

Factors Associated With Umbilical Cord Blood Collection Quality in Japan

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Abstract

Background: Umbilical cord blood (UCB) has become an established alternative source of hematopoietic stem cells with marrow and postmobilization peripheral blood. The presence of a large amount of clots may lead to the deterioration of cord blood quality. To improve UCB quality as a source of hematopoietic stem cells in Japan, we examined factors associated with UCB collection methods from the viewpoint of eliminating the presence of clots.

Methods: In August 2019, we requested the directors of 74 certified facilities to provide information on UCB collection methods in Japan. A total of 46 (62.2%) of them responded with valid information on a total of 2,892 UCB collections. In this study, collected UCB without clots macroscopically was evaluated as a high-quality UCB.

Results: The 2,891 UCB collections described during the study period were divided to those with (n = 760, 26.3%) and without clots (high quality; n = 2,131, 73.7%). Multivariate analysis revealed single puncture as a factor determining high-quality UCB collection (adjusted odds ratio (ORs): 1.80, 95% confidence interval (CI): 1.3 - 5.4, P = 0.01).

Conclusions: Single puncture is an independent effective factor determining high-quality manual UCB collection in Japan.

Keywords: Umbilical cord blood quality; Umbilical cord blood collection; Single puncture; Hematopoietic stem cells; Japan

Introduction

Umbilical cord blood (UCB) has become as an established al-

ternative source of hematopoietic stem cells with marrow and postmobilization peripheral blood [1]. In Japan, about 30% of hematopoietic stem cell transplantation is now performed using UCB [2, 3]. Because the limited number of cells still remains a problem restricting UCB use, maintenance of the quality of harvested UCB will be essential to decreasing the number of discarded units [4, 5]. Collected UCB is cryopreserved after removing red blood cells; however, the presence of a large amount of clots may lead to the deterioration of cord blood quality. To improve UCB quality in Japan, we examined factors associated with UCB collection methods from the viewpoint of eliminating the presence of clots.

Materials and Methods

This study was conducted after receiving approval from the ethics committee of the Japanese Red Cross Society Blood Service and that of the Japanese Red Cross Katsushika Maternity Hospital.

In Japan, UCB collection has been performed manually using a bag containing citrate-phosphate-dextrose (CPD). Some studies have suggested the amount and type of anticoagulant can cause the difference in cell viability in UCB [6-8]; however, in Japan bags of the same standard containing CPD have been used in all regions. In addition, in Japan delayed umbilical cord clamping has not been recommended in order to prevent serious neonatal jaundice [9, 10]. In August 2019, there were 74 certified obstetrical facilities which were actively collecting UCB for five public cord blood banks in Japan, as one site was closed for their facility moving. We requested the directors of the 74 certified facilities to provide information on UCB collection methods in Japan. The inquiries about UCB collection methods as potential factors associated with UCB quality were as follows: 1) Collection during vaginal delivery only; 2) Clamp the tube to prevent air contamination; 3) Puncture with needle hole facing up; 4) Puncture the umbilical cord near the placenta; 5) Puncture the thick part of the Walton Jelly; 6) Single puncture only; 7) Continuous massage of the uterine fundus during collection; 8) Avoid squeezing the umbilical cord; 9) *In utero* collection only; and 10) Continuous stirring of the bag during collection based on the Reports of the Cord Blood Collection Technique Workshop 2014, 2015, 2016 and 2017 conducted by the Blood Service Headquarters of the Japanese Red Cross Society [11]. A total of 46 (62.2%) of the 74 facilities responded with valid information on a total

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of 2,892 UCB collections.

In this study, collected UCB without macroscopic clots was evaluated as high-quality UCB.

Data are expressed as the number (percentage). The EZR (Easy R) Package (<https://cran.r-project.org/web/packages/RcmdrPlugin.EZR/index.html>) was used for statistical analyses. A Fisher's exact test or Chi-square test was used for categorical data, and a P value < 0.05 was considered to be statistically significant. Univariate logistic regression analyses were performed to identify factors associated with UCB collection methods related to UCB quality. Factors with P value < 0.05 in the univariate logistic regression model, as well as those considered clinically important, were evaluated by multiple logistic regression analysis. The logistic regression analyses were used to estimate odds ratios (ORs) and 95% confidence interval (CI).

Results

The 2,891 UCB collections provided from the facilities during the study period were divided into those with (n = 760, 26.3%) and without clots (high quality; n = 2,131, 73.7%).

Table 1 shows the results of univariate logistic regression analyses concerning the association between possible factors of UCB collection methods and the UCB quality (presence or absence of clots). The following five factors were resultantly identified as effective for determining high-quality UCB collection: 1) Puncture with needle hole facing up; 2) Puncture the umbilical cord near the placenta (negative correlation); 3) Single puncture only; and 4) Avoid squeezing the umbilical cord. Following to the selection of possible effective factors through univariable regression, multivariate analysis then revealed that single puncture was a high-quality UCB collection method (adjusted ORs: 1.80, 95% CI: 1.3 - 5.4, P = 0.01), as shown in Table 2.

Discussion

This may be the first report of the factors associated with manual UCB collection quality, and the results of the current study show that single puncture is an independent effective factor (= method) determining high-quality manual UCB collection in Japan.

To date, some studies have observed that delayed umbilical cord clamping and the *in utero* collection mode have some negative correlations with the volume of UCB collection [4, 5]. The current results may be the same for the latter. We understand the WHO recommendation of delayed umbilical cord clamping (not earlier than 1 min after birth) for improved infant health and nutrition outcomes [12]. However, there are many facilities performing early umbilical cord clamping to prevent serious neonatal jaundice irrespective of UCB collection in Japan because the peak period and value of neonatal bilirubin levels have been pointed out to be late and high, respectively [9, 10]. Therefore, we were not concerned about the timing of umbilical cord clamping.

In addition, some obstetric factors such as greater infant and placental weights have also been proposed as effective factors facilitating UCB collection with sufficient cellular richness [4, 5, 13]. However, the weights of Japanese infants and placentae may be lower than those in the countries reported previously [4, 5, 13]. To make up for the obstetric disadvantages, Japanese obstetric staff have honed manual UCB collection techniques through regular Cord Blood Collection Technique Workshops conducted by the Blood Service Headquarters of the Japanese Red Cross Society [11]. As the outcome of the training, we obtained a result that single puncture is recommended. There are two possible mechanisms explaining this result. One is a short collection duration associated with single puncture. It will take some time (nearly 1 - 2 min) to collect a sufficient volume; however, long-term collection will accelerate the blood coagulation properties. The other is the endothelial injury associated with multiple punctures contributing to thrombogenesis. Therefore, it may not be desirable to attempt additional puncture if UCB of 60 mL or more cannot be obtained.

We understand that there are some limitations in this study. Firstly, the proportion of facilities collecting UCB during vaginal delivery only could be examined; the proportion of UCB collected during cesarean section was unknown. To date, there has been disagreement regarding differences in delivery modes [5], and so careful consideration may be required. Secondly, the presence or absence of clots has been left to the trained technicians' visual judgment in Japan; however, the inter-technician error was not examined in this study. In addition, a larger prospective study may be needed because of the large number of missing data concerning the methods of UCB collection.

Based on the current study, single puncture is an independent effective factor determining high-quality manual UCB collection in Japan.

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Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Table 1. Results of Univariate Logistic Regression Analyses Concerning the Association Between Possible Factors of UCB Collection Methods and the UCB Quality (Presence or Absence of Clots)

Factor of UCB collection	Presence of clots		P value	Crude ORs	95% CI
	No	Yes			
Collection during vaginal delivery only					
Yes	1,121	407	0.67	0.963	0.82 - 1.1
No	1,010	353			
Missing data	0	0			
Clamp the tube to prevent air contamination					
Yes	1,379	517	0.34	0.896	0.71 - 1.1
No	333	111			
Missing data	460	136			
Puncture with needle hole facing up					
Yes	1,738	154	0.03	1.47	1.0 - 2.0
No	393	51			
Missing data	0	545			
Puncture the umbilical cord near the placenta					
Yes	1,325	567	< 0.01	0.619	0.48 - 0.79
No	351	93			
Missing data	455	100			
Puncture the thick part of the Walton Jelly					
Yes	1,146	282	0.07	1.21	0.99 - 1.5
No	248	746			
Missing data	737	14			
Single puncture only					
Yes	1,307	585	< 0.01	1.45	1.2 - 1.8
No	269	175			
Missing data	555	0			
Continuous massage of the uterine fundus during collection					
Yes	1,383	509	0.19	1.16	0.93 - 1.5
No	311	133			
Missing data	161	118			
Avoid squeezing the umbilical cord					
Yes	426	18	< 0.01	3.24	2.0 - 5.3
No	1,685	212			
Missing data	25	530			
<i>In utero</i> collection only					
Yes	1,298	594	0.06	1.23	0.99 - 1.53
No	384	160			
Missing data	549	6			
Continuous stirring of the bag during collection					
Yes	1,538	354	0.09	0.691	0.42 - 1.1
No	367	75			
Missing data	226	336			

OR: odds ratio; CI: confidence interval; UCB: umbilical cord blood.

Table 2. Results of Multivariate Logistic Regression Analyses Concerning the Association Between Possible Factors of UCB Collection Methods and the UCB Quality (Presence or Absence of Clots)

Factor of umbilical cord blood collection	P value	Adjusted ORs	95% CI
Puncture the umbilical cord near the placenta	0.09	1.02	0.91 - 1.2
Puncture with needle hole facing up	0.052	1.41	0.98 - 1.8
Single puncture only	0.01	1.80	1.3 - 5.4
Avoid squeezing the umbilical cord	0.11	1.29	0.91 - 1.8

OR: odds ratio; CI: confidence interval; UCB: umbilical cord blood.

Author Contributions

SS contributed to project development, data collection, data analysis, and manuscript writing/editing. TK contributed to project development, data management, data analysis, and manuscript writing/editing. SH contributed to data collection, and manuscript writing/editing. FI was involved in project development, and manuscript writing/editing. MT was involved in project development, data management, data analysis, and manuscript writing/editing.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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