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Review Article

Criteria for Accepting or Rejecting Cord Blood Units

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Abstract

Rare hematopoietic stem cell populations are responsible for the transplantation engraftment process. Umbilical cord blood (UCB) is usually processed to the total nucleated cell (TNC), but not to the mononuclear cell (MNC) fraction. TNC counts are used to determine UCB unit storage, release for transplantation and correlation with time to engraftment [1]. It has been mentioned in the literature that there are several factors that affect harvesting of cord blood stem cells [2]. It was set to analyze the relationship between fetal weight and other factors that led to rejection of CBUs brought to DCRC from public and private donations. In this retrospective study, 375 donations of CBUs from January 2018 to October 2018 at DCRC were recorded. From literature, factors that are usually involved in rejection of CBUs were recorded and analyzed to mark the leading cause of rejection criteria. In this study, it showed that results did not find infants' birth weight or mother's age to have any value in rejection. Other factors' results will be discussed.

Keywords: Private and public donations; Pre-analytic; Recovery; Viability.

Abbreviations

RR:Recovery rate; TNC:Total nucleated cell count; UCB:Umbilical cord blood; CBU:Cord blood unit; BC:Buffy coat; BSC:Biological safety cabinet; DMSO:Dimethyl sulphoxide; CFU:Colony forming unit; WBC:White blood cells; HLA:Human leukocyte antigen; DCRC:Dubai cord blood and research center.

Introduction

Umbilical Cord blood (UCB) is blood that remains in the placenta and in the attached umbilical cord after childbirth. After birth, the doctor clamps the umbilical cord in two places, about 10 inches apart, and cuts the cord, separating mother from baby. Then a needle was inserts and collects at least 40 milliliters of blood from the cord [3]. Cord

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blood is collected because it contains stem cells, which can be used to treat hematopoietic and genetic disorders [4,5]. Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they 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. 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 cell [6].

The volume of umbilical cord blood collection was important for the high yield of TNCs and $CD34^+$ cells concentration [7]. Studies have shown that there are some variables that affect the quality and quantity of the umbilical cord blood, especially those related to maternal and fetal factors [8,9].

In this retrospective study, it was aimed to determine the primarily donor-related variables such as maternal age, weight of the new born before cell processing and their effects on the concentrations of cellular components such as umbilical cord blood volume, TNC numbers, CD34 count, and other criteria.

Methods

Accepted CBUs and maternal blood samples must be properly labelled with donor's name and identity, and follows the DCRC acceptance criteria for CBUs' initial weight shown in Table 1 (Public=Free CBU donations, Private=Paid to preserve CBU).

Criteria	Public	Private
Initial weight of CBU	102g	86g
TNC1 Count	≥ $9.0x10^8$/Unit	≥ $3.0x10^8$/Unit
$CD34^+$Cells	≥ 2.0Million/Unit	≥ 0.4Million/Unit
Viability%	≥ 90%	≥ 85%
Recovery	≥ 60%	≥ 60%

Table 1: Pre-processing and processing criteria for accepting public and private CBUs.

Processing of CBUs and mother's blood

The method of processing a CBUs and mother's blood is briefly described below:

1. Take the properly labelled CBU, mix thoroughly by gentle swirling, disinfect the portal, and mix again.
2. Connect the UCB input bag to the Sepax kit using the pre-installed spike connection under the laminar flow, and withdraw 4.0ml of cord blood from the collection

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bag and distribute it on the labelled cryo-vials.

3. Take the initial sample (1 tube for pre WBC1 count & HLA, 2 tubes for future testing) by slowly aspirating the blood by means of the 10ml syringe.
4. Check WBC1 count with Coulter's ACT diff machine and enter the value of WBC1 count in the database.
5. If TNC1 passed the acceptance criteria shown in Table 1, proceed to next step; if did not pass, proceed with the rejection of unit procedure.
6. Take a Sepax separation kit, and ensure that the sterility indicator on the single use kit blister is GREEN. Remove the kit from the blister and lay it out flat to check that there are no kinks or other visible damage.
7. Connect Sepax kit connector to the blood bag needle port, and follow the SOP on operating the Automated Sepax cell processor.
8. While waiting for Sepax processing to be completed, prepare for the maternal blood samples for send out infectious disease and CMV testing.
9. Sepax machine will start to transfer the buffy coat (BC) to the cryobag.
10. Take the 1ml buffy coat from the segment into cryovials and put 0.8ml into 1 cryovial for post CD34 and WBC2 count and 0.2ml for CFU.
11. Add DMSO to the cryobag, and proceed with cryopreservation lined out in the DCRC SOP. The final BC bag and 8vials from child and mother are placed in a canister, labeled, and transferred into liquid nitrogen tank.
12. Aliquot blood from CBU bag for send out testing (2ml for microbiology lab, 3ml for ABO/Rh grouping, and 2ml to be saved for future testing).

Statistics

Baseline maternal, newborn and cord blood characteristics were reported as means ± standard deviation (and medians along with minimum-maximum range), or frequencies and percentages for continuous and categorical variables, respectively. A p value <0.05 was considered statistically significant, and a p value >0.05 was considered not significant. All statistical analyses were performed using MS® Excel.

Results

Most CBUs came from private donations (288) women (76.8%), and the public donations comprised 87 women (23.2%) of total donations (375CBUs). Total accepted CBUs were 225 (60%), of which 214 (95.1%) were from private donations, and 11 (4.9%) came from public donations. On the other hand, total rejected units were 150 (40%), of which 74 (49.3%) were from private donations, and 76 (50.7%) came from public donations. Mothers' age ranged from 19–49 years old with an average age of 33 years old. The minimum age of mothers with accepted

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CBUs was 21 years, and the maximum age was 49 with an average of 33 years. The minimum age of mothers with rejected CBUs was 19 years, and the maximum age was 46 with an average of 32.9 years. Infants birthweight ranged from 1.04-4.78Kg with an average of 3.094Kg. Infants with accepted CBUs had minimal weight of 1.92Kg and a maximum of 4.78Kg with an average weight of 3.13Kg. Infants with rejected CBUs had minimal weight of 1.04Kg and a maximum of 4.31Kg with an average weight of 3.01Kg. The initial weight of CBU bags for the accepted patients averaged at 115g, while the rejected CBU bags' weight averaged at 100g. The accepted CBU volume averaged at 56ml, while the rejected CBU volume averaged at 41ml. TNC1 from accepted donors averaged at $8x10^8$ cells, while TNC1 from rejected units averaged at $3x10^8$ cells.

Table 2 shows that the total accepted CBUs were 225 (60%), of which 214 (95.1%) were from private donations, and 11 (4.9%) came from public donations.

On the other hand, total rejected units were 150 (40%), of which 74 (49.3%) were from private donations, and 76 (50.7%) came from public donations. It is clear that the number of rejected CBUs from public donations is very high (87.4% of the received public CBUs) when compared with accepted donors (12.6% of the received public CBUs). On the other hand, the number of rejected CBUs from private donations is low (25.7% of the received private CBUs) when compared with accepted private donors (74.3% of the received private CBUs). Results indicate that more samples are being rejected from public donations.

Total Number of CBU's	Nos. of CBU's Received		Nos. of CBU's Accepted		Nos. of CBU's Rejected	
	Private	Public	Private	Public	Private	Public
375	288	87	214	11	74	76

Table 2: Number of accepted and rejected CBUs from public and private donations.

Mothers' age (Table 3) ranged from 19–49 years old with an average age of 33 years old. The minimum age of mothers with accepted CBUs was 21 years, and the maximum age was 49 with an average of 33 years. The minimum age of mothers with rejected CBUs was 19 years, and the maximum age was 46 with an average of 32.9 years. Using t-test analysis to find out whether mother's age affected acceptance or rejection of cord blood samples, indicated that it has no effect on it ($p>0.05$). Further, Table 3 shows infants' birthweight ranging from 1.04-4.78Kg with an average of 3.094Kg. Infants with accepted CBUs had minimal weight of 1.92Kg and a maximum of 4.78Kg with an average weight of 3.13Kg. Infants with rejected CBUs had minimal weight of 1.04Kg and a maximum of 4.31Kg with an average weight of 3.01Kg. Results indicate that mothers' age or infants'

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weight are almost the same between accepted or rejected CBUs. Results of two-tail t-test analysis showed no bearing of infants' weight on accepting or rejecting of samples ($p>0.05$).

	Mother's Age (Years)		Infant's Weight (Kg)	
	Accepted	**Rejected**	**Accepted**	**Rejected**
Min	21	19	1.92	1.04
Max	49	46	4.78	4.31
Average	33	32.9	3.13	3.01

Table 3: Age of mothers and infant's weight at delivery for public and private cord blood donations received at DCRC in 2018 (Jan-Oct).

Table 4 shows that the average weight of CBU bags for the accepted patients was 115g, while the rejected CBU bags' weight averaged at 100g. The accepted CBU volume averaged at 56ml, while the rejected CBU volume averaged at 41ml. TNC1 count from accepted donors averaged at $8x10^8$ cells, while TNC1 count from rejected units averaged at $3x10^8$ cells. Statistical analysis showed that all four criteria were significant ($p<0.05$) in accepting or in rejecting CBUs even though they came from a pool of private and public donors.

	Initial Weight of CBU bags (g)	**Volume of CBU (ml)**	**WBC1 count ($x10^3$cells/ml)**	**TNC1 ($x10^8$cells)**
Accepted	115	56	10	8
Rejected	100	41	8	3

Table 4: Comparisons between accepted and rejected donors in 4 categories.

The criteria expanded that it lead to rejections of samples, and then data compared these criteria among private and public donors. Table 5 shows that 32 (36.8%) low CBU initial weight, 22 (25.3%) low TNC1 recovery, and 14 (16.1%) CBUs that had positive microbial growth were the leading cause of rejecting public donations. The leading causes of private donors were 33 (11.5%) low TNC1 recovery, and 23 (8%) CBUs did not have labeling on the bags. It was compared in terms of percentage the criteria between public and private donors that lead of rejection; it was found that low initial CBU weight, low TNC1, and positive microbial growth were the leading cause for public donors. Collectively, they comprise 78.2% of the total rejection of public CBUs. On the

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other hand, low TNC1 and not labelling of patient CBUs comprised only 19.5% of the rejection of private donors.

Both, public and private donors, had normal $CD34^+$ cells, and this shows that low numbers of $CD34^+$ were not a reason for rejection. However, statistical analysis of causes for rejecting samples between public and private donors revealed that low initial CBU weight is significantly higher in public group ($p<0.05$), while unlabeled CBUs from private donors were significantly higher in the private group ($p<0.05$). Other criteria did not show statistical significance between the two groups ($p>0.05$).

Rejection Criteria	Public	%	Private	%	Total
Low initial CBU Weight	32	36.8	2	0.7	34
Low TNC1	22	25.3	33	11.5	55
Low Recovery	1	1.1	6	2.1	7
Pending Maternal Sample	4	4.6	0	0	4
Positive Serological Test	0	0	3	1	3
Positive Microbial Growth	14	16.1	6	2.1	20
Low $CD34^+$	0	0	0	0	0
Patient Identification: Unlabeled Unit	0	0	23	8	23
Twin samples' errors	3	3.4	1	0.3	4

Table 5: Numbers and Criteria of Rejected CBU's from public and private donors received and processed in DCRC from January to October 2018.

Discussion

Unlike other studies, it showed that the average birth weight of infants was similar both for accepted and rejected donors. Therefore, cannot conclude that infants' weight had any bearing on rejection or acceptance of CBU weights or TNCs [10,11]. In DCRC, do not take in to consideration the infant's weight as a criterion for rejection, and this study just goes to show that this criterion is not significant.

Likewise, mothers' age did not play important role in differentiating any criteria since they were similar as well for both accepted and rejected donors. This is in accordance with other studies that showed similar results [12,13]. However, a recent study has shown that higher TNC came from mothers aged 30-34 years old when compared with mothers aged between 20-24 years old [14].

Volume of CBUs and TNC1 counts were higher in accepted donors than in rejected donors. The average volume of CBU should be about 60ml, which corresponds to 470 million TNC [15].

Depending on the doctor, the procedure for collecting the right UCB amount is important for adequate TNC1 recovery. Further, good hygiene in child delivery is important so that it do not get positive microbial growth.

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The percentage of samples being rejected are higher from public donations than from private donations. The number of rejection percentages of CBUs of public donations were mainly due to initial CBU weight, low TNC1 recovery, and positive microbial growth.

Low TNC1 and improper labeling of CBUs were the main reasons for rejecting private donors. Statistically, low CBU weight and CBU volume were important in rejecting samples for the public group, while incorrect tagging CBUs were the main rejection cause for private group. Attending nurses should be alerted to complete all patient information, and tag it on the CBU prior to sending the CBU to DCRC.

Conclusion

This study indicates that all criteria for rejecting a CBU discussed in this paper are pre-analytical.

Disclosure

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