Original Article

Effect of Timing of Umbilical Cord Clamp on Newborns' Iron Status and its Relation to Delivery Type

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Abstract

Objective: This study was conducted to evaluate the hematological effects of umbilical cord clamp timing and delivery type in term infants 48 hours after birth in Imam Hossein Hospital, Tehran, Iran.

Method: From Oct 2007 – March 2008, 100 mother-infant eligible pairs were selected and divided by cord clamp timing (≤15 s and >15 s) for hematologic value determination between the two groups. Data analysis was performed with SPSS for Windows statistical package (version 13).

Results: Maternal hematological status was assessed upon admission to the delivery room. A total of 100 mother-infant pairs were divided into two groups: delayed cord clamp time within 15 s (n=70) or early cord clamp time [15 s after delivery (n=30)]. The groups had similar demographic and biomedical characteristics at baseline. Forty-eight hours after delivery the mean infant hemoglobin (Hgb; 16.08 gm/dL vs. 14.5 gm/dL; $P<0.001$) and hematocrit (Hct 47.6 vs. 42.8; $P<0.001$) levels were significantly higher in the delayed clamping group. There was no significant difference in ferritin levels (214.7 vs. 173.6 ng/dL; P=0.08).

Fifty infants were born vaginally and 50 were delivered by cesarean section. Infants delivered vaginally had significantly more delayed cord clamp times (>15 s; $P<0.001$).

Conclusion: Delaying cord clamping increases the red cell mass in term infants. It is a safe, simple and low cost delivery procedure that should be incorporated in integrated programs that are aimed at reducing iron deficiency anemia in infants in developing countries. Vaginal delivery facilitates this action.

Keywords: cord clamp, delivery type, hematocrit, hemoglobin

Introduction

Anemia is a major health problem in Iran, whose prevalence amongst children (6 – 60 months) from Yazd is 39%[1] and 57.2% in Kashan (6 – 36 months).[2] During the first six months of life, infants are largely dependent on the iron supply present at birth for growth and hemoglobin (Hgb) production.[3] Maternal supplemental iron is not likely to have a strong effect on breast milk iron concentrations and its effect on fetal iron stores is unclear.[4–6] Direct supplementation of infants with medicinal iron is a challenge because of compliance problems and potential risks of competition for absorption with other nutrients such as zinc,[7] and a possible negative effect on the anti-infective properties of human milk lactoferrin saturation with iron in the breastfed infant's gastrointestinal tract.[8] Delayed cord clamping could increase iron status at birth and reduce anemia among toddlers. It is estimated that up to 50% of children in developing countries become anemic at 12 months[9] of age; therefore, a successful intervention this word can be omitted to prevent iron deficiency could be of global importance. In general, most vaginally delivered neonates that breathe before the cord is

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clamped attain a functional blood volume. Those neonates clamped before the first breath have less than optimal blood volume, and premature, c-section, and depressed babies in this category are prone to severe compromise from hypovolemia and hypotension.[10] The optimal time to clamp the umbilical cord for all infants, regardless of gestational age or fetal weight, is when the circulation in the cord has ceased, the cord is flat and no pulse is evident (approximately three or more minutes after birth). At the present time, both early and late clamping procedures are standard practices with some obstetrical textbooks recommending early clamping[11,12] and others propose delayed clamping.[13] Finally, others give no clear recommendation for either early or delayed clamping, citing a lack of sufficient evidence.[14–16] In our delivery center there is no specific guideline for the time of cord clamping, to date.

The present study was designed to test the effect of cord clamp timing on neonatal iron status and its relation to delivery type.

Materials and Methods

This observational cohort study was designed to assess hospital born newborns delivered by either vaginal or cesarean section from uncomplicated pregnancies (mothers without eclampsia, preeclampsia, severe heart or renal disease, severe antepartum hemorrhage, Hgb greater than 10 gm/dL, and no history of more than five deliveries) from Oct 2007 to March 2008. Newborns were included if there were no twin or asphyxiated deliveries, no first 24 hours after birth icterus, no congenital malformations, no hyaline membrane or respiratory distress syndrome, no sepsis, birth weight <2000 g or gestational age <35 weeks.

In order to detect a 0.7 gm/dL difference in serum Hgb with an SD of 1.5 gm/dL between the two groups after 48 hours of delivery, with a power of 90% and probability of 5% (α=5%), therefore a total sample size of 100 newborns was required for the study. There were 100 mother-infant pairs who fulfilled the enrollment criteria. Cases were matched between vaginal and cesarean deliveries, and 50 cases from each delivery type were selected. Over a 100 day period, one neonate delivered vaginally and one by cesarean section were selected every other day. These cases were watched for cord clamp time

and divided into 30 cases of early cord clamp ($\leq$15 s) and 70 cases for late cord clamp (>15 s). Care was taken to prevent hypothermia in both groups by adequate drying and warmth, and infants were placed under a preheated warmer in the delivery room.

At the time of delivery, maternal venous blood (2 mL) was collected in vials that contained EDTA in order to estimate Hgb and hematocrit (Hct) levels. From the infants, 4 mL of blood was taken 48 hours after delivery in both plain tubes and ETDA-containing vials to estimate Hgb, Hct, and ferritin levels. Ferritin assay samples were centrifuged and the serum was separated into a sealed tube and stored at -20°C until evaluated.

Hgb was estimated with the use of the Sysmex (K 4500) 1000 cell counter. Serum ferritin was estimated by ELISA (Monobind Ferritine ELISA Kit, Germany). The ferritin quantitative test uses a solid phase ELISA technique which was performed according to the manufacturer's instructions. Hct was measured by standard procedures.

Pretested structured questionnaires were used to collect socioeconomic, demographic, and maternal reproductive information in addition to neonate gestational age, Hgb, ferritin, and newborn morbidity. At the time of delivery, an observer used a stopwatch to record the elapsed time before the umbilical cord was clamped, relative to head crowning and appearance of the newborn's shoulders. All anthropometry was performed by the first author, following standard procedures.[17] Weight of the newborns at birth, maternal age, weight, Hgb, delivery type, and number of live children were also measured. Newborn health was assessed within 1 hour of delivery and again 24 hours later by study medical personnel. This examination included a clinical assessment of neurological and motor development, jaundice, as well as gastrointestinal and respiratory functions.

This study was based on observation of cord clamping practices. Blood sampling of infants was performed with the permission of the mothers.

All analyses were done using the SPSS for Windows statistical package (version 13). Baseline characteristics and measurements were compared across groups with the Chi-square statistic for categorical variables and Student's *t*-test for continuous variables. Group means were compared by using the *t* student significant difference test. All results were based on two-tailed tests and a *P* value of 0.05

Table 1. Baseline maternal and infant characteristics

Variables	Less than 15 s	More than 15 s	*P* -value
Mothers' ages			
Mean±SD	25.6±4.5	25.7±4.7	0.9
Range	17–37	17– 38	
Mothers' weights			
Mean±SD	71.2±13.6	70.8±11.8	0.9
Range	50–102	45–112	
Mothers' Hgb			
Mean±SD	12.3±2	13.1±1.27	0.06
Range	8.1–16	9.5–15.5	
Number of live children			
Mean±SD	1.1±0.1	1.3±1	0.5
Range	0–3	0–4	
Birth weight			
Mean±SD	3315±420.4	3284.3±417.8	0.7
Range	2400–4200	2500–4400	
Age at pregnancy			
Mean±SD	37.5±1.7	37.6±1.5	0.8
Range	35–45	35–42	

Table 2. Infants hematological outcome measures

Variables	Less than 15 s	More than 15 s	*P* value
Cord timecut			0.001
Mean±SD	14.5±1.04	28.4±7.5	
Range	10–15	16 – 50	
Newborn Hgb			0.005
Mean±SD	14.5±2.4	16.08±1.9	
Range	11–18.6	12–19	
Newborn Hct			0.003
Mean±SD	42.8±7.1	47.6±5.6	
Range	33–56.7	36-59	
Newborn ferritin			0.08
Mean±SD	173.6±91.7	214.7±124.3	
Range	29–400	20-713	

was used as the criterion for significance. Linear and multivariate regression analysis was used for analysis of confounding and quantitative variables, respectively.

Results

There were 100 mother-infant pairs enrolled in this study who were assigned to either the early (≤15 s) or late (>15 s) cord clamp time groups. The early cord clamp time group consisted of 30 infants, whereas 70 were enrolled in the late cord clamp time group. The groups were comparable with regard to the baseline characteristics of: maternal age, weight, Hgb, number of live children, neonatal birth weight, gestational age (Table 1), and neonatal gender (*P*=0.9) Multivariate-regression analyses were performed to rule out the effects of potentially confounding variables on infant Hct and Hgb at 48 hours postpartum. The differences among groups remained significant after control for: gestational age, mother's age and weight, infant birth weight, and number of children in the family (*P*<0.01). There was no significant difference in ferritin levels between the two groups (Table 2).

Ninety percent of vaginal delivery cases were from the late cord clamping group, which was significant (*P*<0.001). Polycytemia, a complication of delayed cord clamping, was not seen in any of the neonates within both groups.

Simple linear regression analysis between the time of cutting the cord and newborn Hct and Hgb levels 48 hours postpartum showed a positive effect due to early cord clamping on newborn Hgb in the Loess scatter plot (Figure 1).
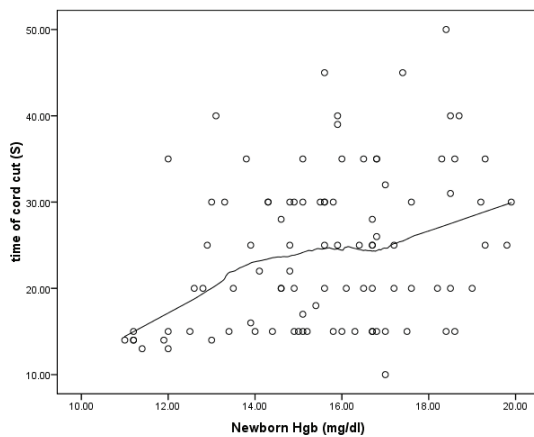
Figure 1: Loess scatter plot between newborn Hgb and cord clamp time

Discussion

Based on the cord clamping time, this study showed a significant difference between newborn Hgb and Hct (≤15 s and >15 s) 48 hours after birth. The equivalence of the groups at baseline (maternal age, weight, Hgb, number of live children, neonatal birth weight and gestational age) support the conclusion that the effect may be casual.

Significant higher ferritin levels and Hgb concentrations have been reported in newborns born with the Leboyer method of delivery (neonates placed on their mothers' abdomens, whose cords where clamped once pulsation ceased).[18] Studies in India and Guatemala in addition to other well-designed, well-executed randomized trials have shown higher venous Hct levels six hours after birth and the sustained effect of late clamping has been demonstrated by other indicators of infant hematologic status (iron stores and ferritin) at age six months.[19–21] This investigation was not undertaken in our study. Similarly, in the preterm population, late clamping has shown some potential benefits in terms of the decreased need for blood transfusion and lower risk of intraventricular hemorrhage as well as a reduced need for packed red cell transfusion 24 hours to 6 weeks after birth.[22–24]

Other uncontrolled studies, particularly in India and China, have shown no significant hematological differences between groups three to six months after birth.[25–26] The majority of trials did not adequately address the hematologic status of recruited mothers as a potential confounder in the relationship between clamping interval and risk of anemia during infancy.[21] We assessed mothers' Hgb levels in the two groups. The complications of late cord clamping, such as the increase in hyperviscosity, stroke volume, heart rate, cardiac output, and left to right shunt across the ductus arteriosus are still controversial.[18] Accordingly, there is no evidence of any significant harm as measured by the need for phototherapy to treat jaundice or by admission to the NICU.[27]

Among different studies, early cord clamping has been described as cord clamping that occurred immediately to 10 s after birth whereas late cord clamping could be prolonged until the time of placental delivery.[21] The volume of placental blood transfusion depends on the time of clamping and the position in which the infant is held prior to clamping and is estimated at approximately 35 mL/kg of birth weight or 32% of blood volume in a term infant kept at vaginal level with the cord clamped three minutes after birth or once pulsation ceased (Leboyer delivery).[28–29] One important issue is the possibility of overlap between the timing definitions of late and early cord clamping. The majority of trials did not provide data about the mean clamping time for the compared groups (Table 2). In this study, the mean difference in cord clamping was 13.9 s and no additional practices, such as neonatal positioning, were concomitantly used.

With multivariate-regression analyses, the differences among the early and late groups in Hct and Hgb levels 48 hours postpartum remained significant. ($P<0.01$). There was no significant difference in ferritin levels between the two groups (Table 2). Simple linear regression analysis between the time of cutting the cord and newborn Hct and Hgb levels 48 hours following delivery showed no statistical significance regarding the effect of these variables and cord time cut (Figure 1). Thus the effects of cord clamp time on neonate Hgb are shown at the lowest and highest time measurements, therefore a linear effect cannot be maintained. As such, the recommendation regarding the optimal time to clamp the umbilical cord for all infants (approximately three or more minutes after birth), is completely logical.[30]

The majority of randomized and unrandomized trials that have researched cord clamping divide

vaginally delivered births into two groups with the exception of two recent trials in 2006 that choose to include infants delivered by cesarean section.[28,30] In this study, 50 cases, each, of infants delivered vaginally and by cesarean section were enrolled. Most infants in cesarean section group had delayed cord clamping (*P*<0.05). Delivery type can affect the time for cord clamping. Cesarean sections are performed in an operating room and the duration of cord clamp depends on the surgical procedure and cannot be delayed because of surgical complications to the mother (hemorrhage and infection). Elimination of this limitation gives permission to prolong this time manually in vaginal delivery; this can be another benefit of vaginal delivery as opposed to a cesarean section.[31]

Perhaps the most important finding is that the beneficial effects of late cord clamping appear to extend beyond the early neonatal period. Documented results estimated a significant (47%) reduction in the risk of anemia and a 33% reduction in the risk of having deficient iron stores at ages two to three months that occur with late clamping. Although this is of particular importance for developing countries in which anemia during infancy and childhood is highly prevalent, it is likely to have an important impact on all newborns, regardless of birth setting.[29]

Acknowledgements

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