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ORIGINAL ARTICLE

Umbilical cord milking in term infants delivered by cesarean section: a randomized controlled trial

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Objective: The study's objective was to compare hematocrit (Hct) levels at 36 to 48 h of age in term infants delivered by cesarean section exposed to immediate cord clamping or umbilical cord milking (UCM).

Study Design: In this randomized controlled trial, 24 women scheduled for elective cesarean section were randomized to either immediate clamping (<10 s) or UCM (milked ×5 by the obstetrical provider) at birth.

Result: All subjects received their allocated intervention. The milking group had a smaller placental residual blood volume (13.2 ± 5.6 vs $19.2 \pm 5.4\ ml\ kg^{-1}$, $P = 0.01$) and higher Hct levels at 36 to 48 h (57.5 ± 6.6 vs 50.0 ± 6.4 %, $P = 0.01$). Five infants (42%) in the immediate group had a Hct of ⩽47%, indicative of anemia.

Conclusion: UCM results in placental transfusion in term infants at the time of elective cesarean section with higher Hct levels at 36 to 48 h of age. *Journal of Perinatology* (2012) **32,** 580–584; doi:10.1038/jp.2011.159; published online 17 November 2011

Keywords: umbilical cord stripping; umbilical cord clamping; cord clamping; placental transfusion; placental residual blood volume

Introduction

At the time of cesarean section, the customary practice in the United States is to immediately clamp and cut the infant's umbilical cord. When the cord is cut immediately after birth, approximately $20\ ml\ kg^{-1}$ of the infant's whole blood[1] and $25\ mg\ kg^{-1}$ of iron[2] remains in the placenta and is routinely discarded as medical waste after birth. This has the potential to affect iron stores and may place the infant at risk for iron deficiency and anemia.[2–5] The practice of immediate cord clamping (ICC) is not based on a specific rationale or supporting evidence. Yet, the practice impacts approximately 1.5 million infants each year.

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Umbilical cord milking (UCM) can be used as a proxy for delayed cord clamping (DCC), as the benefits of UCM are similar to those associated with DCC and include improved blood and red cell volume, red blood cell counts and hemoglobin (Hb) and hematocrit (Hct) levels. Eight controlled trials and one randomized controlled trial published over the past 60 years have documented the safety and utility of UCM in term and preterm infants ($n = 827$).[6–14] Colozzi[9] reported that milking the cord five times, at the time of birth, was associated with higher blood volume, red cell volume and Hb and Hct levels without adverse effects when compared with infants exposed to ICC ($n = 100$). He recommended that UCM should be considered for all infants born by cesarean section in order to maximize placental transfusion. Hosono *et al.*[14] demonstrated in a randomized controlled trial of very low birth weight infants ($n = 40$), born vaginally or by cesarean section, that those who received UCM had higher initial Hb levels, better initial mean blood pressures, fewer blood transfusions and required less oxygen use when compared with very low birth weight infants exposed to ICC without causing harm.

Although these studies make a valuable contribution to the growing body of evidence surrounding placental transfusion, they are limited by (1) the variety of definitions of the variables, (2) the wide variation in cord milking practices and (3) small sample size in studies. Additionally, clinicians have voiced concerns about undesired neonatal outcomes such as jaundice requiring treatment and polycythemia when techniques that promote placental transfusion (UCM or DCC) are used. However, a recent meta-analysis ($n = 1921$) suggests that these concerns may be unfounded.[15]

The main objective of this study was to assess Hct levels at 36 to 48 h of age in term infants delivered by elective cesarean section exposed to ICC or UCM. The primary hypothesis stated that term infants, born by elective cesarean section, who received UCM would have higher Hct levels at 36 to 48 h of age compared with infants who received ICC. The secondary hypothesis stated that placental residual blood volume (PRBV) would be less in infants with UCM compared with infants who received ICC. Examination of any differences between groups in adverse neonatal outcomes such as symptomatic polycythemia, Neonatal Intensive Care Unit

admission, hyperbilirubinemia requiring prolonged hospitalization for phototherapy and hospital readmission would be recorded.

Methods

This was a randomized controlled trial conducted at Women and Infants' Hospital in Providence, Rhode Island. The study was approved by the Institutional Review Board of Women and Infants' Hospital and the University of Rhode Island. Women with uncomplicated term pregnancies who were scheduled for an elective cesarean section were assessed for eligibility. The eligibility criteria included (1) singleton pregnancy, (2) gestational age of 37 to $41^{6/7}$ weeks confirmed by a first trimester ultrasound, (3) no evidence of active labor, (4) $\geqslant 18$ years of age, and (5) a written consent given by the woman. Exclusion criteria included maternal medical and obstetric complications, severe anemia ($\leqslant 9.0\,g\,dl^{-1}$ Hb), clotting disorders and suspected intrauterine growth restriction. Women who smoked in pregnancy or who were non-English speakers were excluded. After delivery, the infant was excluded if there was a confirmed diagnosis of intrauterine growth restriction or serious congenital anomalies.

There were no contemporary DCC or UCM trials with data on Hct levels at 36 to 48 h of age for power analysis. Thus, the primary outcome for power analysis was based on a study by Nelle,[16] who found mean (s.d.) hematological differences of 53 (7)% vs 62 (6)% ($P<0.05$), between term infants with ICC and DCC at 2–4 h of age. A power analysis with a 1.38 effect size, two-tailed test, an alpha of 0.05 and a power of 0.80 revealed that a sample size of 24 pregnant women would be sufficient to test the study's primary outcome. A potential 25% drop out rate was factored into the sample size calculation.

All women who presented for an elective cesarean section were screened for eligibility. Following informed written consent, the women were randomized into one of the two groups: ICC (the control) or UCM (the intervention group). Just before surgery, a randomization card was opened by the investigator who informed the obstetrician of the group assignment. After the infant was delivered, the obstetrician either immediately clamped and cut the cord (within 10 s) or initiated the milking protocol. For the intervention, the obstetrical provider supported the umbilical cord with his/her non-dominant hand near the cord insertion site on the placenta and then used the thumb and index finger of the dominant hand to milk the entire length of the cord (towards the infant) five times before clamping. The infant was kept below the level of the placenta. Infants from either group were handed to the awaiting pediatric staff and moved to an infant warmer. All subsequent newborn care was directed by the supervising pediatrician. Uterotonic medications were not given before the umbilical cord was clamped.

As it was not possible to blind the randomization assignment, the obstetrician, pediatrician and OR staff were asked not to document or discuss which group the infants were assigned. Nursery and laboratory personnel were not informed about the infants' randomization groups.

After the delivery of the placenta, the PRBV was measured by the investigator. The placenta was drained in a supported funnel device. The drained placental blood volume was measured in milliliters and the PRBV was recorded as total blood volume in milliliters divided by the infant's birth weight in kilograms.

There were four data collection points: (1) birth, (2) 36 to 48 h of age, (3) the time of hospital discharge and (4) at 10 to 14 days of age. At birth, cord clamping time, infant gender, Apgar scores, resuscitative measures, birth weight, PRBV and maternal-estimated blood loss were recorded. Cord blood for Hct analysis (Coulter LH750 Hematology Analyzer, Beckman-Coulter, Miami, FL, USA) was collected. At 36 to 48 h of age, to avoid unnecessary discomfort for the newborn, a capillary Hct sample was drawn simultaneously with the routine newborn blood work. It was collected and analyzed by the laboratory personnel. The following infant data was collected at the time of hospital discharge: admission temperature (axillary, °F), initial mean blood pressure (~ 3 h of age measured by Dynamap, GE Healthcare, Milwaukee, WI, USA), feeding type, discharge weight, percentage of weight loss or gain, an assessment of bilirubin levels using the AAP Hour Specific Nomogram for Bilirubin Risk Stratification (http://www.bilitool.org), any evidence of polycythemia (venous Hct >65%),[17] anemia (capillary Hct $\leqslant$47%)[18] and any undesired neonatal conditions. At 10 to 14 days postpartum, a phone interview was conducted and the mother was queried about infant feeding status, any infant evaluation or treatment for jaundice, as well as any emergency room visits and/or hospital readmission since being discharged.

The statistical analyses were done using SPSS Version 15.0 (SPSS, Chicago, IL, USA) and intention-to-treat protocol was followed. There were no protocol violations. Differences in Hct levels and PRBV were examined using a student's *t*-test for independent groups. A contingency table analysis and Pearson's χ^2-test or Fisher's exact test for independent groups were used to examine whether there were any differences in the observed frequencies of symptomatic polycythemia, admission to the neonatal intensive care unit, hyperbilirubinemia requiring prolonged hospitalization for phototherapy, hospital readmission or exchange transfusion.

Results

Between October 2008 and January 2009 (the enrollment period), 167 women were admitted for a term elective cesarean section. Overall, 24 women and their fetuses were enrolled and randomized and 23 women/infant pairs participated in follow-up out to 2 weeks (Supplementary Figure 1). No significant differences in maternal

Table 1 Neonatal hematologic levels at 36–48 h of age

Variables	*ICC* (n = 12)	*UCM* (n = 12)	P *value*
36–48 Hb, g dl^{-1} [a]	17.2±2.1 (14.1–19.7)	19.4±2.2 (15.3–22.4)	0.03
36–48 Hct, %[a]	50.0±6.4 (41.0–58.3)	57.5±6.6 (43.3–65.7)	0.01
Capillary Hct >65%[b]	0	1 (8%)	0.31
Venous Hct >65%[b]	0	1 (8%)	0.31
Capillary Hct ⩽47%[a]	5 (45%)	1 (8%)	0.07

Abbreviations: Hb, hemoglobin; Hct, hematocrit; ICC, immediate cord clamping; UCM, umbilical cord milking.
Data presented as mean±s.d. (range) or *n* (%).
[a]*t*-test.
[b]χ^2.

Table 2 Jaundice and hyperbilirubinemia

Variables	*ICC* (n = 12)	*UCM* (n = 12)	P *value*
Clinical observation of jaundice[a]	10 (83%)	12 (100%)	0.48
No. of infants tested-TSB[a]	5 (42%)	9 (75%)	0.21
Peak total serum bilirubin, mg dl^{-1} [b]	11.8±3.8 (8.8–18.4)	12.4±2.1 (9.9–15.6)	0.73
Bilirubin >95%[a,c]	1	2	NS
Phototherapy[a]	0	2	0.48
Re-admit for phototherapy[a]	0	1	NS
Exchange transfusion[a]	0	0	NS

Abbreviations: ICC, immediate cord clamping; NS, not significant; TSB, total serum bilirubin; UCM, umbilical cord milking.
Data are presented as mean ± s.d. (range) or *n* (%), or as analyzed by Fischer's exact test.
[a]χ^2.
[b]*t*-test.
[c]AAP Hour Specific Nomogram for Bilirubin Risk Stratification.

demographics and pregnancy characteristics were reported at the time of enrollment (Supplementary Table 1).

There were no significant differences in neonatal demographic characteristics. The average time for milking the cord was 18 ± 5 s. Infants in the ICC group had more blood left behind in the placenta (a mean volume of 19 ml kg^{-1}). This was approximately 30% more than in the UCM group (a mean volume of 13 ml kg^{-1}). There were no group differences in Apgar scores, method of resuscitation, cord blood Hb, cord blood Hct, nursery admission temperature, initial mean blood pressure or glucose assessment. There were no admissions to the Neonatal Intensive Care Unit (Supplementary Table 2).

Table 1 reports neonatal hematologic status at 36 to 48 h of age. Infants in the UCM group had significantly higher Hct levels. One infant in the UCM group had a venous Hct >65% with no clinical symptoms indicative of asymptomatic polycythemia.[17] Five infants from the ICC group (45%) had a capillary Hct level of ⩽47%, suggestive of anemia.[18]

Table 2 provides information about jaundice and hyperbilirubinemia. Total serum bilirubin (TSB) levels were ordered by the pediatricians when jaundice was suspected. The mean peak TSB levels were similar amongst the two groups, but TSB levels were not tested on all infants. Three infants had a TSB level >95% as assessed by the AAP Hour Specific Nomogram for Bilirubin Risk Stratification (http://www.bilitool.org). One infant was from the ICC group, who was discharged on day of life 4 and was followed by outpatient TSB evaluations through day of life 7; phototherapy was not required. Two infants from the UCM group received a brief course of phototherapy. Neither infant had polycythemia. One was diagnosed with an ABO incompatibility. The second infant was discharged on day of life 4 and readmitted on day of life 7 for phototherapy, with the admission diagnosis of milk protein jaundice. No further treatment was necessary.

Discussion

Our study demonstrates that milking the cord in term infants, delivered by elective cesarean section, results in higher Hct levels at 36 to 48 h of age when compared with ICC. Infants who have their cords cut immediately at the time of birth leave 30% more residual blood volume behind in the placenta. Although the sample size is small, we have added information in the literature that shows that UCM is safe and does not result in undesirable complications such as hypothermia, hyperbilirubinemia, symptomatic polycythemia and Neonatal Intensive Care Unit admission.

The timing of the clamping and cutting of the umbilical cord has a significant impact on the infant's blood and red cell volume and early iron stores.[1–2,5] In utero, at term gestation, one-third of the fetus's blood volume is in the placenta at any one time. At the time of birth, a major shift occurs in the cardiac output to the lungs—changing from 8 to 10% in fetal life to 50% in neonatal life. This shift requires a rapid increase of blood volume to fill the capillary beds surrounding each alveolus to assist with lung tissue recruitment and expansion.[19] The placenta serves as the blood reservoir designed to meet this immediate demand for increased blood volume. A delay in cord clamping or milking the cord supports placental transfusion and results in a 20 to 30% increase in whole blood and a 50 to 60% increase in red blood cell volume.[1] When the cord is cut immediately, the infant does not receive the additional blood volume from placental transfusion, representing a loss of 25 mg kg^{-1} of iron or 33% less body iron.[2] This loss can affect iron stores and may place the infant at risk for iron deficiency and anemia during infancy.[1–5]

Although delaying the clamping and cutting of the cord at birth optimizes placental transfusion, it is not always feasible at the time of cesarean section. Waiting up to two or three minutes (or until pulsations cease) before clamping the cord can seem like a long time during a cesarean section. Cord milking appears to be a viable alternative to DCC when timing is critical. In our study, we found

that milking the cord took <20 s, yet resulted in less PRBV and demonstrated significantly higher Hct levels at 36–48 h of age when compared with infants with ICC. These findings suggest that cord milking is easy to implement and takes only a few seconds to improve an infant's hematologic status.

The greatest barrier to the clinical application of placental transfusion is the long held belief that overtransfusion can lead to symptomatic polycythemia and hyperbilirubinemia. In a meta-analysis involving 1912 infants, Hutton and Hassan[15] reported a slightly higher rate of asymptomatic polycythemia at 24 to 48 h of age with delayed clamping, but treatment was unnecessary and not associated with higher levels of jaundice and hyperbilirubinemia. Another recent meta-analysis found no differences in the amount of asymptomatic polycythemia or clinical jaundice, but did report a small increase in jaundice requiring treatment although bilirubin levels were not reported.[20] In our study, there was no report of symptomatic polycythemia and no significant differences between the ICC and UCM groups in the incidence of clinical jaundice, peak TSB levels, hyperbilirubinemia requiring hospitalization or readmission for phototherapy. Although these findings are consistent with previously published controlled trials,[3–14, 21–24] not all infants in this study had a TSB evaluation during the hospital stay. We recommend that in future studies, all infants should be assessed in order to draw stronger conclusions about jaundice and hyperbilirubinemia.

Of greater concern are the infants who are iron deficient and anemic in early infancy secondary to ICC. Similar to our study results in which almost half of the infants in the ICC group were anemic at 36 to 48 h of age, Ceriani Cernadas *et al*.[4] found a higher incidence of anemia in the ICC group. Available evidence (animal and human studies) suggests anemia of infancy may contribute to neurodevelopment impairment.[25] There are no long-term studies (>6 months) with follow-up of children with ICC, DCC or UCM. Examining the neurodevelopment of these children is a priority in light of the significant role iron has during the critical time of infant brain development.

A major limitation of this study is its small sample size. Although the study was not powered to detect significant differences in neonatal morbidity between groups, we were able to find significant differences in the primary outcome variable. Because the pertinent neonatal morbidities (that is, hyperbilirubinemia and polycythemia) have a low event rate, a very large sample size is needed to detect significant differences in these variables between UCM and ICC.

Cord milking is a low-cost intervention that accelerates placental transfusion at the time of cesarean section. Placental transfusion appears to have an important role in enriching early infancy iron stores and assists in availability of iron for the developing brain. Although DCC is the preferred method of transferring iron-rich blood from the placenta to the infant in the first few minutes after birth, it is not always feasible at the time of cesarean section. UCM is a viable alternative.

Conflict of interest

The authors declare no conflict of interest.

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Supplementary Information accompanies the paper on the Journal of Perinatology website (http://www.nature.com/jp)