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ORIGINAL ARTICLE

Effect of Umbilical Cord Milking on Maternal and Neonatal Outcomes in a Tertiary Care Hospital in South India: A Randomized Control Trial

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Abstract

Background and Aim Umbilical cord milking (UCM) has been theorized to increase placental blood transfusion then again, the optimal method of cord clamping at birth is still contested. We aimed to analyse the effects of UCM on the neonatal haematological parameters at 72 h and 6 weeks of age and its association with any adverse effects.

Materials and Methods In this randomized control trial, mothers ≥ 34 weeks were randomized into two arms. Under the intervention group, the cord was milked three times before clamping and cutting whereas the controls had the cord clamped and cut without milking. Haemoglobin and haematocrit levels were measured at 72 h. and at 6 weeks.

Results A total of 170 mothers were enrolled with 85 subjects in each arm. Baseline characteristics were comparable. In the intervention arm, the mean haemoglobin [18.1 (2.4) g/dL] and haematocrit [54 (7) %] were significantly higher as compared to the control arm [16.4 (2.1) g/dL and 48 (6) %], at 72 h of age. There was also significant increase in the mean haemoglobin [11.6 (1.3) g/dL] and haematocrit [34 (4) %] compared to the controls [10.1 (1.1) g/dL and 30 (3) %], at 6 weeks. No statistical difference was found in the incidence of PPH and duration of third stage. There was no significant rise in hyperbilirubinaemia, phototherapy requirement and polycythaemia among neonates in the intervention group.

Conclusion Umbilical cord milking is a sound practical approach to raise the haemoglobin and haematocrit levels up to 6 weeks thereby decreasing the proportion of anaemic infants.

Keywords Cord milking · Neonate · Anaemia · Placental transfusion

Introduction

Immediate cord clamping (ICC) was introduced as part of routine care without meticulous evaluation. This method reduces placental transfusion and potentially deprives the new born baby of 20–30 mg/kg of iron, sufficient for the needs of a neonate for around 3 months (RCOG scientific impact paper, 2018). Conversely, umbilical cord milking (UCM), performed on a 30 cm length of the cord would transfuse approx. About 18 ml/kg of whole blood to the infant equivalent to 13 ml of packed red cells [1]. But studies on cord milking were limited and delayed cord clamping has gained favour for term and preterm infants (ACOG committee opinion, 2017) as standard practice. However, a recent systematic review inferred that UCM resulted in haemoglobin (Hgb) and haematocrit (HCT) levels similar to delayed clamping with the benefit of being completed in a short time [2]. Also, a meta-analysis had not found any association of UCM with increased incidence of hyperbilirubinaemia or other neonatal complications [3]. Albeit, currently evidence is insufficient to confirm or refute the benefits from UCM in infants and before we adopt it universally, we need to analyse the potential dangers as well.

We aimed to investigate (1) the effects of UCM on the haematological parameters at 72 h and 6 weeks of age among late preterm and term neonates when compared to

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ICC and (2) if this intervention resulted in any maternal or neonatal sequelae.

Materials and Methods

This was a single centre, blinded, placebo-controlled parallel-group study with balanced randomization (1:1) conducted from November 2017 to May 2018 in the Department of Obstetrics and Gynaecology in MOSC Medical College, Kolenchery, Kerala, India. The primary investigator approached expectant mothers beyond 34 weeks who were admitted to the labour ward. An informed consent was obtained and their demographic details were collected through interview. Gestational age was determined from the last menstrual period (LMP) and corrected with the first trimester ultrasound if the mother had irregular cycles. We included all infants from $34^{0/7}$ to $40^{6/7}$ completed weeks. We excluded mothers with multiple pregnancies, pregnancy complicated with diabetes, hypertensive disorders and antepartum haemorrhage as well as Rh-negative mothers and those with foetal complications like IUGR or a major congenital anomaly.

Randomization was done by permuted block randomization with allocation concealment. When a woman enters active labour, a single opaque sealed envelope with computer generated numbers was opened and appropriate intervention performed. The blinding was achieved by not disclosing the allocation arm before measuring the haemoglobin and haematocrit levels.

Sample Size Estimation

The sample size was calculated using the nMaster sample size software developed in CMC Vellore, India (https://www.cmc-biostatistics.ac.in/nmaster). A previous study [4] in North India showed a mean increase in Hgb of 1.1 ± 1.2 g/dl at 6 weeks when infants were subject to UCM. Using this data, we estimated that to detect a mean increase in Hgb of 0.6 g/dl with UCM compared to ICC with 80% power and a 2-tailed alpha value of 0.05 we had to enrol 71 subjects in each group (total 142 neonates). Since a follow-up was required, a drop out of 15% was anticipated and 170 mothers were included in the study.

Intervention

Under the intervention arm, the cord was held at the introitus or at the wound in caesarean delivery with one hand and milking of the umbilical cord was done for its remaining accessible length (approx. 20 cm). The milking was performed at an average speed of 10 cm per sec., three times after which the cord was clamped and cut. A standard stop watch was used to ensure that the procedure was completed in < 30 s. This technique of umbilical cord milking—its length, with time to be taken were standardized through repeated demonstrations to all attending obstetricians before the onset of the study. This group was allocated as the UCM group. Neonates who underwent ICC were designated as the control group. Both groups had the neonate held at the level of the uterus in normal delivery and at the level of the thighs in caesarean. All neonates were provided routine care and attended to by a neonatologist who assessed the general condition of the neonate.

After delivery, mothers were strictly monitored for any third stage complications. All of them received intravenous oxytocin, 5 units IV, 10 units IM and 20 units in 500 ml Ringer Lactate at 60 drops per minute as per institute protocol.

Outcome Measurement

The primary outcome of the study was Hgb and HCT at 72 h and 6 weeks. Secondary outcomes were (1) maternal complications, i.e. post-partum haemorrhage, duration of third stage (2) neonatal complications like hyperbilirubinaemia requiring phototherapy, symptomatic polycythaemia and unplanned admissions to NICU.

Post-partum haemorrhage (PPH) was estimated through weighing all the blood-soaked delivery pads and mops along with the blood in the delivery pan and those with a blood loss > 500 ml for normal delivery and > 1000 ml for caesarean section was taken to have PPH. The need for extra uterotonics and blood transfusions were recorded. The time to delivery of the placenta after delivery of the infant defined as the third stage duration was measured by wall mounted digital clocks available in the labour room or operation theatre.

At 24 h of age, all neonates had their bilirubin level (TcB) measured using a transcutaneous bilirubinometer and the infants were treated with phototherapy if the value was > 13.5 for term and > 13 for preterm infants (Institute Protocol). The duration of phototherapy was charted and any pathological causes for the same were investigated. All neonates were closely monitored for any complications and the required data were collected from case sheets. At 72 h, the Hgb and HCT levels were measured in the capillary blood sample (heel-prick sample) using the portable Hgb meter—Mission® Hb meter that has a measuring range of 5–25.6 g/dl. The duration of phototherapy required to correct the hyperbilirubinaemia was also noted. Polycythaemia was defined as a HCT value ≥ 65% at 72 h

of age, those infants who developed polycythaemia were closely observed for any symptoms.

Follow up

We listed the contact numbers of the parents and followed them up via phone to detect any untoward events and ensure an attendance for a postnatal visit at 6 weeks of age. At visit, the Hgb and HCT values of the infant was measured using the Hgb meter, in the out-patient department. All the infants who had a Hgb < 9.4 g/dL [5] were taken to be anaemic and referred to the paediatrician for further evaluation.

Statistical Analysis

Data was input using Microsoft excel spread sheet and analysed using the SPSS software. Quantitative variables were represented using mean and standard deviation. Qualitative variables were expressed in proportions. Repeated measure ANOVA was performed for the comparison of quantitative variables at two time points. Rest of the quantitative variables were measured using Student '*t*' test. Chi-square/Fisher exact test and Mann Whitney U were used for the analysis of qualitative variables. A p-value of less than 0.05 was taken as statistically significant.

Ethical Considerations

Ethical clearance was obtained from the Research Ethics Committee of the Institutional Review Board in MOSC Medical College, Kolenchery, India. Confidentiality was strictly maintained. No additional cost was incurred by the participants. The trial was prospectively registered under the Clinical Trial Registry of India. www.ctri.nic.in (CTRI/2017/10/009970).

Results

During our study period, 300 mothers presented in spontaneous labour to the labour ward. Of them 94 participants were excluded based on our selection criteria. The remaining mothers were randomized into the control group and intervention group with 85 mothers in each. Of the 170 neonates enrolled, 144 (125 term and 19 late preterm) completed the trial (Fig. 1). Characteristics of both groups are comparable (Table 1).

At 72 h and at 6 weeks, the mean Hgb and HCT levels were significantly higher in the intervention group that underwent cord milking compared with the controls ($p < 0.001$) (Table 2). The 95% confidence interval (CI) of gain in Hgb due to cord milking was 2.4–1.0 g/dl and HCT was 7–3% at 72 h and the gain had a CI of 1.9–1.1 g/dl for Hgb and 6–3% for HCT at 6 weeks. The decreasing trend of the Hgb and HCT from the 3rd day of life to the 6th week is consistent with the natural physiological process and Fig. 2 indicates that a higher Hgb and HCT at 3 days will result in better levels at 6 weeks. On subgroup analysis, similar findings were observed in late preterm and term infants. We have observed that the proportion of anaemic infants were similar at 72 h between the two groups (5.6% in intervention arm and 2.7% in the control arm), but there was rise in the proportion (31%) by 6 weeks in the control arm compared to the intervention arm ($n = 0$). Twenty-five neonates were born through caesarean section and rest vaginally, on sub group analysis the Hgb levels were not significantly higher at 72 h but there was a significant difference at 6 weeks with the mean Hgb in the intervention arm being 11.1 g/dl and in the controls, being 9.9 g/dl.

We analysed the bilirubin levels (TcB) at 24 h and there was no significant difference in the levels among the two groups even though a total of 100 infants (81 term infants, 19 preterm infants) developed hyperbilirubinaemia of which all required phototherapy (Table 3). Five infants (3-intervention group, 2-control group) in our study required Phenobarbitone injections to lower the bilirubin levels. Two infants were DCT positive (control group) and were excluded from further analysis. There was no statistically significant difference in the hours of phototherapy required to correct the hyperbilirubinaemia between the two groups. Only term neonates developed polycythaemia in our study with seven neonates being in the intervention group compared to one neonate among controls, but all of them were asymptomatic and this difference was not statistically significant. Among the late preterm, three infants from both groups required admission to the NICU but among the term infants more infants ($n = 17$) in the intervention group required NICU admission compared to controls ($n = 10$) but this difference was not statistically significant and none of them developed severe complications. On follow up, one preterm and one term neonate (both controls) developed sepsis and were excluded from the study.

We also monitored for maternal complications and found that only one patient in the intervention arm developed PPH which was well controlled with uterotonics. And, there was no significant change in the third stage duration as a result of cord milking.

Discussion

In our study, we have found that UCM results in a mean increase of the Hgb and HCT levels at 72 h and at 6 weeks in the term neonates when compared to ICC.

Fig. 1 Study flow diagram

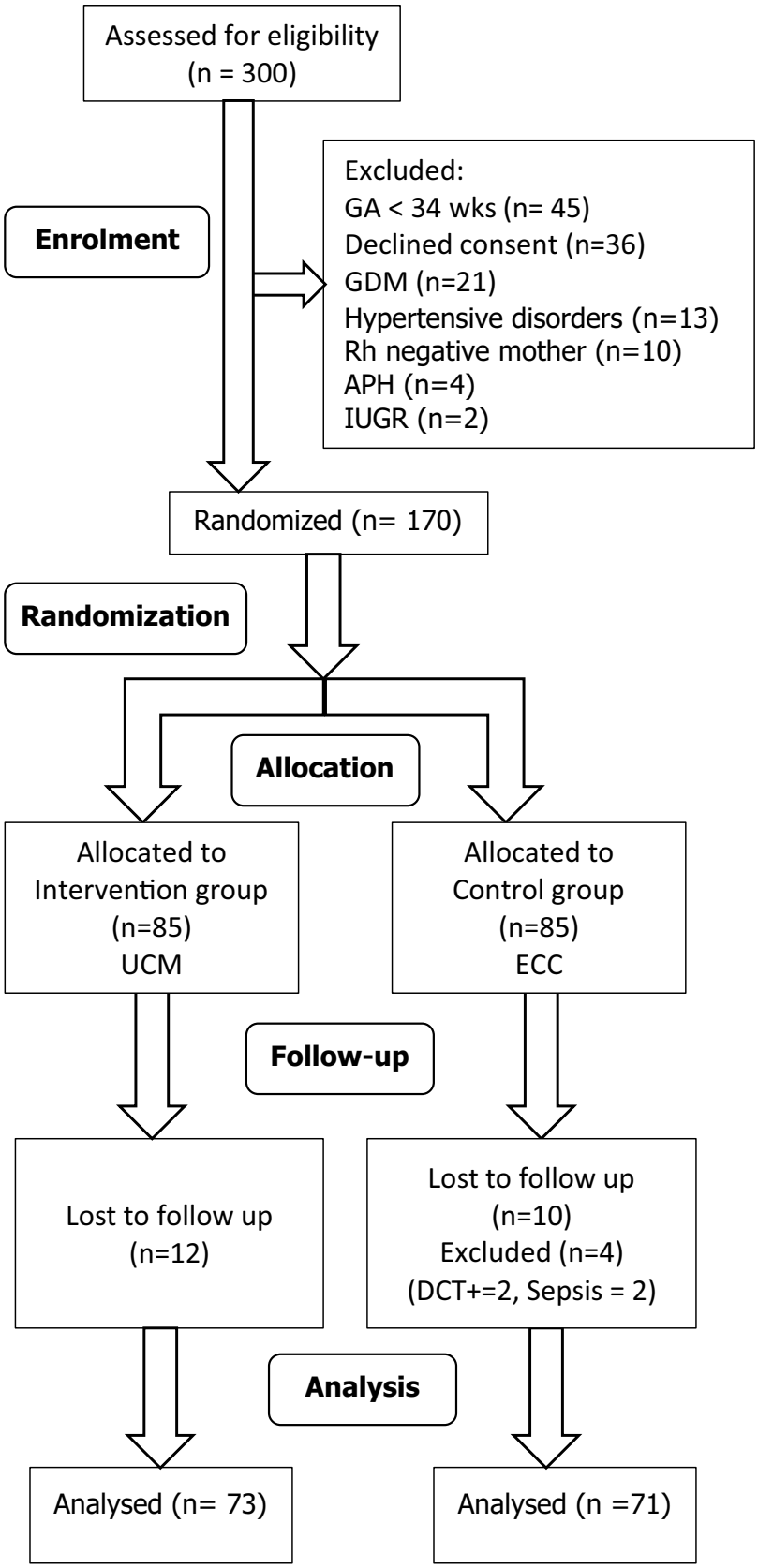

Table 1 Baseline characteristics

Characteristic	Intervention group ($n=85$)	Control group ($n=85$)	p value
Maternal age (years)	26.75 (4.16)	27.11 (3.87)	0.57
Middle socio-economic status[#]	79 (93%)	79 (93%)	0.07
Maternal BMI (kg/m^2)	23.77 (4.31)	24.24 (4.15)	0.47
Nulliparous[#]	45 (53%)	44 (52%)	0.88
Maternal Hb (g/dl)	11.22 (0.90)	11.25 (0.91)	0.83
Vaginal delivery[#]	72 (85%)	73 (86%)	0.83
Gestational age (days)	270(9)	270 (10)	0.79
Birth weight (kg)	3.06 (0.42)	3.02 (0.47)	0.54
Gender, female[#]	41 (48%)	40 (47%)	0.88
ABO incompatibility[#]	3 (3.5%)	5 (6%)	0.45
Exclusive breast feeding at 6 weeks[#]	85 (100%)	85 (100%)	1

Mean (SD), value (percentage)

Hgb, haemoglobin, test of significance, Student t test (continuous data)

[#]Fisher's exact test/χ^2 test (non-continuous data)

Table 2 Haematological parameters

	Overall infants		Late preterm infants		Term infants		p value for all groups
	Intervention group ($n=85$)	Control group ($n=85$)	Intervention group ($n=11$)	Control group ($n=13$)	Intervention group ($n=74$)	Control group ($n=72$)	
Hb at 72 h, g/dl	18.1(2.4)	16.4(2.1)	17.4(1.5)	16.1(1.7)	18.2(2.5)	16.4(2.1)	<0.05
Hct at 72 h, %	54(7)	48(6)	51(4)	47(5)	54(7)	48(6)	<0.05
TcB at 24 h	12.1(3.6)	12.2(3.6)	12.8(3.3)	14.2(1.4)	12.0(3.6)	11.9(3.8)	>0.05
Hb at 6wks, g/dl	11.6(1.3) ($n=73$)	10.1(1.1) ($n=71$)	11.0(1.0) ($n=10$)	10.2(1.2) ($n=9$)	11.7(1.3) ($n=63$)	10.1 (1.1) ($n=62$)	<0.05
Hct at 6wks, %	34(4) ($n=73$)	30(3) ($n=71$)	32(3) ($n=10$)	30(4) ($n=9$)	35(4) ($n=63$)	30(3) ($n=62$)	<0.05

Mean (SD). Test of significance was repeated measure ANNOVA

Hb, Haemoglobin; Hct, Haematocrit; TcB, Transcutaneous Bilirubin

Number of subject at birth is mentioned in this table top and number of subjects at 6 weeks is mentioned in relevant boxes below

Our haemoglobin levels are similar with a previous study where milking five times of a clamped cord results in a higher Hgb at 6 weeks after birth in term infants [6]. Among the preterm neonates also, the results are similar and the mean increase in Hgb is concurrent with a previous study that showed Hgb at 24 h of age were significantly higher in the UCM group compared to ICC [7]. We have milked the cord at the perineum three times while the umbilical cord is still attached to the placenta as performed by Katheria et al [8]. This method was found to increase the amount of blood volume transfused when compared to milking after cord clamping that results in transfusion of a fixed blood volume [9]. We adopted this method as a meta-analyses of seven trials that involved UCM with an intact cord in premature new-borns revealed, an increase in Hb and decreased IVH of all grades in the milked arm compared with those who underwent ICC, with no adverse effects in the immediate postnatal period [3]. All parameters were tested using a portable haemoglobinometer as this requires only 10 µl of blood and many studies [10, 11] have shown comparable results with the standard automated haematology analyser. The rise in Hgb due to cord milking resulted in no infants becoming anaemic in the intervention group compared to the controls at 6 weeks. Hence, UCM may play a role in venting undetected childhood anaemia that is essential for the cognitive development and the linear growth of a child, particularly in low resource settings [12]. It is postulated that during caesarean sections, lack of a good uterine tone, and time constraints of a major surgery hinders the natural placental transfusion. Zanardo et al. conducted a trial that showed, intact UCM is an efficacious and safe procedure

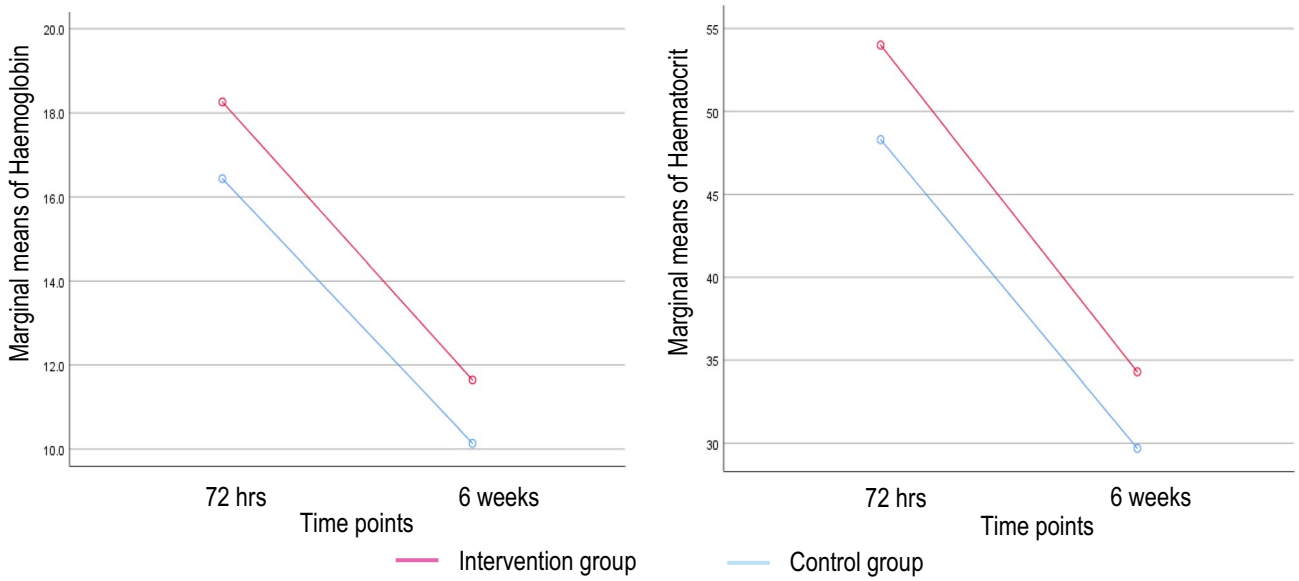

Fig. 2 Profile plots of haemoglobin and haematocrit at 72 h and at 6 weeks in whole sample

to enhance placental transfusion among neonates born via elective caesareans [13]. Among the caesarean sections in our study, the mean Hgb was significantly higher in the intervention group compared to controls at 6 weeks. However, our inferences are limited as we have not quantified the iron status of the mother and the neonate.

Concerns about short-term adverse effects, such as hyperbilirubinaemia needing phototherapy, symptomatic polycythaemia, increased hospital length of stay (LOS) is a major hindrance to performing milking in term infants. Sixty-five per cent of the term infants in our study developed hyperbilirubinaemia requiring phototherapy but there was no statistical difference between the two groups, similar to data from previous studies [14, 15]. Of late a cohort study demonstrated that UCM in term infants was not associated with increased incidence of phototherapy, symptomatic polycythaemia, NICU admissions or readmissions for phototherapy compared with cohort of infants who received ICC [16]. We observed that, though all the preterm neonates in our study developed hyperbilirubinaemia there was no statistical association with cord milking. Also, there was no significant rise in the incidence of polycythaemia in the intervention arm which is in par with studies that have suggested, babies who receive UCM do not have an increased risk of polycythaemia [15, 17]. Nevertheless, in our study, the proportion of preterm infants (14%) is less which makes

Table 3 Complications

	Intervention group ($n=85$)	Control group ($n=85$)	p value
Maternal			
Presence of PPH	1	0	> 0.05
Duration of third stage (min)	4.96 (1.18)*	5.08(1.53)*	> 0.05
Neonatal			
Hyperbilirubinaemia	48	52	> 0.05
Duration of phototherapy (h)	24[24,48]# ($n=48$)	24[24,57]# ($n=52$)	> 0.05
Polycythaemia	7	1	> 0.05
Term neonates admitted to NICU	23% ($n=74$)	14% ($n=72$)	> 0.05

Test of significance is Fisher's exact test/χ^2 test

*Mean (SD), test of significance is student t test

#Median [Q_1, Q_2], non-parametric Mann–Whitney U test

it underpowered to detect the risk of intraventricular haemorrhage which has been described as a probable complication among preterm neonates in a recent study [18].

The active management of third stage of labour that was developed by the World Health Organization (WHO) initially advocated that early cord clamping was required to reduce the risk of PPH. However, evidence has showed that among the key components only prophylactic utero-tonic therapy actually reduces the risk [19]. Accordingly, we also did not observe any increase in the incidence of PPH and third stage duration by performing cord milking. However there has been contrasting studies where Piyadigama et al. [20] showed that there was a Hb drop of 1.0 g/ dl when the cord was milked whereas Song et al. observed there was no difference in maternal haemoglobin levels after delivery and incidence of PPH due to cord milking [7].

As the debate on the optimal method of cord clamping at childbirth continues, we hope this study could heighten our current knowledge on cord milking which could help incorporate the practice into standard care.

Conclusion

UCM could be universally adopted in lieu of immediate clamping without causing any adverse maternal or neonatal effects and eventually become a cost-effective intervention for the primary prevention of anaemia in childhood.

Acknowledgements The trial was registered prospectively under the Clinical Trial Registry of India. (CTRI/2017/10/009970).

Declaration

Conflict of interest Both authors declare that they have no conflict of interest.

Human and Animal Right Statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with Helsinki Declaration 1975, as revised in 2008.

Ethical Standards This study was approved by the institutional ethical committee.

Informed Consent Informed consent was obtained from all mothers for being included in the study.

References

1. Hosono S, Hine K, Nagano, N et al. Residual blood volume in the umbilical cord of extremely premature infants. Pediatr Int. 2015;57(1):68–71.
2. Basile S, Pinelli S, Micelli E, et al. Milking of the umbilical cord in term and late preterm infants. Biomed Res Int. 2019;11(2019):1–9.
3. Al-Wassia H, Shah PS. Efficacy and safety of umbilical cord milking at birth: a systematic review and meta-analysis. JAMA Pediatr. 2015;169(1):18–25.
4. Upadhyay A, Gothwal S, Parihar R, et al. Effect of umbilical cord milking in term and near term infants: randomized control trial. Am J Obstet Gynecol. 2013;208(2):120.e1-120.e6.
5. Wang M. Iron deficiency and other types of anemia in infants and children. AFP. 2016;93(4):270–8.
6. Alzaree F, Elbohoty A, Abdellatif M. Early versus delayed umbilical cord clamping on physiologic anemia of the term newborn infant. Open Access Maced J Med Sci. 2018;6(8):1399–404.
7. Song S-Y, Kim Y, Kang B-H, et al. Safety of umbilical cord milking in very preterm neonates: a randomized controlled study. Obstet Gynecol Sci. 2017;60(6):527–34.
8. Katheria AC, Truong G, Cousins L, et al. Umbilical cord milking versus delayed cord clamping in preterm infants. Pediatrics. 2015;136(1):61–9.
9. Katheria A, Garey D, Truong G, et al. A randomized clinical trial of umbilical cord milking vs delayed cord clamping in preterm infants: neurodevelopmental outcomes at 22–26 months of corrected age. J Pediatr. 2018;194:76–80.
10. Olatunya OS, Olu-Taiwo A, Ogundare EO, et al. Evaluation of a portable haemoglobin metre performance in children with sickle cell disease and implications for healthcare in resource-poor settings. J Trop Pediatr. 2016;62(4):316–23.
11. Olatunya O, Ogundare O, Olaleye A, et al. Point-of-care testing for anaemia in children using portable haematocrit meter: a pilot study from Southwest Nigeria and implications for developing countries. Ethiop J Health Sci. 2016;26(3):251–8.
12. Onyeneho NG, Ozumba BC, Subramanian SV. Determinants of childhood Anemia in India. Sci Rep. 2019;9(1):16540.
13. Zanardo V, Guerrini P, Severino L, et al. A randomized controlled trial of intact cord milking versus immediate cord clamping in term infants born by elective cesarean section. Am J Perinatol. 2019;0039:1697673.
14. Yadav AK, Upadhyay A, Gothwal S, et al. Comparison of three types of intervention to enhance placental redistribution in term newborns: randomized control trial. J Perinatol. 2015;35(9):720–4.
15. Jaiswal P, Upadhyay A, Gothwal S, et al. Comparison of two types of intervention to enhance placental redistribution in term infants: randomized control trial. Eur J Pediatr. 2015;174(9):1159–67.
16. Chiruvolu A, Medders A, Daoud Y. Effects of umbilical cord milking on term infants delivered by cesarean section. Am J Perinatol. 2020;0040:1701617.
17. Agarwal S, Jaiswal V, Singh D, et al. Randomised control trial showed that delayed cord clamping and milking resulted in no significant differences in iron stores and physical growth parameters at one year of age. Acta Paediatr. 2016;105(11):e526–30.
18. Balasubramanian H, Ananthan A, Jain V, et al. Umbilical cord milking in preterm infants: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2020;105(6):572–80.
19. Vogel JP, Williams M, Gallos I, et al. WHO recommendations on uterotonics for postpartum haemorrhage prevention: what works, and which one? BMJ Glob Health. 2021;4(2). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6509591/
20. Piyadigama I, Devasurendra LC, Dissanayake AD, Gunawardana K. Effects of umbilical cord milking compared to differed cord clamping in term infants, a randomized controlled trial. Sri Lanka J Obstetr Gynaecol. 2017;39(4):63.

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