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Research Article

Impact of Delayed Cord Clamping versus Umbilical Cord Milking on Neonatal and Maternal Outcomes

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Abstract

Background

Delayed cord clamping (DCC) at delivery is currently recommended to increase neonatal hemoglobin levels and reduce the risk of infant anemia.

Given the benefits to most newborns and concordant with other professional organizations, the American College of Obstetricians and Gynecologists now recommends a delay in umbilical cord clamping for at least 30-60 seconds after birth in vigorous term and preterm infants.

Although effects of umbilical cord milking (UCM) have been assessed in preterm neonates such evidence is sparse for term neonates.

Objectives

To investigate the effects of DCC and UCM on the hematological, hemodynamic and clinical parameters of full term neonates, and the postpartum maternal hemoglobin reduction in vaginal and caesarean deliveries.

Methods

Eligible full term neonates were involved in a prospective interventional trial. Neonates of DCC group had the umbilical cord clamped after 30 to 60 seconds of delivery; whereas in the UCM group, the umbilical cord milking was done after cutting and clamping the cord at 25cm from the umbilicus. Both groups got similar routine care. Neonatal hemoglobin, bilirubin and hemodynamic parameters, and postpartum maternal hemoglobin level were assessed after 24 hours of delivery.

Results

107 participants underwent DCC while 103 participants underwent UCM.

There were no significant differences between the DCC and UCM groups with regard to mean neonatal hemoglobin (17.4 ± 2.1 vs 17.3 ± 1.5 P= 0.96), and mean neonatal total bilirubin (5.3 ±1.5 vs 5.2 ± 1.5 P=0.82). All the neonates had the similar birth APGAR at 1 and 5 minutes.

The mean blood pressure was significantly higher but within normal range in the DCC group. No significant difference was observed in oxygen saturation, heart rate, respiratory rate and NICU admissions in the 2 groups. The postpartum hemoglobin reduction was also comparable in the 2 groups.

Conclusion

In term neonates, the DCC and UCM had comparable effect on neonatal and maternal outcomes. This study may give support to the practice of UCM in term deliveries when DCC is not feasible.

Introduction

For centuries, dynamic debate had surrounded the question of when to clamp and cut the umbilical cord of the newly born infant, and practices have ranged from one extreme to the other [1].

One essential goal of neonatal critical care is to deliver adequate oxygen to meet tissue demand. Increasing fetal hemoglobin by placental transfusion is a highly effective method of increasing cardiac output, enhancing arterial oxygen content and improving oxygen delivery. Placental transfusion is the transfer of residual placental blood to the baby during the first few minutes of age, its aim is to facilitate transfer of blood volume from the placenta to the newborn and can be accomplished by three different methods: delayed cord clamping (DCC), intact umbilical cord milking (I-UCM), and cut-umbilical cord milking (C-UCM) [2].

Around the 18 to 20 weeks of pregnancy, the blood is equally divided between the fetus and placenta. At birth around one third of the blood is retained in the placenta. Early cord clamping deprives the fetus from 20-35ml of blood for each kilogram of its body weight. If the cord clamping is delayed and placenta transfusion is completed, it gives a higher number of red blood cells that results in 20-30mg/kg of iron, which is enough for the fetus need for at least three months. On the other hand, the resulting bilirubin will lead to increased risk for jaundice requiring phototherapy [3].

The umbilical cord of a full term human neonate averages 50 to 70cm in length and 2cm in diameter [4]. It is estimated to contain approximately 108ml of blood, about one third of the blood volume in a term infant, which is approximates about 300ml [5]. The umbilical cord is easily accessible to the operator and if the umbilical blood can be forced in to the fetus this will invariably improve the fetal circulation with minimal delay. Umbilical cord milking or stripping has been considered as a method of achieving increased placental transfusion to the newborn in a rapid time frame, usually less than 10-15 seconds. However, umbilical cord milking has not been studied as rigorously as delayed umbilical cord clamping. Several ongoing studies are evaluating the possible benefits and risks of umbilical cord milking compared to delayed cord clamping, especially in extremely preterm infants. Currently, there is insufficient evidence to either support or refute umbilical cord milking in term or preterm infants [6].

Methods

Study Design

The study was a prospective interventional trial that was conducted in the Department of Pediatrics, Neonatal Unit and Department of Obstetrics, at Makassed General Hospital, between August 2017and February 2018. The study was approved by the Institutional Ethical Committee (IEC), at Makassed General Hospital. Consent was from the eligible mothersWe included pregnant females who had singleton term pregnancies (37-42 weeks of gestation) planned for vaginal delivery or cesarean section.

We excluded those with cord anomalies like true knots or cord prolapse, non-vigorous babies, major congenital anomalies, in utero growth restriction, placental abruption, placental implantation disorders, Rh and ABO incompatibility, ante-partum hemorrhage, maternal diabetes.

Methodology

The primary outcome was the hemoglobin level (Hb) at 24 hours of life of neonates.

Secondary outcomes were the following

(A) Hemodynamic Parameters: heart rate, respiratory rate, blood pressure, temperature, oxygen saturation, blood glucose at birth and at 24 hours of life

(B) Clinical Parameters: respiratory distress, indirect hyperbilirubinemia requiring phototherapy

(C) Maternal postpartum hemoglobin level

Bilirubin levels were interpreted by using phototherapy and exchange transfusion charts of American Academy of Pediatrics.

Eligible neonates between August and November 2017 underwent delayed cord clamping for 30-60 seconds after delivery (DCC group).

While in the following period (December 2017 till February 2018), umbilical cord milking after immediate clamping (UCM group) was performed.

In DCC, the delivering obstetrician was informed about the intervention to delay the clamping for 30-60 seconds which was noted by using the Apgar timer on the resuscitation bed.In vaginal deliveries, the babies were held at the level of the introitus and over the thighs of mother in caesarean section while the intervention was done.

In UCM group, the cord was cut at approximately 25cm of length from umbilical stump, and then the baby was placed under the radiant warmer. The umbilical cord was raised and milked from the cut end toward the infant 3 times with speed at 10cm/ sec, and then clamped 2-3cm from the umbilical stump. Resident doctors involved in delivery and newborn resuscitation were trained for technique of cord milking.

In both groups neonates received the same routine care at birth and early breast feeding was encouraged.

Data Collection

The maternal data and other demographic characteristics were collected from mother and clinical notes which includes maternal age, gestational age, gravidity, mode of delivery, BMI, smoking, IV iron during pregnancy, and medical illnesses during pregnancy.

Neonatal Assessment

At birth, neonates were assessed for the following: gender, Apgar score, resuscitative measures, birth weight, temperature, oxygen saturation, heart rate, blood pressure (systolic, diastolic and mean BP), respiratory rate and blood glucose.

Late neonatal outcomes at 24 hours of life include oxygen saturation, heart rate, blood pressure (systolic, diastolic and mean BP), respiratory rate, hematological parameters (complete blood count), total bilirubin level, and the need for admission to NICU.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS, version 24) was used for data entry, management, and analysis. Categorical variables were presented as a number and percent, whereas continuous variables were presented as mean and standard deviation. Bivariate analysis was carried out by using the Chi square for comparing categorical variables, whereas continuous ones were compared using the Student's t-test. A p value ≤ 0.05 was indicated statistical significant.

Results

Two Hundred and ten pregnant mothers were assessed for eligibility. 107 underwent DCC while 103 underwent UCM.

Table 1: *Baseline maternal and neonatal characteristics*

Characteristics	**DCC n=107**	**UCM n=103**	**P -value**
Maternal age			
< 20	5 (4.7%)	1 (1.0%)	0.32
20-30	58 (54.2%)	60 (58.3%)	
>30	44 (41.1%)	42 (40.8%)	
Gestational age (weeks) Mean (SD)	38.5 (0.9)	38.6 (1.0)	0.32
Gravidity, Mean (SD)	2.5 (1.5)	2.7 (1.8)	0.39
Primi gravida (G1)	31 (29.0%)	31 (30.1%)	0.35
2nd gravid (G2)	32 (29.9%)	30 (29.1%)	
3rd gravida (G3)	22 (20.6%	13 (12.6%)	
Multi gravida (G>3)	22 (20.6%)	29 (28.2%)	
Maternal mode deliver			
C section delivery	70 (65.4%)	65 (63.1%)	0.73
NVD	37 (34.6%)	38 (36.9%)	
Maternal BMI Mean (SD)	29.6 (4.7)	30.8 (4.8)	0.07
Maternal Smoking	44 (41.1%)	32 (31.1%)	0.13
IV iron during pregnancy	1 (0.9%)	2 (1.9%)	0.62
Anemia during pregnancy	6 (5.6%)	2 (1.9%)	0.28
Hypertension during pregnancy	5 (4.7%)	3 (2.9%)	0.72
Preterm labor during pregnancy	9 (8.4%)	7 (6.8%)	0.66
Infections during pregnancy	6 (5.6%)	1 (1.0%)	0.12
Hypothyroidism during pregnancy	4 (3.7%)	3 (2.9%)	1.00
Neonate Gender			
Male	57 (53.3%)	43 (41.7%)	0.09
Female	50 (46.7%)	60 (58.3%)	
Birth weight mean (SD)	3146.9 (401.9)	3082.4 (406.6)	0.25

Table 2 presents a comparison between DCC and UCM groups regarding the neonatal investigations at 24 hours of age, the mean hemoglobin and hematocrit were comparable in both groups, the neonatal hemoglobin was 17.4 ± 2.1gm/dl and 17.3 ±1.5gm/dl in DCC and UCM respectively (P=0.96). Furthermore, there were no significant differences between the DCC and UCM groups with regard to mean serum bilirubin level 5.3 ± 1.5 vs 5.2 ±1.3, P= 0.82).

Table 2: *Hematological outcomes at 24 hours of life*

Parameters at 24 hours	DCC n=107	UCM N=103	P-value
Neonatal Hemoglobin (g/dl) Mean (SD)	17.4 (2.1)	17.3 (.5)	0.96
Neonatal Hematocrit Mean (SD)	52.6 (6.7)	53.4 (4.8)	0.34
Less than 15	11 (10.3%)	5 (4.9%)	0.11
15-18.5	63 (58.9%)	76 (73.8%)	
18.5-21.5	30 (28.0%)	21 (20.4%)	
More than 21.5	3 (2.8%)	1 (1.0%)	
Neonatal wbc Mean (SD)	17.8 (5.2)	18.7 (5.2)	0.25
Neonatal Platelets Mean (SD)	284.9 (74.5)	273.9 (67.7)	0.27
Serum Bilirubin (mg/dl) Mean (SD)	5.3 (1.5)	5.2 (1.3)	0.82

Comparison between DCC and UCM groups concerning vital signs at birth, showed no statistically significant differences between both DCC and UCM groups regarding their oxygen saturation, neonatal temperature, systolic, diastolic BP, respiratory rate and glucose level at birth. Although, a higher mean blood pressure at birth and at 24 hours of life were observed in DCC.

A higher heart rate was observed at birth in UCM group and no difference at 24 hours of life (table 3).

Table 3: *Hemodynamics and related neonatal outcomes*

	DCC n=107	UCM n=103	P-value
APGAR 1 min mean (SD)	8.7 (0.5)	8.7 (0.5)	0.98
APGAR 5 min mean (SD)	9.7 (0.4)	9.7 (0.5)	0.63
Oxygen saturation mean (SD)			
Birth	97.4 (2.4)	97.2 (2.5)	0.52
24 hours	98.3 (1.2)	97.9 (1.4)	0.09
Temperature mean (SD)			
Birth	36.7 (0.2)	36.7 (0.2)	0.42
SBP (mmHg) mean (SD)			
Birth	71.5 (6.9)	70.4 (6.1)	0.19
24 hrs	74.2 (6.7)	71.1 (5.9)	0.001
DBP (mmHg) mean (SD)			
Birth	39.9 (6.7)	39.2 (6.1)	0.46
24 hrs	42.9 (7.3)	41.4 (4.4)	0.08

MBP (mmHg) mean (SD) Birth 24 hrs	50.5 (5.8) 53.3 (6.9)	48.6 (5.7) 50.9 (4.6)	0.01 0.004
HR(b/min) mean (SD) Birth 24 hours	143.9 (11.9) 136.1 (11.1)	147.8 (10.8) 138.3 (10.5)	0.02 0.13
RR (b/min) mean (SD) Birth 24 hours	52.9 (11.7) 49.1 (9.9)	53.2 (10.2) 49.5 (7.9)	0.89 0.78
Glucose, mean (SD) Birth	61.7 (12.5)	61.7 (10.1)	0.97
Hypoglycemia, ≤ 40	5 (4.7%)	4 (3.9%)	1.00
RR at birth, ≥ 60	18 (16.8%)	10 (9.7%)	0.13
NICU admission	11 (10.3%)	8 (7.8%)	0.53
Need for oxygen	10 (9.3%)	7 (6.8%)	0.49
NICU admission for respiratory distress	9 (8.4%)	7 (6.8%)	0.66

Figure 1 reveals that NICU admissions after birth were similar in both groups (p=0.53).

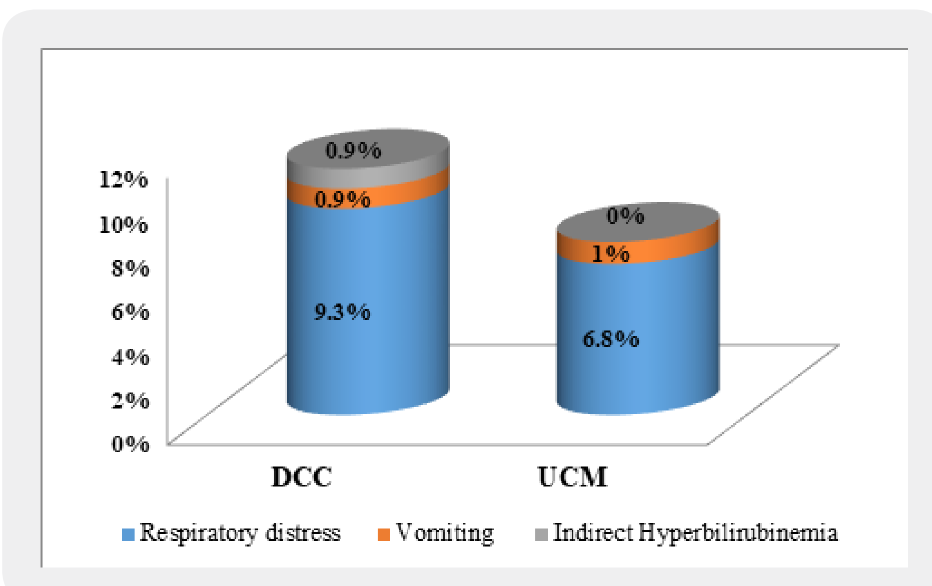

***Figure 1:** Comparison between DCC and UCM regarding neonatal need for NICU admission*

According to figure 2, there was statistically significant differences (p =0.77) between both DCC and UCM groups in relation to postpartum mean hemoglobin level and postpartum hemoglobin reduction, nor in the postpartum use of blood products (table 4).

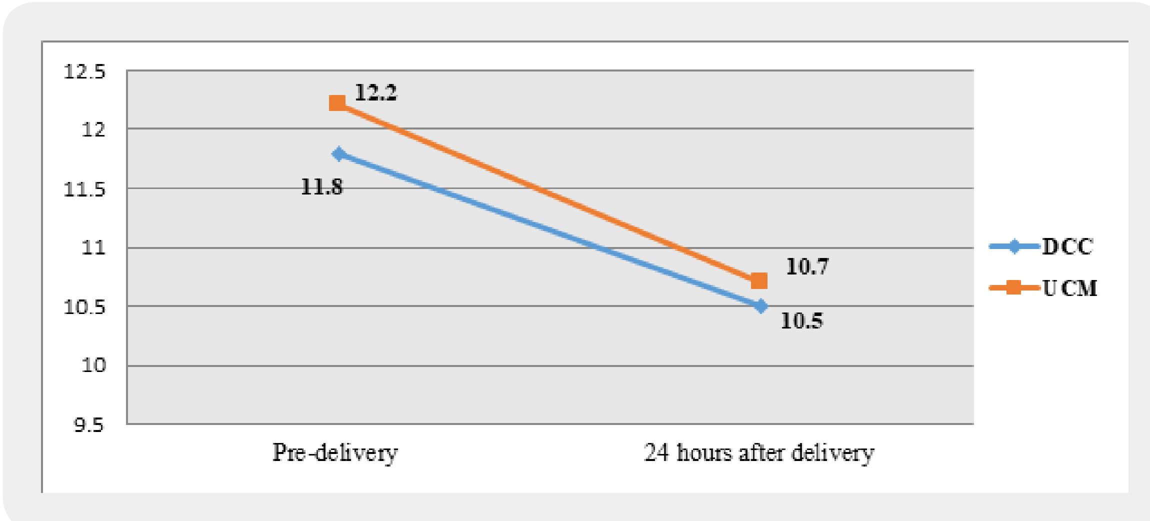

Figure 2: *Comparison between DCC and UCM regarding maternal hemoglobin reduction*

Table 4: *Postpartum use of blood products*

	DCC n=107	UCM n=103	P- value
Post delivery medications			
None	96 (89.7%)	90 (87.4%)	0.83
Post delivery IV iron	10 (9.3%)	12 (11.7%)	
PRBC transfusion	1 (0.9%)	1 (1.0%)	

Discussion

The term *early clamping*, before the mid-1950s, was defined as umbilical cord clamping within 1 minute of birth, in contrast to *late umbilical cord clamping* that was defined as umbilical cord clamping more than 5 minutes after birth. Studies have showed that blood volume changes after birth was reported as 80-100mL of blood that transfers from the placenta to the newborn in the first 3 minutes after birth [7] and up to 90% of that blood volume transfer was achieved within the first few breaths in healthy term infants [8]. The interval between birth and umbilical cord clamping began to be shortened based on these early observations and the lack of specific recommendations regarding optimal timing and it became common practice to clamp the umbilical cord shortly after birth, usually within 15-20 seconds. Nonetheless, more randomized controlled trials of term and preterm infants as well as physiologic studies of blood volume, oxygenation, and arterial pressure have evaluated the effects of early versus *delayed umbilical cord clamping* (usually defined as cord clamping at least 30-60 seconds after birth) [9,10].

The World Health Organization recommends that the umbilical cord not be clamped earlier than 1 minute after birth in term or preterm infants who do not require positive pressure ventilation. Recent Neonatal

Resuscitation Program guidelines from the American Academy of Pediatrics recommend delayed umbilical cord clamping for at least 30-60 seconds for most vigorous term and preterm infants. The Royal College of Obstetricians and Gynaecologists also recommends deferring umbilical cord clamping for healthy term and preterm infants for at least 2 minutes after birth. Additionally, the American College of Nurse-Midwives recommends delayed umbilical cord clamping for term and preterm infants for 2-5 minutes after birth [11].

Given the benefits to most newborns and concordant with other professional organizations, the American College of Obstetricians and Gynecologists now recommends a delay in umbilical cord clamping for at least 30-60 seconds after birth in vigorous term and preterm infants [6].

Different methods are utilized to calculate the magnitude of placental transfusion in clinical studies. Extending the time before cord clamping leads to a gradual increase in fetal-neonatal blood volume with a corresponding decrease in residual placental blood. Measurement of hemoglobin or hematocrit during the first 24h can provide a crude assessment of placental transfusion.

Several factors including cord clamping time, uterine contractions, umbilical blood flow, respirations and gravity have an important role in determining placental transfusion volumes. During fetal life, around 29% of the combined ventricular output flows through the umbilical arteries to the placenta and returns to the fetus via the umbilical vein. After birth, during the third stage of labor, and within 45 seconds, the umbilical arteries constrict, therefore diminishing the blood flow from the neonate to the placenta, whereas the umbilical vein remains patent facilitating placental transfusion [2]. 25 to 60% of the total blood circulating in the fetal-placental circulation at term is found in the placental circulation including 60% of the fetal red blood cells [7]. Clamping of the cord within the first 5 to 10 seconds of birth was reported to deprive the neonate of about 20-40ml/kg of blood, with concomitant deprivation of iron, which increases the risk of hypovolemia, anemia, and the consequences of loss of hematopoietic stem cells.

Cut-umbilical cord milking is a technique that involves clamping and cutting a long segment of the umbilical cord immediately at births then milking the entire contents into the baby [12].

The cord vein contains approximately 20ml of placental blood [13]. Rabe *et al* concluded that neonates could receive approximately 18ml/kg of whole blood by one-time milking of 30cm umbilical cord [14].

A randomized controlled trial conducted by Upadhyay *et al.* on 200 term babies, reported that UCM after birth leads to higher hemoglobin and better iron status at 6 weeks of age as compared to babies receiving early cord clamping [15]. Studies that compare either UCM [15] or DCC [16] to early cord clamping in term neonates, but only limited trials directly comparing the effects of DCC and UCM in term neonates.

The current study results pointed out that there was no significant difference between DCC and UCM groups regarding hemoglobin levels at 24 hours of life, the mean neonatal hemoglobin was 17.4 ± 2.1 and 17.3± 1.5 in DCC and UCM. Theoretically, delaying the cord clamping for a longer period of time could lead to more passage of transcord blood than milking due to connectivity to bigger pool of blood in placenta, however, this has not been observed in our study.

Our result is congruent with the results published by Piyadigama I *et al* [17]. That evaluated the effects on Hemoglobin, bilirubin and hemodynamic parameters in neonates, and the blood loss in the mother between UCM and DCC during elective caesarean delivery at term, it showed that mean neonatal hemoglobin at 24-48 hours after delivery was almost comparable in both groups (17.6g/dl ± 2 vs 17.4g/dl ± 2.4, P=0.67). Furthermore, Jaiswal *et al* [18], who had conducted a study entitled 'Comparison of Umbilical Cord Milking and Delayed Cord Clamping in Term Neonates: A Randomized Controlled Trial' the mean hemoglobin at 48 hours of life was 15.9 ±2.2 and 16.2 ±2.4 in DCC and UCM groups respectively.

There is a widespread belief that placental transfusion through DCC or UCM increases the risk of jaundice, which hindered the adoption of placental transfusion techniques in practice The finding of the current study indicated that, the mean total bilirubin level at 24 hours of life in the two groups was statistically insignificant. Although we report one case in DCC group that developed indirect hyperbilirubinemia that was admitted at hours 96 of life to NICU, bilirubin level reached 20mg/dl that required intensive phototherapy. Jaiswal P *et al* showed no statistical difference in the NICU admission for phototherapy, although a higher percentage was seen in DCC group.

We found a higher mean blood pressure and systolic blood pressure at 24 hours of life in DCC and within normal range of gestational age-specific normograms. There are some concerns about adverse effects of flushing the extra blood into the pressure passive cerebral circulation of neonates, healthy neonates can autoregulate their cerebral blood flow and thus can avoid transmitting fluctuation in the systemic blood pressure [19], Although this might not have been clinically significant in term healthy infants, a gain of 4mm Hg may be important in hypotensive babies because of hypovolemia.

Additionally, the current study had reported that no significant difference was observed regarding the rate of NICU admission among the two groups. Although the percentage of neonates that required NICU admission for respiratory distress, and need for oxygen was higher in DCC group but it was not statistically significant. The current study results revealed that no significant differences were observed between DCC and ECC groups in relation to postpartum maternal complications, need for IV iron therapy or PRBC transfusion. In our study the hemoglobin drop was 1.4g/dl in both groups.

We demonstrated that in full term neonates, the hematological and hemodynamic effects of umbilical cord milking (UCM) were similar to those of delayed cord clamping (DCC) after 30-60 seconds of birth. Both interventions led to comparable hemoglobin at birth, without any significant side effects at 24 hours of life.

Limitations of the study are the lack of randomization, and a longer follow up till 6 to 12 months after birth is desirable.

Conclusion

Although AAP has recommended DCC for all newborns yet, it may not be feasible in all deliveries, especially in babies who require resuscitation at birth. UCM also increases the placental and cord blood transfusion to the newborn and can potentially improve their hematological status.

UCM offers the primary advantage of speed. The actions can be completed in a matter of seconds, the maneuvers are readily accomplished at caesarean section, and the baby can be immediately transferred to the pediatric team for any needed resuscitation. Entire surgical teams do not need to pause during a caesarean section Transfer of blood occurs as a bolus rather than a process of equilibration as with delayed cord clamping; milking often is accomplished in 15s or less [20,21].

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