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The Importance of Cord Blood and Cord Tissue Stem Cells: Today vs Tomorrow

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Introduction

Once considered medical waste, umbilical cord blood and cord tissue are now recognized as important and rich sources of hematopoietic and mesenchymal stem cells. Hematopoietic stem cells play an important role in cellular therapy, while mesenchymal stem cells have the potential to be used in the treatment of a broad range of clinical conditions including immunologic conditions, cardiovascular disease, and neurologic injuries.

Providing expectant parents with information about the current and potential applications of newborn stem cells and options for collection and banking is an important part of patient education in early pregnancy. Parents have only one window of opportunity to arrange for the preservation of newborn stem cells and many expectant parents remain under-informed about their options. This article reviews the current uses in transplant medicine and the potential future applications in regenerative medicine. We also emphasize key education points for providers to use when discussing newborn stem cell preservation decisions with families that can have implications for both individual and public health.

DISCLOSURES: Dr. Weinthal reports that he is on the speakers' bureau and advisory board, and a consultant, for CBR®, Cord Blood Registry®.

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Background

The first allogeneic hematopoietic stem cell transplantation (HSCT) utilizing umbilical cord blood (UCB) was performed in 1988 in a pediatric patient with Fanconi anemia who received a human leukocyte antigen (HLA)-identical cord blood unit from a sibling.[1] This initial milestone in transplant medicine was followed by the introduction of unrelated cord blood transplantation in both children and adults.[2-4]

For over 25 years, UCB has been documented to be a suitable alternative source of hematopoietic stem cells to bone marrow and mobilized peripheral blood for use in transplant medicine. UCB stem cells have multiple advantages over stem cells obtained from adult tissues. Cord blood collection is simple and noninvasive as it is performed at the time of birth after the cord has been clamped and cut. As compared to other sources of stem cells, cells from cord blood are less likely to have been exposed to viruses or to have suffered environmental or age-related degradation.[5,6] UCB stem cells also require less stringent HLA matching when used in allogeneic transplantation as compared to other stem cells sources, such as bone marrow. To this end UCB transplants are

associated with a lower incidence of graft-versus-host-disease (GvHD), a significant cause of transplant-related morbidity and mortality.[5,6] Since UCB is cryopreserved after collection and processing, these stored units can be made immediately available if needed for use in treatment, rather than the long delays often encountered when trying to identify a suitable donor from a registry.[2,3]

As a result of these advantages, clinical use of cord blood has greatly increased in the past decade, and the infrastructure needed to store the cryopreserved units, and connect patients to available HLA-matched units, also has grown. In the United States, private banks that preserve UCB for family use and public banks that store units from volunteer donors for use in unrelated recipients began to emerge in the early 1990s. Today, worldwide, there are more than 5 million cord blood units stored in more than 130 private cord blood banks, and more than 800,000 units in over 100 public banks.[7,8] To date, more than 35,000 stem cell transplants using UCB have been performed worldwide.[5]

Applications of Cord Blood Stem Cells

In the United States, the lifetime odds of an individual requiring an autologous or allogeneic stem cell transplant using hematopoietic stem cells from any source are estimated to be 1 in 217.[9] Autologous and allogeneic HSCT are used clinically to treat pediatric and adult hematologic cancers, and nonmalignant hematologic, immune, and certain metabolic disorders. To date, HSCT with cord blood has been used in the treatment of over 80 diseases.

Ongoing Research with Cord Blood

In addition to the use of UCB in traditional transplant medicine, ongoing research suggests that cord blood may play an important role in the future of cellular and regenerative therapy. This rapidly advancing field focuses on developing treatments that augment the body's healing and repair mechanisms in tissues damaged by disease or illness. Clinical trials are currently examining the use of UCB as a potential treatment for conditions such as autism, cerebral palsy, and acquired hearing loss.

Autologous Stem Cell Transplantation in Autism Spectrum Disorder

UCB is currently being evaluated as a potential treatment for autism spectrum disorder (ASD), a developmental disorder characterized by various degrees of deficits in communication, behavior, and social interactions.[10] ASD has no medical treatment or cure and is reported to affect 1 in 68 children in the United States, with annual total costs ranging from $11.5 to $60.9 billion.[11] The pathophysiology of ASD is unknown, but multiple underlying features have been identified including altered neural connectivity and inflammation.[12] Potential immune system involvement in ASD has led some researchers to hypothesize that immune effector cells found in UCB may have a potential therapeutic benefit as these cells appear to modulate the immune system and decrease neuro-inflammation via paracrine signaling.[12]

An open-label phase I trial was conducted at Duke University in Durham, North Carolina, to assess the safety and feasibility of a single intravenous infusion of UCB in children diagnosed with ASD whose cord blood had been banked.[12] A total of 25 children participated in the study, 21 patients were male, median patient age was 4.62 years (range, 2.26–5.97), and 72% were considered to have moderately severe or severe ASD symptoms.[12] Patients were evaluated at baseline, and 6 and 12 months after the infusion. The evaluation included a battery of behavioral and other clinical tests. The study results showed that the UCB infusion was safe and feasible in the study population.[12]

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While not designed to evaluate efficacy, there was reported improvement in some symptoms of ASD in a subset of study participants. Specifically, statistically improved outcomes in both clinician- and parent-reported measures of communication and behavior were observed in some patients. Verbal ability improved in 68% of patients, and these changes were not found to be correlated with age.[12] Presently, investigators advise caution when interpreting these results, noting that the uncontrolled, open-label trial design make it impossible to discern changes potentially brought about by the UCB versus changes that occurred as a natural part of aging or through other therapy.[12] A phase II, double-blind study evaluating the efficacy of autologous and matched, unrelated cord blood infusions is now underway at Duke University.[13]

The Sutter Neuroscience Institute in Sacramento, California, launched in 2012 a placebo-controlled trial evaluating the effects of a single infusion of cord blood stem cells on language skills and behavior in children with ASD. Investigators enrolled 29 children between 2 and 7 years of age who, in a blinded fashion, each received a cord blood infusion or a placebo infusion during a 13-month period. The study hypothesized that cord blood stem cells may repair damage to the nervous system caused by immune system dysfunction in some children with ASD. Results are now pending publication.[14]

Ongoing Research with Cord Tissue

Umbilical cord tissue is a rich source of mesenchymal stem cells (MSCs) and also contains endothelial and epithelial progenitor cells, all of which may have clinical utility in future regenerative applications. While clinical applications have yet to garner US Food and Drug Administration approval, there are more than 400 active clinical trials utilizing this cell type from a multitude of different tissue sources listed on the NIH Clinical Trials registry (https://www.clinicaltrials.gov). The treatment implications for MSCs from a variety of tissues are vast, and areas of research being explored include: osteogenic diseases and injuries, autoimmune and inflammatory conditions, gastrointestinal disease, cancer, diabetes, transplant complications such as chronic GvHD, neurologic disease and injuries, and repair of damaged cardiac tissue.[15] The epithelial and endothelial cells found in umbilical cord tissue are being investigated as possible treatments for wounds, burns, ulcers, ocular surface disease, and vascular damage.

Patient Education and Counseling

Educating families about their cord blood banking and tissue preservation options is important so that an informed decision can be made in a non-emergent fashion. Despite advances in newborn stem cell research, most expectant parents remain poorly informed about the science and applications of cord blood. In 2005, the Institute of Medicine (IOM) issued a comprehensive report to Congress on cord blood banking. The report contains clear recommendations that health care professionals should provide all expectant parents with fair and balanced education on cord blood preservation prior to labor and delivery, thereby enabling families to make an informed decision regarding their options: preserve the stem cells for future family use, donate the cells for public use or research, or dispose of the cord blood.[16]

When and Who to Educate

It is recommended that newborn stem cell education be introduced to all expectant parents as early as the 2nd trimester as a means of ensuring the opportunity to consider, research, and discuss all available options. Parents should optimally make a decision well in advance of the delivery date. Given that expectant parents, particularly first-time parents, are often anxious and excited during this time, it is important to provide families with written information that can be reviewed at home and discussed again during follow-up visits. Additional education may be appropriate for families with a history of malignant and nonmalignant hematologic diseases treatable with stem cell transplantation since these families may have the greatest future need for banked cord blood. Likewise, families of racial and ethnic minorities, or families with certain special circumstances also might benefit from additional education, as donors for these families can be more difficult to find in existing registries.[17] Therefore, the best approach is to provide informed education, so that expecting families may decide what is best for their family.

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Banking Options

Expectant parents also require education on the differences between discarding umbilical cord blood and tissue and preserving samples in either public or family banks. Education on the public health benefits of cord blood donation and banking need to be addressed. From a public health perspective, donation is overwhelmingly preferable to discarding cord blood even if public banks are not widely available. Specifically, it is important that patients understand that once a sample is donated they no longer retain access to that sample, and it is unlikely to be available to the family should the need arise. Families also should be informed that public banks store roughly 25% of donations, and their child's cord blood ultimately may be discarded.[7] Conversely, family banks store cord blood and tissue that meet preservations standards, and these samples remain available for individual and family use. For patient's in need of a stem cell transplant, a treating physician often will look first within the family as relatives have the best chance of being a suitable match. This may be especially true for families of minorities or mixed ethnicities where a donor match is more difficult to find in the public banks.

Science and Education

The educational content and materials presented to families should include the science and process of blood and tissue collection. The differences among cell types (eg, pluripotent, multipotent, and differentiated), as well as the advantages of stem cells collected from newborn stem cells versus units collected from other sources (eg, bone marrow and peripheral blood) also should be described in as nontechnical a fashion as possible.

Patients should be educated on the current indications as well as the potential breadth of new clinical applications that may utilize newborn stem cells, as well as the current and future uses of both autologous and allogeneic transplants. This discussion may include information on HLA matching, differences between related and unrelated donors, and the more favorable outcomes reported with matched family members.

Ongoing research in transplantation and regenerative medicine should be discussed, noting that although there are currently no established treatments using cord tissue, there is an enormous amount of research and potential being explored in the field of regenerative medicine.

Expectant parents also likely will have questions about collection procedures. This is a useful moment to reiterate to patients that this stage of delivery is the one and only opportunity to collect cord blood and tissue. The process of collection should be described in detail, emphasizing that the cord blood and tissue are collected only after the baby is delivered and the umbilical cord is cut, posing no risk to the infant or mother. They should be informed that sometimes circumstances can arise in which the cord blood collection must be abandoned, such as during fetal distress or maternal hemorrhage or other emergency situations.

Questions about delayed cord clamping (DCC) likely will arise during this discussion, and parents should be advised that DCC does not prevent cord blood and tissue collection, although it may result in a sample with a lower volume of cord blood.

Selecting Banks and Costs

If a family decides to store cord blood privately, they must also research and select a cord blood banking company. Key qualities parents should look for are a company's financial stability and longevity, experience and reputation in the field, investment and participation in cord blood and tissue research, availability of genetic counselors and physicians to answer questions, and experience in facilitating transplants. Other important resources include the availability of financial planning and assistance for families. The cost of one-time, initial courier and processing at a family bank is approximately $1500, and $150 per year for storage.[7,18]

Conclusion

Cord blood is a state-of-the-art source of stem cells for the clinical care of patients with life-threatening diseases in transplant medicine. Cord blood and tissue hold promise for the future of cellular therapy in regenerative medicine with many potential applications for conditions that have no current cure. Providing expectant parents with balanced and comprehensive education about current and potential future applications will help them make decisions regarding cord blood banking for the future health of their family, as well as the public's future health care needs. ■

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