system & other organs and inherited metabolic diseases.
- ix. Stem cells are providing to be a promising therapy for a wide range of paediatric disorders from neonatal hypoxic-ischemic encephalopathy to paediatric leukaemia [7].

Cord blood banking

Human Umbilical cord blood can be banked in two ways:

a. Private cord bank: The umbilical cord is stored at a certain cost which can be sometimes a bit expensive. And, the components of it can be used only by the child or his/her parents and by their siblings when the need arises, the sample remains the property of the child in the trust of the parents. They are committed to storing the cells absolutely safe and the complete processing, testing, freezing, storage and release for therapy, is highly monitored and controlled. It uses special state-of-the-art techniques to ensure full traceability from the client to the laboratory and storage facilities. The quality management and processes are structured according to ISO, AABB, NABL and WHO-GMP accreditations [8].

b. Public cord bank: These are quite like blood banks in which any pregnant lady can enroll to donate umbilical cord, after her delivery at free of cost. But if anyone in need of those components can access to it at a certain cost [9] Table 1.

Table 1: Cord banks treasure all the nucleated cells from the blood for their therapeutic use.

Type of bank	Private bank	Public banks
Cost	Approximately Rs.85,000/- to 1,50,000	Free of cost
Cord blood owner	Donor and family	Bank itself
Who uses blood?	Donor and family	Unrelated transplant patients or scientists
How the blood is used	Related transplants or for cell therapy	Unrelated transplants, For research, Discards
Income to bank	By parents	Approximate cost per transplant is paid via insurance or sold for research.

Cord banks treasure all the nucleated cells from the blood for their therapeutic use. These include the WBC's required for hematopoietic stem cell transplant and also the highly immature stem cells with potential application for the treatment of non-hematopoietic diseases. The pioneers of cord tissue preservation ensure to preserve Epithelial, stromal /mesenchymal, smooth muscle and endothelial cells from all the parts of the cord [10]. These can treat bone and cartilage related diseases, heart, and vascular system-related diseases, cancers, neurological diseases and injury, autoimmune diseases, liver diseases, etc [11,12]. Jeevan was the only public cord blood bank in India that has public cord blood units listed on the WMDA international registry. Due to the scarcity of funds, it has to be temporarily stopped accepting cord blood unit donations. To date, India does not have any public cord blood units listed on the WMDA international registry.

Common types of questions arisen by the public are

- i. What are the benefits of banking in, cord constituents?
- ii. What is cord blood bank accreditations, quality, professional expertise, transparency approach necessary to be known?
- iii. Does the concerned schedule need to be known to register for cord blood donation?
- iv. What is the proprietary system that is completely automated in delivering the best possible results consistently with no contamination?
- v. What is cord blood insurance?

Major Challenges in Umbilical Cord Blood Banking

- i. Regulatory issues, such as licensure, have increased the cost to bank UCB units.
- ii. Less than 1 in 10 stored UCB units are used for transplantation, also increasing the costs 5 times more.
- iii. When the obstetrician procrastinates in cord clamping, it may alter the proportions, volume and cell contents to be collected.
- iv. But from some of the sources, the public can be misinformed by the cord banks for their commercial purposes, regarding unrealistic future needs, to be "birth tissue profiteers". Experts would not recommend this kind of banking for unproven therapies [13].

Ethical Aspects of Umbilical Cord Blood Banking

- i. Every parent should have awareness of minimum information regarding the benefits of Umbilical cord blood constituents and their need for research to further develop its potential.
- ii. A wide range of surgeons and obstetricians usually care for pregnant women regarding, care for the mother and baby, but

provide limited or no information on UCB collection, their utility and future trends of stem cell therapy [14,15].

Banking the stem cells of the newborn is equally important as opening a savings account to ensure the financial & educational future of the child as it helps in ensuring the medical future of the child. It is a boon and the best gift we can give our children-the miracle of good health.

- i. Sign-up for the services by deciding earlier with relevant details and knowledge
- ii. The sample will be transported to the processing facility by a certified courier service.
- iii. They examine, process and cryo-preserve the stem cells in an accredited facility.
- iv. The bank must issue a certificate of storage to the holder with a unique number corresponding to the baby's stem cells.

What is cord blood bank accreditation?

Accreditations are quality standards. Cord blood laboratories that are located in certain countries are required by federal law to follow high standards which include:

- i. Good manufacturing practices (GMP) in Germany,
- ii. Health assessment technology (HTA) in the UK,
- iii. Swiss medic in Switzerland is the surveillance authority for quality standards of medicines and the handling of devices.
- iv. Therapeutic Goods Administration (TGA) in Australia.
- v. Public cord blood banks should be under license of FDA, but private cord blood banks should necessarily register with the FDA in the USA.

But FDA warns about stem cell therapy centres that make false claims in treating serious health conditions like Alzheimer's, through advertising commercials, as the FDA has not approved such kind of practices. None are proven to work to treat these conditions, some may cause harm. The FDA has only approved for treating certain blood disorders. And had cautioned to beware of unapproved stem cell therapies have led to serious infections, blindness, and death. If you are considering stem cell therapy, ask questions and don't become a victim of dishonest and dangerous stem cell clinics. Three major voluntary accreditation systems have been developed specifically for cord blood banking and are based on inspections of the laboratory procedures were:

AABB: an international accreditation for blood banking and transfusion services

- i. FACT: an international accreditation for cellular therapies devoted to educating in regenerative medicine.
- ii. International Organization for Standardization (ISO): an accreditation on certain aspects of their operations like quality

management systems, medical devices, and laboratories, testing, and calibration of laboratories.

iii. In our 2015 Cord Blood Industry Report, it was found that accredited cord blood banks are NOT more expensive on average than banks with no accreditation [16].

Stem cell Transplantation

The main goal of stem cell therapies is to promote cell replacement in organs that are damaged beyond their ability for self-repair. One of the most difficult tasks in transplantation is finding a compatible donor. Stem cells from a relative (preferably a sibling) are generally the first option for a transplant when considering the source of stem cells. A large part of allogeneic transplants uses stem cells from a family member. There are 2 options to transplant stem cells:

i. Allogeneic transplantation: when the recipient gets transplants delivered from a donor by some other individuals who might or might not be compatible with it. To avoid graft rejections by the body the recipient must be tested for compatibility before the transplantation and according to the needs, additional assessments should be performed. Even then, in the majority of cases 100% compatibility is not guaranteed.

ii. Autologous transplant: when patients receive cells from their bodies. This kind of transplant is 100% compatible with the owner and, depending on the disease, can be the preferred option for the patients.

To steer clear of alterations in the efficacy, contradictory effects and dreadful circumstances of transplanting stem cells in recipient, it is necessary to evaluate the stem cell's set of proteins which gets secreted into extracellular spaces to recognize and amplify the crucial paracrine signals secreted by those stem cells that could lead the way to provide neuro-armed effects to stem cell transplantation [7]. Human umbilical cord blood from kin or akin donors, compatible or un-compatible with either one or more antigens, is now broadly considered as another donor source to get matched marrow or circumferential blood for allogeneic transplantation in both elders and children in a wide range of disorders like cancerous or non-cancerous comorbidities. The utility of cord blood compellingly increases accessibility to transplantation therapy for patients lacking matched, related or unrelated adult donors. Dr. Kurtzberg said, "In the future, umbilical cord blood may emerge as a source for cellular therapies focused on tissue repair and regeneration [17]." It reinforces the observations of the earlier studies. The cord cell material is not considered dangerous to the patient receiving the injection in any way, even if the patient is in no way of co-relation with the donor. Fluids and cells from the cord blood matrix, placenta, and amniotic fluid are immunologically privileged as they meant to cause no reaction even between completely unrelated donors and recipients.

Objectives to be followed

Health care professionals and the resourced persons who have the proficiency in cord blood banking must propagate to the would-be parents as it is a foremost step that needs to be taken. Any Informed or written consent, indications and claims related to medical benefits, type of transplants, legal authority works, quality affirmation, relative expenditure, commercialization and obtaining patent, safeguarding the personal profiles, and have to maintain liaison relationships among banks, doctors, recipients, and donor's to make this work out successfully. According to Good Manufacturing Practices (GMP), for the clinical applications of cord cells in regenerative medicine are having more expectations in future aspects like one of them might include assessing/evaluate the cell product activity with the help of serum-free media with a spread of reagents. The ex-vivo culture can lead the route to an accurate pre-clinical evaluation [18]. The composition of UCB is a copious source of stem cells, which has been discarded as medical waste for centuries. Their cells are authentic and can fight with many catastrophic consequences of pathological conditions in the future as they are naïve and have much lesser chances of graft rejections by the host and can make huge progress in producing an attenuated donor-derived immune response. The OB/GYN, Paediatricians, and any other health care professional should step forward and should take up the responsibility as a primary task to extend/ educate about cord blood donations and their prominence along with pre-natal/post-natal care [19,20]. An epidemiological study from India had surveyed a certain number of the general public and a set of doctors. The study was found that 58% of the doctors and 82% of the people were either unaware or misinformed about the indications of UCB transplants. The study concluded that the obstetricians and therefore the paediatricians should take a pivotal role in furnishing the precise information to would-be parents to assist them in taking a good decision [21,22].

A Word of honor by Regenerative Medicine

Imagine a world where incurable diseases can be cured, without surgical transplants or donor organs. We are the victims of devastating diseases. Regenerative medicine accelerates this natural healing process by harnessing advances in biology, immunology, pharmacology, and other sciences to restore health and function to damaged tissues and organs. Regenerative medicine is truly a GAME CHANGER, if we can take a patient or genetically related person's cells and get them working on the patient's problem, we can have a tremendous amount of impact on the care of medicine. This is something we need now as we see as this is the end of a line for a lot of patients, and this is easily translatable to the bedside. Recognizing the vast potential of this emerging field many pharmaceutical companies have established the center for regenerative medicine. The center catalyzes advancing the practice of regenerative therapies across the medical and surgical specialties educating the next generation addressing patients' unmet needs with next-generation solutions.

Many patients are already benefitting from proven regenerative therapies, for example, physicians use patients' materials from the body to assist in a healing process. Osteonecrosis is essentially the death of bone material. Sometimes it might be caused by the use of chemotherapy in cancer patients. Regenerative therapy can help treat this condition.

Curing the incurable, with low impact of non-invasive therapies to create a better quality of life for patients of all ages, in providing hope. The idea of regenerative medicine in stem cell biology understands which kind of stem cell we can transplant into which part of the body to help regenerate and help the body from within by growing into tissues and organs later. The health professionals must be able to acknowledge and educate the people what the hope and what the hype is of stem cells in the regenerative medicine of today. Numerous Pharmaceutical companies use the human placenta as a source of hormones, drugs, and blood; portions of placentas are also used for burn coverage. Umbilical cord MSCs from donated, live, healthy birth are usually called as an "injury drug store" as their job is to maintain status equilibrium in the body so that if something is disrupted in the status quo then they are the first line of defense to rectify it through secreting certain trophic factors as Anti-apoptotic as it prevents programmed cell death, well, in that case, the MSCs will donate their mitochondria to the injured cell as an energy source. Habitually, autism spectrum disorder can be treated by social

skills training, early intensive behavior therapy, applied behavior analysis, speech therapy, occupational therapy, psychotropic drugs, alternative treatments, and supplements. Most of the children are prone to autism spectrum disorder and parents opt for the above-mentioned ways to treat the symptoms. But they must be aware to consider Stem Cell Therapy- Anti-inflammatory, paracrine, immunomodulatory effect as also access to treat [23]. Stem cell therapy is based upon three criteria that MSCs can release anti-inflammatory drugs over an extended amount of time and they also have a paracrine effect. MSCs are a viable treatment option for autism, many studies are going on globally. Stem cell clinics assign patients before they come to the ASD protocol and any of the four variants depending on their weight, height, age particulars the dosages for the patient is selected. They derive MSCs from the human umbilical cord of healthy pregnancies. ASD protocol includes:

1st day- Evaluation + Blood work

2nd to 5th day: Physical signs examination, pre-conditioning of patient and vitals check is important before and after initiating the Treatment (40/60/100 Million HUC – MSC total IV infusion syringe push).

5th day: Discharge the patient with information on the number of cells they received.



Figure 1: Umbilical Cord in Regenerative Medicine.

Follow up (ATEC) at 3-month intervals is very important because it tells us how the patients or a recipient is doing. And also it is crucial to check-up the patient to find out any relevant medical conditions associated with treatment as they may lead to adverse events like psychomotor hyperactivity, restlessness,

warm skin, fatigue, and anxiety. These adverse events may last for a short duration and are mild in intensity. Or anything they need to disclose to their doctor, which can improve their state of health [24]. They are anti-scarring and also they can be Angiogenic as they induce new blood vessels to grow and mitotic. They also

can modulate the immune system that WBCs particularly that of overactive. These cells can be given intravenously and then the cells are collected there at the target site. These cells can modulate the immune system and increase the number of T-regulatory cells and block the clonal expansion of activated T cells. But the MSCs from parents don't work properly. According to the indices of age including oxidative damage, ROS levels, and p21 and p35 all increased suggesting a loss of MSC fitness with age. There is an age-related decline in overall Bone marrow MSCs "fitness" which might lead to problems when using autologous aged MSC for cell-based therapies. Hence, it is better to opt for the collection of MSCs from the cord at the neonatal stage itself helps to restore a wide range of MSCs. Compared with stem cells of adult bone marrow harvests, the UCB stem cells have greater proliferative and regenerative potential Figure 1.

Major Challenges in the utilization of Cord Blood Transplantation in Regenerative Medicine

- i. Regulatory hurdles for large-scale use of these products.
- ii. The use of autologous UCB units from private banks for regenerative medicine indications may affect UCB public banking [23].

Discussion

Stem cell therapies raise ethical and socially contentious issues that must be addressed in parallel with scientific and medical opportunities. This society has great diversity concerning religious beliefs, concepts of individual rights, tolerance for uncertainty and risk, and boundaries for scientific interventions should be used to alter the outcome of diseases. Ultimately there will be medical interventions that are scientifically feasible but ethically or socially unacceptable to some members of society. Stem cell research raises fundamentally difficult questions about the definition of human life, and it has raised deep fears about the ability to balance issues of justice and safety with the needs of critically ill patients. Health care providers and experts with backgrounds in ethics, law, and sociology, must help guard against the premature or inappropriate use of vulnerable population groups. Open dialogue among the scientific community, physicians, patients, and their advocates, lawmakers, and address important ethical issues and balance the benefits and risks associated with stem cell transfer.

Conclusion

I presume that, saving and storing cord blood is the new way to go for a long and safe future for the near and dear ones. Recent developments in stem cell therapies are a source of hope to several individuals suffering from currently incurable diseases. Cord blood banking may necessarily become the ticket to survival for some in the future. Cord blood stem cell collection

is one of the most important break-through in recent medical and pharmaceutical history. Progress of science is such that in a few years many diseases can be treated with stem cell therapy. Stem cell therapies are going to be the pillar of 21st-century medicine. Health care professionals should recommend availing the opportunity of cord blood banking and save these precious cells for life.

Limitations

These stem cell-based therapies are still at a very early stage of development, and the perfection of techniques for clinical transplantation of predictable, well-characterized cells is going to be a difficult and lengthy undertaking. In terms of disadvantages, cell dosage and the possibility of delayed engraftment represent the main challenges to be fully resolved for the widespread use of UCB [16].

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