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EFFECTS OF UMBILICAL CORD MILKING ON HEMATOLOGICAL PARAMETERS IN TERM NEONATES: A CASE CONTROL STUDY IN A TERTIARY CARE HOSPITAL

Summary

Delayed cord clamping (DCC) and Umbilical cord milking (UCM) are the two methods of placental transfusion. Both interventions improve hemoglobin, are safe with no risk of polycythemia and hyperbilirubinemia. UCM is beneficial in situation where DCC is not feasible or contraindicated.

Objectives. 1) Comparison of UCM and DCC on following hematological parameters in term neonates-Cord Hemoglobin at birth, Hemoglobin, Hematocrit and Bilirubin at 48 hours of life. 2) To compare Hb and ferritin levels of infants born with UCM to that of DCC at 6 weeks of age.

Material and methods. A Prospective Case-Control Study. Newborns delivered by normal vaginal and elective lower segment cesarean section underwent DCC. Neonates in whom DCC was not feasible underwent UCM. 56 neonates in each group were followed up to 6 weeks. Cord hemoglobin at birth, hemoglobin, hematocrit and bilirubin were sent at 48 hours, and during 6 weeks of life, Hb and serum ferritin was estimated in both groups and compared.

Results: At 48 hours, mean hemoglobin is 18.75 and 19.38 g/dL, mean hematocrit is 52.20 and 53.94 %, and mean total bilirubin is 11.56 and 10.39 mg/dL in the DCC and UCM groups, respectively. Mean hemoglobin at 6 weeks is 11.37 and 11.6 gm/dL and mean serum ferritin is 207.2 and 252.63 mcg/L in the DCC and UCM groups, respectively. No increase in the incidence of neonatal jaundice or polycythemia was observed in either group.

Conclusion. Both the methods of placental transfusions DCC and UCM are equally effective and have comparable benefit on hematological parameters in full term neonates at 48 hours of life and at 6 weeks of life.

Key words: Umbilical Cord Milking; UCM; Delayed Cord Clamping; DCC; Placental Transfusion.

Introduction

Iron deficiency anemia of infancy is associated with poor cognitive, physical, social, and emotional outcomes. The most important finding regarding iron deficiency anemia of infancy is that its effects are usually permanent and do not improve with iron supplementation [1]. The lifelong, irreversible effects of iron deficiency anemia during infancy underscore the notion that prevention of iron deficiency anemia is better than treatment, especially during infancy and early childhood [2]. Iron stores at birth determine iron status during infancy and early childhood. Therefore, any intervention that increases total body iron stores at birth is important [3]. Blood continues to flow through the umbilical arteries (from the newborn to the placenta) for 20-25 seconds after birth and then becomes negligible by 45 seconds. Blood continues to flow from the placenta to the newborn in the umbilical vein for up to 3 minutes after birth [4, 5].

Early Cord Clamping (ECC) or Immediate Cord Clamping (ICC) is the clamping of the umbilical cord within 30 seconds of birth. It may not be beneficial to the newborn and can deprive the newborn of up to a quarter of its blood volume and iron stores [6].

Placental transfusion is an additional volume of blood transferred to the newborn during birth. Within 1 minute of birth, approximately 80 ml of placental blood is transferred to the newborn, reaching 100 ml by 3 minutes in term newborns. This provides about 40-50 mg/kg of iron to term newborns, which can prevent iron deficiency anemia during the first year of life [7].

In delayed cord clamping (DCC), placental transfusion occurs passively at a slow rate and is usually dependent on uterine contractions. In umbilical cord milking (UCM),

placental blood transfusion is done actively by milking the blood towards the baby. It's preferred in cases where a depressed infant needs resuscitation and DCC is not possible or appropriate [10].

UCM increases circulating blood volume, decreases the need for blood transfusion, reduces the incidence of high-grade intraventricular hemorrhage in preterm infants, increases iron stores, and improves hemoglobin by 6 months of age [12]. When UCM is performed at birth, increased ferritin levels are observed in late preterm infants at 6 weeks of age [13]. There is evidence strongly suggesting that umbilical cord milking effectively increases placental blood transfusion, which is rich in stem cells and red blood cells at birth, resulting in benefits superior to immediate cord clamping (ICC) [14]. UCM is more beneficial in neonates where DCC is not possible.

Objectives. 1) Comparison of UCM and DCC on following hematological parameters in term neonates-Cord Hemoglobin at birth, Hemoglobin, Hematocrit and Bilirubin at 48 hours of life. 2) To compare Hb and ferritin levels of infants born with UCM to that of DCC at 6 weeks of age.

Material and methods

Study design. The present study is a hospital based prospective case-control study conducted at Department of Paediatrics Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital (SDMCMS&H), Dharwad, India. The study period was one year from December 2019 to November 2020. The study was approved by the institutional ethics committee. All the relevant data were collected in a pre-designed proforma after obtaining informed consent from the parents or guardians.

All term neonates (37 weeks to 41+6 weeks of gestation) delivered by either vaginal delivery or lower segment cesarean section (LSCS) to non-anemic mothers (with maternal Hb more than 11 g/dl) during the study period were included in the study.

Neonates born to mothers with conditions such as hemodynamic instability, abnormal placentation, abruptio placentae, placenta previa, maternal hemorrhage (i.e. Neonates born to mothers with conditions such as hemodynamic instability, abnormal placentation, abruptio placenta previa, maternal hemorrhage (i.e., bleeding placenta previa), active maternal seizure, placental and neonatal conditions in which placental circulation is not intact (e.g., tight nuchal cord, vasa previa, cord avulsion, IUGR with abnormal Doppler evaluation), Rh isoimmunization, twins/multiples, or major congenital malformations were excluded from the study.

These neonates were divided into groups based on the intervention performed. The neonates without risk factors underwent DCC and those term neonates in whom DCC is not feasible were assigned to UCM. Neonates who required resuscitation at birth, umbilical cord milking was done simultaneously by two separate persons involved in neonatal resuscitation without disturbing/delaying for resuscitation. The neonates in whom UCM was performed were considered as cases and the neonates in whom DCC was performed were considered as controls.

In our study, DCC was defined as delay in clamping the umbilical cord until pulsation stops or up to 2 to 3 minutes after delivery. UCM is defined as a procedure in which an

intact cord or a cut cord is grasped and blood is pushed 3-4 times towards the neonate in a time frame of about 20 seconds.

All the details of the newborns were recorded in a pre-designed proforma. All neonates included in the study were sent for umbilical cord hemoglobin. After 48 hours of birth, hemoglobin hematocrit and bilirubin levels were sent and the results were compared between both the groups. Both groups of newborns were monitored daily for clinical signs of jaundice and polycythemia. These newborns were followed up at OPD at 6 weeks of age. These neonates were advised to breastfeed exclusively and were not given any supplements other than vitamin D3. At 6 weeks, serum hemoglobin and ferritin were measured and compared between the two groups. Hemoglobin and hematocrit levels were estimated using a Sysmex XN1000 fully automated analyzer, bilirubin levels were estimated using a SEIMENS EXL-200 machine, and serum ferritin was estimated using a SIEMENS ADVIA CENTAUR X P machine by chemiluminescence immunoassay.

Statistical Analysis. All data were entered into Microsoft Excel version 2203 and analyzed using SPSS software version 23.0 for Windows (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as percentages and continuous variables as mean + SD or median. Chi-squared test was used to analyze categorical variables, and Student's independent t-test was used to analyze continuous variables. p-value <0.05 was considered significant.

Results. There were 5201 deliveries during the study period. A total of 866 mothers were eligible for the study.

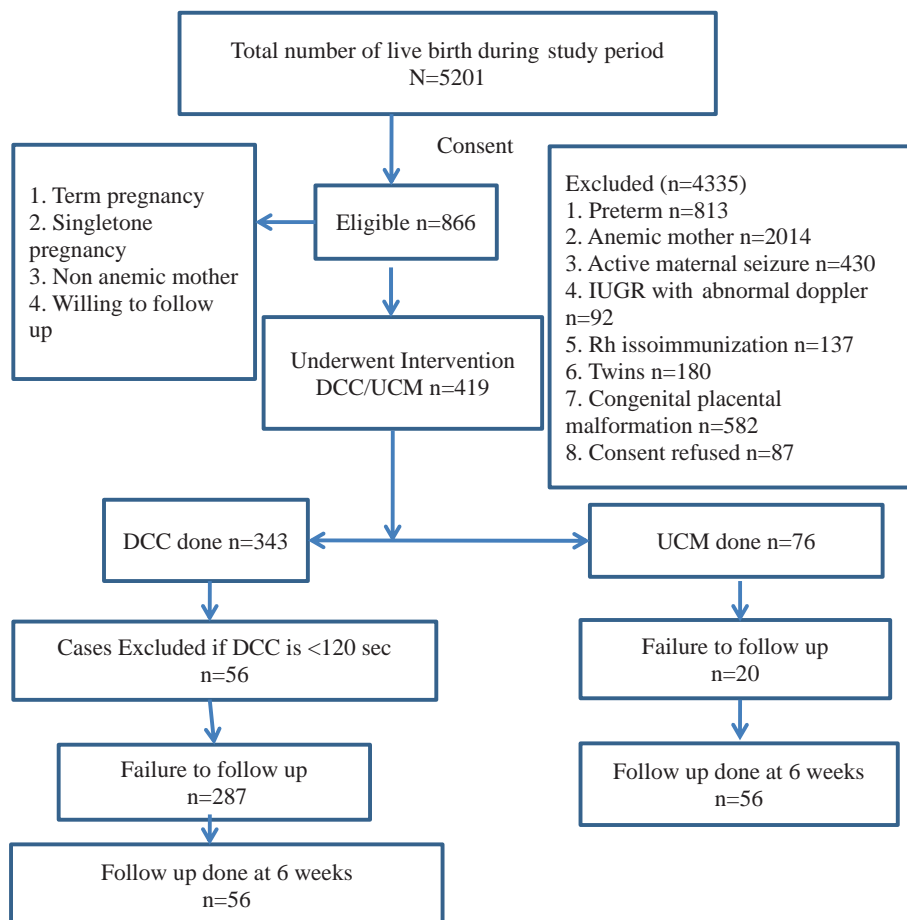


Fig. 1. Flow chart of study

As shown in Figure 1, 419 neonates underwent the intervention. The 56 neonates of UCM group were taken as cases and 56 neonates of DCC group were taken as controls and all the relevant data were collected from both the group and the results were compared between two groups. Neonates of both the groups were followed up till 6 weeks of age.

In our study, out of 112 infants, 48 were boys (20 in DCC group and 28 in UCM group) and 64 were girls (36 in DCC group and 28 in UCM group) as shown in Figure 2 above. There was no significant statistical difference in gender between the two groups.

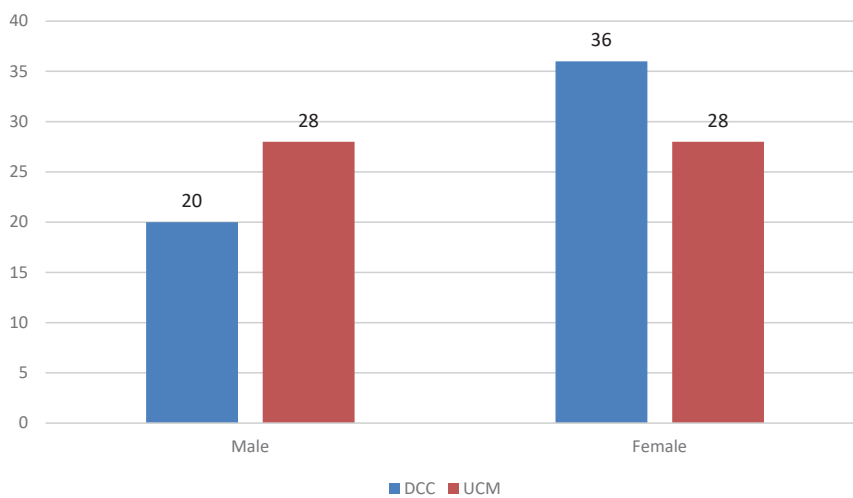
The mean birth weight in DCC group was 2.92 kg and in UCM group was 2.84 kg with mean difference of 0.09, it was not statistically significant with p value of 0.227.

As shown in Table 2, the mean hemoglobin and hematocrit levels were higher in UCM group compared

to DCC group, but the difference was not statistically significant. The mean TSB (total serum bilirubin) at 48 hours is 11.56 mg/dL in DCC group and 10.39 mg/dL in UCM group. TSB levels are higher in the DCC group than in the UCM group and this difference was statistically significant.

As shown in the Table 1, there is no statically significant difference in the cord hemoglobin between both the groups.

8.92 % (n=5) neonates in each group had hyperbilirubinemia requiring phototherapy for 12 to 24 hours. The mean peak serum total bilirubin among infants admitted for phototherapy was 14.976 mg/dL in the DCC group and 15.548 mg/dL in the UCM group, with a mean difference of 0.572. None of the babies in both the groups had hyperbilirubinemia of exchange transfusion range. Both methods of placental transfusion are safe and have no risk of hyperbilirubinemia.



*p-value = 0.127

Fig. 2. Gender wise comparison of both study group

Table 1

Comparison of both group for cord hemoglobin, g/dL

Group	Mean Hb	SD	p value
DCC	15.58	1.01	0.0706
UCM	15.74	1.08	

Table 2

Comparison of hematological parameter between both the groups at 48 hours

Group	DCC		UCM		p-value
	Mean	SD	Mean	SD	
Hb, g/dL	18.75	1.80	19.38	1.81	0.0693
Hematocrit, %	52.20	4.70	53.94	4.86	0.0500*
Total bilirubin, mg/dL	11.56	2.43	10.39	3.30	0.0339*
Direct bilirubin, mg/dL	0.38	0.14	0.35	0.17	0.3347

*p-value < 0.05

Table 3

Comparison of two groups cord Hb, Hb at 48 hours and 6 weeks

Time points	DCC group		UCM group		p-value
	Mean	SD	Mean	SD	
Cord Hb, g/dL	15.58	1.01	15.74	1.08	0.0706
Hb at 48 hours, g/dL	18.75	1.80	19.38	1.81	0.0693
Hb at 6 weeks, g/dL	11.37	1.23	11.61	1.36	0.3172

As shown in Table 3, the mean cord hemoglobin in the DCC group is 15.28 g/dL and in the UCM group is 15.74 g/dL. The mean difference was 0.16. Mean hemoglobin at 48 hours of life in DCC group is 18.75 g/dL and in UCM group is 19.38 g/dL and mean difference is 0.63. Hemoglobin value done during follow up at 6 weeks in both groups showed that, mean Hb of 11.37 and 11.61 g/dL in DCC group and in UCM group

respectively and mean difference was 0.25. There was no statistically significant difference in hemoglobin values between both the groups at 48 hours, 6 weeks and cord hemoglobin.

As shown in the Figure 3, mean increase in hemoglobin levels at 48 hours in both groups. And we also noticed fall in hemoglobin levels at 6 weeks follow-up both groups, which corresponds to physiological anaemia of infancy.

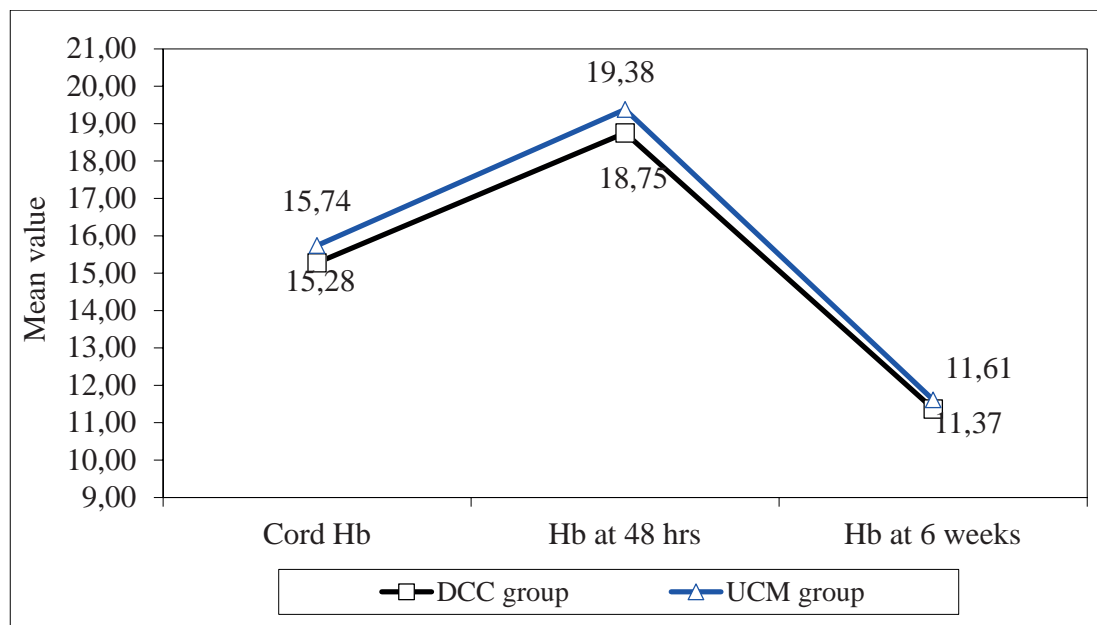


Fig. 3. Comparison of trends of change in hemoglobin (g/dL) value in both the groups

Table 4

Comparison of two groups ferritin at 6 weeks, mcg/L

Time points	DCC group		UCM group		p-value
	Mean	SD	Mean	SD	
Ferritin at 6 weeks	207.2	69.98	252.63	130.02	0.0233*

* $p < 0.05$

Table 4 shows that the mean serum ferritin level in DCC group is 207.2 and in UCM group is 252.63 (mcg/L). Mean difference is 45.39, there is statistically significant difference in serum ferritin levels (corresponding to iron storage levels) at 6 weeks of follow-up. Neonates who underwent UCM have comparatively more iron stores than the neonates who underwent DCC. During the 6-week follow-up period, none of the infants were readmitted to the hospital or received a blood transfusion.

Discussion. We compared the effects of cord milking with those of delayed cord clamping on hematologic parameters at 48 hours and 6 weeks of age in term neonates. We observed that cord milking in term neonates is as safe and effective as delayed cord clamping in improving hemoglobin levels and iron stores.

In the present study, there was no statistically significant difference between the mean hemoglobin levels in both the groups, hence both the groups, cases and controls were comparable. The results were in par with the results of the study done by Jaiswal et al [12], Panburana et al [7], Yadav et al and Singh and Gupta et al [15, 16].

It was observed that at 6 weeks follow-up of both the study groups the mean hemoglobin levels remains same, there was no statistically significant difference in mean hemoglobin values. These results were comparable to the studies done by Jaiswal et al and Yadav et al [12, 15]. However, Hb levels and serum ferritin levels were significantly higher in our study as compared to the study conducted by Jaiswal et al [12]. In the study conducted by Upadhyay et al [13], the serum ferritin levels are higher in UCM group than in DCC group at 6 weeks follow-up, which correlates with the results of our study. However, the serum ferritin level of DCC group was higher in the study of Yadav et al [15].

In a study conducted in 2006 by Chaparro et al [17], the ferritin level at 6 months of age was higher in the DCC group than in the ECC group (mean difference of 11.80 $\mu\text{g/L}$). In the study by R. Bora et al [3] in 2012-13, the mean serum ferritin at 6 months of follow-up in the ECC group was 70.8 ng/mL, while in the UCM group it was 113.9 ng/mL, with a mean difference of 43.9 ng/mL, which was statistically significant. In another study by Upadhyay A. et al [11] in 2013, the mean serum ferritin at 6 weeks follow-up was significantly higher in UCM

group (355.9 mcg/L) than in ICC group (177.5 mcg/L). In the present study, serum ferritin at 6 weeks follow-up was higher in DCC group compared to UCM group.

In our study, 8.92 % (n=5) neonates in each group had hyperbilirubinemia requiring phototherapy which was higher than the study of Upadhyay A. et al [11] where none of the neonates had peak hyperbilirubinemia requiring intensive phototherapy or exchange transfusion. The studies by Panburana et al, Upadhya A. et al, Jaiswal et al and Yadav et al [7, 11, 12, 15] showed a difference in the development of polycythemia between the immediate and delayed cord clamping groups. But in these studies, the results were compared with groups that had ICC and DCC. In our study, the DCC group was compared with the UCM group, but none of the group neonates had polycythemia requiring monitoring or intervention.

Conclusions. UCM is as effective as DCC in achieving higher hemoglobin and ferritin levels in term neonates. At 48 hours of life, both interventions yield

similar results in terms of hematological parameters such as hemoglobin, hematocrit and serum bilirubin levels. UCM has resulted in higher iron reserves at 6 weeks in short-term follow-up, thus helping to reduce the burden of anemia in these infants. UCM is a safe and effective intervention with no additional increase in risk of polycythemia and neonatal hyperbilirubinemia compared to DCC. UCM is beneficial in neonates where DCC is not feasible and/or contraindicated, particularly in neonates who require resuscitation at birth. Since DCC has already been universally recommended by WHO, American Academy of Paediatrics and ACOG as the standard of care for placental transfusion, we recommend the use of UCM in term neonates when DCC is not an option.

Conflict of interest. The authors have no conflicts of interest to declare.

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ВПЛИВ ЗЦІДЖУВАННЯ ПУПОВИННОЇ КРОВІ НА ГЕМАТОЛОГІЧНІ ПАРАМЕТРИ У ДОНОШЕНИХ НОВОНАРОДЖЕНИХ: ДОСЛІДЖЕННЯ «ВИПАДОК-КОНТРОЛЬ» В ЛІКАРНІ ТРЕТИННОГО РІВНЯ МЕДИЧНОГО ОБСЛУГОВУВАННЯ

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Резюме.

Відстрочене перетискання пуповини (Delayed cord clamping, DCC) і зцідження пуповинної крові (Umbilical cord milking, UCM) є двома методами плацентарної трансфузії. Обидва втручання підвищують рівень гемоглобіну, є безпечними, не викликають поліцитемії та гіпербілірубінемії. UCM є корисним у ситуації, коли DCC неможливий або протипоказаний.

Мета дослідження. 1) Порівняння UCM і DCC щодо наступних гематологічних параметрів у доношених новонароджених: гемоглобін пуповинної крові при народженні, гемоглобін, гематокрит і білірубін через 48 годин життя. 2) Порівняти рівні гемоглобіну та феритину у немовлят, народжених із застосуванням UCM, порівняно з технологією DCC, у віці 6 тижнів.

Матеріал і методи дослідження. Проспективне дослідження типу «випадок-контроль». Дітям, народженим шляхом звичайного вагінального та планового кесаревого розтину нижнього сегмента, проведено DCC. У випадках, де DCC не було можливим, проведено UCM. За 56 новонародженими у кожній групі спостерігали до 6 тижнів. Гемоглобін пуповини при народженні, гемоглобін, гематокрит і білірубін визначали через 48 годин, а протягом 6 тижнів життя оцінювали рівень гемоглобіну та феритин сироватки в обох групах.

Результати дослідження. Через 48 годин середній рівень гемоглобіну становив 18,75 і 19,38 г/дл, середній гематокрит становив 52,20 і 53,94 %, а середній рівень загального білірубину – 11,56 і 10,39 мг/дл у групах DCC і UCM відповідно. Середній рівень гемоглобіну через 6 тижнів становив 11,37 і 11,61 г/дл, а середній рівень сироваткового феритину – 207,2 і 252,63 у групах DCC і UCM відповідно. В обох групах не спостерігалось підвищення частоти неонатальної жовтяниці або поліцитемії.

Висновок. Обидва методи плацентарної трансфузії DCC і UCM є однаково ефективними та мають порівнянну користь щодо гематологічних параметрів у доношених новонароджених на 48-й годині та на 6-му тижні життя.

Ключові слова: зцідження пуповинної крові; UCM; відстрочене перетискання пуповини; DCC; плацентарна трансфузія.

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