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Effects of in utero cord blood collection on post-cesarean hemoglobin levels

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ABSTRACT

Objective: To assess effects of in utero cord blood collection on postoperative hemoglobin, hematocrit levels.

Study design: Elective cesarean deliveries in which cord blood was collected were compared with match paired elective cesarean deliveries without cord blood collection. Pre–post-operative hemoglobin and hematocrit level differences were compared between study groups with Student's *t* test. Multivariate regression models were used to address confounders. Correlation between volume of collected UCB and mean decrease in blood count parameters was analyzed.

Results: A total of 399 cesarean deliveries during a 12 months period were included in the analysis. Mean decrease in hemoglobin levels was 1.08 g/dL (SD = 1.0) in UCB collected group compared to 0.84 g/dL (SD = 1.0) in control group ($p = 0.002$). Mean decrease in hematocrit levels was 3.1% (SD = 3.4) in cord blood collected cesarean delivery group compared to 1.9% (SD = 2.4) in control group ($p = 0.002$). Univariate analysis has shown the collected UCB volume to be uncorrelated with the change in hemoglobin levels ($r = 0.013$). Multivariate regression models, after adjusting for birth weight, age and number of prior cesarean, have shown the UCB collection to be significantly associated with the mean decrease in blood count parameters (estimate = 0.23 g/dL, $t = -2.23$, $p = 0.02$).

Conclusion: In utero UCB collection is associated with a small increase in bleeding of little clinical importance. Amount of UCB is not associated with amount of change in hemoglobin and hematocrit levels. In utero UCB collection seems to be safe for expectant mothers scheduled for low-risk cesarean delivery.

Introduction

Umbilical cord blood (UCB) transplantation is a rapidly advancing field in hematology due to UCB's use in the treatment of many diseases, including but not limited to, Fanconi anemia, thalassemia, leukemia and metabolic storage diseases [1–3]. Umbilical cord blood is a potent stem cell source which can be cryopreserved and is available upon request within a few days [4]. UCB transplantation has lower rates of graft versus host disease than traditional bone marrow transplants as human leukocyte antigen mismatch is better tolerated with UCB [5,6]. Autologous use of cord blood is still subject to debate [7]. A major issue of UCB transplantation is the small volume of umbilical cord blood unit compared to bone marrow which limits it's clinical use to either pediatric population or for adults, double units are required. Therefore, efficient collection of UCB to increase the volume of collected UCB is of great importance.

Primarily, there are two ways for UCB harvesting, first in utero collection and second ex utero collection. Intrauterine harvesting requires placenta to be still in the uterus while UCB is being collected. A recent research by Bassiouny et al. has suggested in utero collection to be superior to extra uterine collection adding to body of literature in support of in utero collection of UCB [8–10]. In their research they have found intrauterine harvesting yields a greater volume of UCB and total number of nucleated cells, which are both crucial to the success of UCB transplantation. However, depending on the amount of UCB collected, in utero collection

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practice prolongs the operative time of cesarean delivery and speculatively increases intraoperative blood loss.

UCB collection is offered to expectant mothers worldwide during their antenatal follow-up. However, there is limited data in the literature regarding health effects of UCB collection on the mothers. Some reports suggest an increase in maternal hemorrhage during delivery when UCB is collected [11]. The aim of this study is to determine effects of in utero UCB collection on pre/postoperative hemoglobin and hematocrit changes as a measure of intraoperative bleeding in women undergoing elective cesarean delivery.

Materials and methods

Elective cesarean deliveries of singleton, term pregnancies that occurred in Ankara University Department of Obstetrics and Gynecology between March 2014 and February 2015 were used in the study. Deliveries that were performed by the same group of surgeons for both UCB collected cesareans and regular cesareans were selected. Surgical teams consisted of one of the four senior residents with 3 years' experience with cesarean delivery coupled with one of the two specialists (TY and DCK) supervising the surgery. Deliveries were divided into two groups depending whether cord blood was collected or not. All cord blood collected cases were characterized according to maternal age, number of prior cesarean and birth weight. A case matched group of cesarean deliveries whose cord bloods were not collected were used as the control group. According to the Ankara University Cord Blood Bank standard operational procedures, maternal consents were obtained before deliveries for UCB collection. Deliveries were performed via Joel–Cohen incisions. Vesicouterine plica was prepared and low-uterine segment was transversely incised for two centimeters then incision was bluntly extended to sides. Cord blood was harvested in utero, i.e. while leaving the placenta inside the uterus, after delivery of the baby and clamping of the cord. After UCB collection, placenta was delivered and then the corners hysterotomy site were clamped to prevent further bleeding. Hysterotomy site was repaired in one layer with continuous locking. Electrocoagulation was used for bleeding small vessels. A single dose of 0.2 mg methylergonovine maleate was administered for postpartum hemorrhage prophylaxis. Postoperatively patients were hydrated with 100 cc per hour infusion of isotonic liquids and bloods were drawn at eight hours postoperatively for control blood counts. Amount of blood loss was estimated by subtracting preoperative hemoglobin and hematocrit levels from postoperative hemoglobin and hematocrit. Mean decrease in hemoglobin and hematocrit levels was compared between two groups. Correlation between amount of UCB collected and blood loss was analyzed.

Patients with history of bleeding 30 days prior to delivery were excluded from analysis. Emergent cesarean deliveries, postpartum bleeding due to uterine atony, retained placenta, cesarean deliveries performed due to placental adhesion abnormalities (placenta previa, placenta accreta), patients on anticoagulation regimens (aspirin, low molecular weight heparin, heparin) were all excluded from the study. Patients were matched from the birth register by two people who are blind to pre and post-operative blood count results.

With an enrolment ratio of 1:2 and 126, 252 patients in UCB collected cesarean group and control cesarean group respectively, the study would have 80% or more power to detect a mean between-group difference in the increase from baseline postoperative minus preoperative hemoglobin level of 0.4 g/dL, assuming a standard deviation of 1.18, a two-sided type I error rate of 0.05.

All statistical analysis was performed using R 3.1.3 for Windows. Delta values of each group were compared with Student's *t*-test. Multivariate regression models were used to assess association of UCB collection with change in hemoglobin values adjusted for number of prior cesarean, age, and birth weight. *p* Values below 0.05 were considered as statistically significant. Institutional review board of Ankara University deemed this study exempt from ethical approval.

Results

A total of 399 deliveries were included in the analysis (152 in case group, 247 in control group). Baseline characteristics of participants are given in Table 1.

There was a mean decrease of 1.08 g/dL (SD = 1.0) in cord blood collected cesarean delivery group compared to a mean decrease of 0.84 g/dL (SD = 1.0) of control cesarean delivery group (Fig. 1). Student's *t*-test showed the difference between groups to be statistically significant ($p = 0.02$). A change from baseline hematocrit levels of 3.1% (SD = 3.4) were observed in cord blood collected cesarean delivery group compared to 1.9% (SD = 2.4) of control cesarean delivery group (Fig. 1). Again Student's *t*-test showed the difference between groups to be statistically significant ($p = 0.002$).

Sample correlation between collected UCB volume and delta hemoglobin values was extremely weak with a correlation coefficient of $r = 0.013$ (Fig. 2). In a multivariate regression model adjusting for effects of age, and birth weight and number of prior cesarean; UCB collection was significantly associated with mean decrease in hemoglobin values (estimate = −0.23 g/dL, $t = -2.28$, $p = 0.02$).

There was one case in UCB collection group who had a change in hemoglobin levels from 11.4 g/dL to 6.8 g/dL and she was treated with blood transfusion. None of the control group patients needed transfusions.

Comment

In this study, we aimed to study effects of UCB collection on intraoperative bleeding in women undergoing elective cesarean delivery. Results have shown, UCB collection is associated with a minor increase in intraoperative bleeding. Cohen et al., in their similar study, demonstrated UCB collection is associated with increased intraoperative blood loss. Although the mean change in hemoglobin levels were small, blood loss requiring transfusion and a drop of 3 g/dL or more in hemoglobin levels were more common

Table 1
Study population characteristics.

Parameters	Cord blood collected cesarean deliveries $n = 152$ Median, Minimum–Maximum	Routine cesarean deliveries $n = 247$ Median, Minimum–Maximum
Age (years)	31 (22–50 years)	30 (18–50 years)
Parity	1 (0–3)	1 (0–4)
Birth weight (g)	3365 (2330–4450)	3330 (2150–4750)
Collected UCB volume (mL)	115 (36–194.5)	N/A
Preoperative hemoglobin levels (g/dL)	12.3 (9.8–14.9)	12.1 (9–15.1)
Negative delta hemoglobin between 0 and 2 g/dL (*n*, percent)	108 (71%)	181 (73%)
Negative delta hemoglobin more than 2 g/dL (*n*, percent)	33 (20%)	28 (11%)