The Collection And Banking Of Umbilical Cord Blood At A Military Treatment Facility

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Abstract

Objective. This study reports results of the first 22 months of partnership between Womack Army Medical Center (WAMC) and the Carolinas Cord Blood Bank (CCBB) at Duke Medical Center, Durham, North Carolina in cord blood donations for public banking. Methods. In 2009, WAMC formalized an agreement with the CCBB to become the first military hospital to serve as a cord blood collection site for public cord blood banking in the United States. Interested pregnant mothers were identified, screened, educated and consented for cord blood donation. Collected cord blood was transported to the CCBB laboratory, processed, tested, cryopreserved and listed on the National Marrow Donor Program's Be the Match donor registry. Results. From 3 July 2009 to 31 December 2012, 2204 maternal donors were consented and 1502 cord blood units were collected. Of these, 463 were processed, cryopreserved and banked. The median volume of units collected was 67.0 ml. The median cell count of units banked was 1.4x10e9 total nucleated cells. Unavailability of collection staff and small collection volume/cell counts were the primary reasons for failure to collect units from consented mothers or store collected units. Eligible units were banked and of these 50.5% were from non-white donors. Fifteen banked units have been released for transplant. Conclusion. WAMC has a large population of racially and ethnically diverse donors and have made a significant contribution to the CW Bill Young Cell Transplantation Program's National Cord Blood Inventory. This program can serve as a model for cord blood collection at other military treatment facilities.

INTRODUCTION

Umbilical cord blood is rich in hematopoietic stem and progenitor cells, but has long been considered medical waste and is routinely discarded after delivery. In 1988, Gluckman, Boxmeyer, Auerback, et al. performed the world's first successful umbilical cord blood (UCB) transplantation in a 6-year-old child with Fanconi anemia from North Carolina with cryopreserved UCB from an HLA-matched related donor. (1) In subsequent years several groups reported successful UCB transplantation with human leukocyte antigen (HLA) matched and unmatched donors to patients with hematopoietic conditions. Realizing the importance of this new therapy, the New York Blood Center established the first UCB public banking program in 1991 with support from the National Institutes of Health. (2) By 2012, approximately 800,000 units of UCB have been banked worldwide and more than 30,000 UCB transplants have been performed from unrelated donors for the treatment of patients with malignant and non-malignant conditions. (3) There are several advantages of umbilical cord blood as compared to adult bone marrow as a source of human stem cells for transplantation. First, the collection of cord blood is easy, safe and non-invasive for the donor. Second, cord blood units are stored in advance and therefore rapidly available, while bone marrow must be collected just before transplantation. Finally, HLA type does not need to be a perfect match in cases of allogeneic cord blood cell transplantation because the cells are less likely to induce an immunological reaction called graft versus host disease that is more common after transplantation of bone marrow cells. Due in part to the immaturity of the cells, UCB has a reduced graft-versus-host reactivity compared to adult-derived marrow grafts. (4)

Collection sites for cord blood donation have been established by public cord blood banks in the U.S. Access to large numbers of donors with diverse racial and ethnic backgrounds has been challenging. Womack Army Medical Center (WAMC) currently has the busiest obstetrical service in the U.S. Army. With over 3,000 live births annually, there is a large pool of healthy, ethnically diverse potential cord blood donors. In July 2009, WAMC entered into an agreement with the Carolinas Cord Blood Bank (CCBB) at Duke Medical Center to become the first military facility to offer a public cord blood donation program. Through this

formal partnership, WAMC has joined a group of researchers whom for the past 22 years have been intimately involved in evaluating the safety and efficacy of using unrelated donor allogeneic cord blood units for transplantation in malignant and non-malignant diseases. The WAMC program was implemented in part to examine the effects of military collection site on donor recruitment and the quality of cord blood units collected from racial and ethnic minority donors. If successful, the WAMC collection site could serve as a model for other military health care facilities.

METHODS

The CCBB is a public, unaffiliated donor cord blood banking facility established in 1997 with support from the National Heart Lung and Blood Institute as part of the Cord Blood Transplantation (COBLT) Study. (5) The program collects, processes, tests and stores over 24,000 ethnically diverse, high cell dose cord blood units. These are listed on the single point of access "Be the Match" registry of the CW Bill Young Cell Transplantation Program operated by the National Marrow Donor Program (NMDP). (6) The CCBB currently operates collection sites at 7 facilities in North Carolina and one in Boston, Massachusetts. As of 2012, the CCBB has released over 2,000 cord blood units for unrelated donor transplantation and is registered with the Federal Drug Administration (FDA) and accredited by the Foundation for the Accreditation of Cellular Therapy (FACT). On October 4, 2012, a biologic license application for the CCBB (BLA) was approved by the FDA.

Cord blood donation is considered an experimental therapy; therefore, the CCBB protocol was submitted and approved by the WAMC Institutional Review Board. Subsequently, a Cooperative Research and Development Agreement were entered into with Duke University. Under this ongoing agreement, the CCBB provides staff to educate and consent potential donors, performs cord blood collections (Monday through Friday during business hours), arranges the transport of cord blood units to the CCBB laboratory, and processes, tests and then cryopreserves the cord blood units. To improve the likelihood of cord blood collection after hours and on weekends, delivering providers were trained. Trained obstetrical providers can collect cord blood units only from women who have been appropriately consented for participation by CCBB staff.

Education for potential donors occurs through posters, videos and brochures that are placed throughout the Obstetrics and Gynecology (OB/GYN) clinic, the labor and delivery unit (L&D) and other approved sites in WAMC. Additionally, CCBB staff frequently set up booths during the semi-annual WAMC maternity fairs and other local health care festivals. CCBB personnel are available on L&D daily and in the OB/GYN clinic as needed to answer patient questions and to consent potential donors.

Eligibility criteria for cord blood donation are strictly mandated by the U.S. Department of Health and Human Services, Health Resources and Services Administration, FACT and the FDA. Cord blood donors must be 18 years of age or older; be at or greater than 34 weeks gestation at the time of delivery; have a singleton pregnancy with no known congenital defects; be negative for HIV, hepatitis B and C, tuberculosis, or active sexually transmitted infections; have no history of intravenous drug abuse; and be able to consent for cord blood donation in their native language. Donors should not have a known history of cancer, immunodeficiency or bone marrow failure in first degree relatives of the baby.

Informed consent to participate in cord blood donation is performed by CCBB staff prior to labor (as early as 28 weeks gestation). Patients who present to L&D in early labor who have not previously consented can complete an abbreviated consent form, but must sign a full consent document after delivery. Key components of the informed consent include: the voluntary nature of the donation with no cost to the patient or their insurance; minimal risk to mother or infant; the possibility that cord blood will not be collected or banked; the understanding that cord blood is not stored exclusively for the family; the maintenance of strict confidentially even if the cord blood is used for transplant; and the need for an additional blood draw to evaluate for possible infectious diseases that may need to be reported. Cord blood is collected and processed on a case-by-case basis for directed donation from mothers who have family members diagnosed with malignant and non-malignant conditions that can benefit from UCB transplant.

Cord blood is collected by either in-utero or ex-utero techniques based on the clinical scenario. Approximately 30 ml of maternal blood is drawn after delivery to test for hepatitis, Cytomegalovirus, Human T-lymphotropic virus Type I and Type II, Human Immunodeficiency Virus, syphilis and West Nile virus. Cord blood units that fail to meet the criteria for cord blood donation (< 60 ml in volume or cell count < 1 billion stem cells) may be used for research at Duke University Medical Center or other facilities.

Cord blood is transported to the Duke CCBB laboratory for processing and evaluation within 48 hours of collection by a CCBB courier. A cell count is determined from a small

sample of the cord blood unit to determine its adequacy for banking and transplantation. CBUs meeting the criteria for transplant are further tested for stem and progenitor cell content, sterility, HLA typing and possible genetic and metabolic disorders (see Table 1.) If necessary, the cord blood units are tested for metabolic disorders such as Gaucher's Disease, Krabbe Disease, Hurler Syndrome or other mucopolysaccharidoses. Maternal donors are screened for infectious diseases transmittable through blood in CLIA approved donor screening laboratories. For positive results, every feasible effort is made to contact the donor through donor provided contact information. If this is impossible, the donor's obstetrician and/or pediatrician are contacted.

Table 1

Cord Blood Unit Laboratory Analysis

Cord Blood Testing	Source
Cord blood unit stem cell count	CCBB processing laboratory, Duke University, Durham, NC
Hepatitis B Hepatitis C Cytomegalovirus HTLV I, II West Nile Virus Chagas disease Nucleic Acid Testing	American Red Cross National Testing Laboratory, Charlotte, NC
HLA testing	The Transplant Immunology Lab, Walter Reed National Military Medical Center, Bethesda, MD

RESULTS

Between July 2009 and December 2012, 2,204 donors were consented for cord blood donation. Of those consented, 1,502 (68.1%) units were collected; 1,177 (78.4%) units were collected by the in-utero technique; 325 (21.6%) units were collected ex-utero after Cesarean delivery.
Of the 1,502 collected units, 1,039 (69.2%) cord blood units were not banked, due primarily to low volume and low cell count (see Table 2).

Table 2

Reasons for Cord Blood Units Not Banked

Number	Percent	Reason
331	50.0	Insufficient volume
179	27.0	Insufficient cell count
50	7.5	Low viability
25	3.8	Other
16	2.4	Maternal sample problem
14	2.1	Failed sterility
14	2.1	Reassigned for directed donation
11	1.7	Insufficient nuclear/ mononuclear cell recovery
8	1.2	Maternal history exclusion
5	0.7	Collection to cryo > 48 hrs
4	0.6	Child with Type I diabetes (directed donation)
4	0.6	Shipped for transplant
3	0.5	Subsequent medical problem

Ultimately, 463 cord blood units (30.8%) met cell-count and volume criteria for cord blood banking. Volume and cell counts for collected units and banked units are summarized in Tables 3 and 4. Overall, the mean volume/cord blood unit was 70.5 ml and the mean cell count was 14 x 108. As of 2012, 15 cord blood units have been transported for transplant.

Table 3

Volume and cell counts for all collected cord blood units

	Volume mL	Post-Processing Viability	TNCC[a] x10e8	DTNCC[b] x10e8	Total CD34[c] Frozen x 10e3	CFU[d] x 10e5
Cord blood units	1502	562	644	585	439	439
Mean	70.5	93.8	16.4	14.0	5156.0	37.0
Maximum	204.0	100.0	92.8	38.7	26292.4	127.2
Minimum	0.0	42.0	5.2	4.7	513.9	2.6
Median	67.0	95.0	14.8	13.0	4168.9	32.3

[a] Total Nucleated Cell Count
[b] Post-processing TNCC
[c] Protein found on the surface of stem cells
[d] Colony Forming Units

Table 4

Volume and cell counts for all banked cord blood units.

	Volume mL	Post-Processing Viability	TNCC[a] x10e8	DTNCC[b] x10e8	Total CD34[c] Frozen x10e3	CFU[d] x 10e5
Cord blood units	463	462	461	461	417	417
Mean	100.1	95.7	17.3	14.4	5218.0	37.5
Maximum	204.0	100.0	54.0	38.7	22678.2	127.2
Minimum	40.0	90.0	9.2	7.1	513.9	2.6
Median	95.0	96.0	15.9	13.3	4211.9	32.7

[a] Total Nucleated Cell Count
[b] Post-processing TNCC
[c] Protein found on the surface of stem cells
[d] Colony Forming Units

The overall racial mix of donors was reflective of the WAMC population with 50.8% white, 11.3% black and 15.5% Hispanic.
The main reason that cord blood was not collected was due to the lack of availability of CCBB staff after hours (71.7%) (see Table 5).

Table 5

Reasons Cord Blood Not Collected

Number	Percent	Reason
264	71.7	CCBB staff not available
26	7.1	CCBB staff not notified of delivery
22	6.0	Hospital chart review revealed medical exclusion
16	4.3	Stat Caesarian section
15	4.1	Torn cord or placenta
11	2.9	Delivery complications
10	2.7	Cord clamp not applied
7	1.9	Chorioamnionitis
7	1.9	Cord too short
4	1.1	Cord drained
2	0.5	Clotted cord
2	0.5	Single umbilical artery

The main reason that collected cord blood units were discarded was low cell count or low volume (77%).

DISCUSSION

Only 20-25% of candidates for bone marrow transplantation have an available HLA- matched sibling donor. As a result, there is a need for alternative sources including HLA-matched unrelated donors. Approaches to identify non-related donors have focused on volunteer living donor registries such as the NMDP. (6) Due to the extreme polymorphism of the HLA system, the probability of finding a matched, unrelated donor through a registry is approximately 20% and even lower for recipients of ethnic minority heritage (black, Asian, Hispanic, Native America, etc.). (4)

The issue is further compounded by the cumbersome process of identifying, typing, and harvesting bone marrow from an unrelated donor with a minimum average time interval from identity to donation of approximately 4 months.

Options for cord blood donation include public and private UCB banks. (7) Currently, there are a number of private for-profit companies that encourage parents to bank their children's cord blood for their own autologous use as a form of "biologic insurance." In a review by Sullivan, 16 publications are cited that give negative opinions about the value of private cord blood banking. (8) Obstetricians are frequently asked by parents to collect umbilical cord blood for private cord blood banking. In our institution, only 30.8% of collected cord blood units collected by trained personnel were adequate for banking. One would anticipate an even higher rejection rate in umbilical cord blood collections performed by untrained personnel. Regardless of what parents choose to do with cord blood, they need to be provided with scientifically accurate information and should also be advised of the potential that collected cord blood may be inadequate for transplantation.

There are still some significant challenges that need to be addressed. Because CCBB personnel are only available weekdays during business hours, many persons consented did not undergo cord blood collection. WAMC has plans to use CCBB personnel primarily for patient and provider education and consenting, while relying more heavily on the OB providers to perform cord blood collection. This strategy is expected to increase the yield of eligible cord blood units.

We believe that this model works well in the military health care system, but requires commitment and support at all levels. WAMC has been an ideal location for a cord blood collection site with a very busy obstetrical service, an ethnically diverse population, and close proximity to the CCBB at Duke Medical Center. Obstetrical and neonatal care is one of the leading medical product lines in the military health care system. The model that has been established at WAMC could easily be applied to other military treatment facilities.

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