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Research Article

Effect of Umbilical Cord Milking on Severity of Hypoxic Ischemic Encephalopathy in Asphyxiated Neonates: A Pilot study

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ABSTRACT

Background: The present study was aimed to evaluate the effect of umbilical cord milking technique on severity of Hypoxic Ischemic Encephalopathy (HIE) in asphyxiated neonates and assessed by Modified Sarnat's staging as primary outcome, APGAR score at 5 minutes and respiratory support requirement as secondary outcome.

Methods: This was a randomized, controlled pilot study conducted in neonatology department at a tertiary care center, Thrissur, Kerala for one year starting from March 2020. The neonates were divided into two groups non milking group, control (n=38) and umbilical Cord Milking, case [UCM] (n=32) and their outcomes were compared. In the intervention group, the cord was cut at 30 cm from umbilical stump within 30 seconds of birth and euthermia was maintained. The umbilical cord was raised and milked from the cut end towards the infant 3 times with speed at 10 cm/sec and then clamped 2-3 cm from the umbilical stump. In the control group, the umbilical cord was clamped without doing cord milking.

Results: In this study moderate to severe HIE were less in case group 46.9 % than control group 55.1% and less neonates 44.7% had Mild HIE in control group compared to case group 53.1% even though result was statistically not significant as primary outcome (p value not significant). Eight neonates (21.6%) in control group had Apgar at 5 min score 0-3, whereas only 4 (12.5%) neonates in cord milking group.

Conclusion: The insufficient knowledge of placental transfusion limits and benefits leads to a wide variation in the management of cord clamping. It would be useful to standardize the UCM procedure in order to offer protocols applicable to clinical practice, and to spread knowledge among professionals through educational programs.

Keywords: Perinatal asphyxia; Umbilical cord milking; Hypoxic ischemic encephalopathy; Noninvasive mechanical ventilation; Invasive mechanical ventilation

INTRODUCTION

Neonatal Resuscitation Protocols (NRP 2015 and 2020) recommend Delayed Cord Clamping (DCC) as part of normal neonatal resuscitation, after International Liaison Committee on Resuscitation (ILCOR) systematic review found that interventions to enhance placental transfusion like DCC are beneficial in neonates. DCC is associated with less intraventricular haemorrhage, higher blood pressure and blood volume, less need for transfusion after birth, and less necrotizing enterocolitis [1]. Umbilical Cord Milking (UCM), another intervention to enhance placental transfusion has been shown to be a safe procedure that improves the haemoglobin and iron status at 6 weeks of life among term and late preterm neonates [2,3]. In a comparison of two types of intervention (DCC and UCM) to enhance placental transfusion in term infants, there was no difference in haemodynamic status, Cranial Doppler indices, and adverse neonatal outcomes among the two groups [4]. Currently Neonatal Resuscitation Protocols (NRP 2020) states that cord milking is

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being studied as an alternative to delayed cord clamping but should be avoided in babies less than 28 weeks gestational age , because it is associated with brain injury [5].

Birth asphyxia accounts for 20%-30% of neonatal deaths in India and surviving infants are at risk for development of cerebral palsy and neuro developmental disabilities in later life. Hypoxic Ischaemic Encephalopathy (HIE) is a brain injury seen in these neonates due to inadequate blood flow and oxygen delivery to the brain. Currently only therapeutic hypothermia (whole body temperature maintained at 33.5°C) initiated within 6 hours of birth and continued for 72 hours is known to be effective in preventing secondary neuronal injury in neonates with moderate to severe HIE. UCM may act as an adjunctive to cooling and can potentially improve brain injury in neonates with HIE [3,6].

UCM is proposed as a simple, safe intervention in depressed neonates [7,8] which if found to be beneficial, could be recommended as a standard protocol for all depressed neonates in resource limited settings like primary and community health center. UCM could then reduce the need for neonatal resuscitation interventions (positive pressure ventilation, chest compressions, and medication and fluid boluses). It may also prove to be a useful adjunct to whole body hypothermia for those neonates with moderate to severe HIE. This simple intervention can be widely adopted in both developed and developing countries, thereby helping the latter to achieve the Millennium Development Goals.

Placenta being a rich source of stem cells, UCM may potentially improve brain injury in neonates with HIE. UCM may prove to be a relatively harmless and simple intervention feasible among the initial steps in the resuscitation of a depressed newborn [9]. If found to be beneficial in preventing brain injury, it has immense therapeutic value in resource limited settings like primary and community health center, where birth asphyxia otherwise carries a very poor outcome.

The present study was conducted to investigate severity of HIE of Umbilical cord milking in term infants who are depressed at birth using Modified Sarnat Score. Later investigations such as APGAR score of 0-3, 4-6 and 7-10 at 5 minutes, respiratory off support at 48 hours, Non Invasive Mechnanical Ventiltation (NIMV) and Invasive Mechanical Ventiltation (IMV) requirement and MRI abnormality were evaluated on the study participants.

MATERIALS AND METHODS

This was a randomized, controlled pilot study conducted in neonatology department at a tertiary care center, Thrissur, Kerala for one year starting from March 2020. The study was approved from the Institutional Ethical Committee. The trial was registered under the Clinical Trials.gov (ClinicalTrials.gov Identifier: NCT03123081). All depressed neonates (defined as per NRP 2015 and 2020 criteria) of gestation 35 weeks and above, delivered either vaginally or by lower segment caesarean section with in the hospital were enrolled into the study after receiving informed consent from the parents. Cases such as MCDA Twin pregnancy (including DCDA twins), triplet or quadruplet pregnancy, short umbilical cord length (< 25 cm), hydrops foetalis, major chromosomal or congenital anomalies, severe placental abruption and cord prolapse and cord abnormalities such as true knots were excluded from the study.

Randomization

A computer generated random number of all term depressed neonates were allocated to intervention and control group. Consent of all term parents was taken before delivery. Ethical clearance no: 01/17/IEC/JMMC and RI

Details of the intervention

All doctors and nurses involved in delivery and newborn resuscitation were trained for a standardized cord-milking technique, by showing three live demonstrations by the principal investigator and also showing a video available on the internet [10-24], In all cases after birth, the babies were held at the level of the uterus in vaginal delivery and on the thighs of mother in caesarean section while the umbilical cord was cut and clamped.

In the intervention group, the cord was cut at approximately 30 cm of length from umbilical stump within 30 seconds of birth (early clamping). Then the baby was placed under the radiant warmer for resuscitation as per NRP 2015 guidelines. The umbilical cord was raised and milked from the cut end towards the infant 3 times with speed at 10 cm/sec and then clamped 2-3 cm from the umbilical stump.

In the control group, the umbilical cord was clamped early (within 30 seconds) near the umbilicus and cut without doing cord milking.

The primary outcome of the study was to investigate the severity of HIE of UCM in case and control group using Modified Sarnat Score. Secondary outcomes were to investigate APGAR score of 0-3, 4-6 and 7-10 at 5 minutes, respiratory off support at 48 hours, Non Invasive Mechnanical Ventiltation (NIMV) and Invasive Mechanical Ventiltation (IMV) requirement and MRI abnormality on the study participants.

Statistical analysis

Data were analyzed using Chi-square test, student t-test, percentage analysis, odds ratio. Means were compared using the t-test. Adjustments for multiple comparisons were made using Fisher's least significant difference method. Adjusted were obtained using analysis of covariance, and differences were compared using Fisher's least significant difference t-test (Figure 1).

RESULTS

A total of 70 babies were recruited for this study that fulfilled the inclusion criteria. These babies were randomized in to two groups: intervention group (38) and control group (32). The baseline characteristics of the two groups were compared in 70 new born enrolled for the study (Table 1).

When primary outcome was compared in both the groups, it was observed that moderate HIE was present in 46.9% in intervention group as compared to 55.3% in control group, indicating a trend towards better outcome in intervention group (p value – not significant).

When secondary outcomes were compared (Table 2), in intervention group, 12.5% had APGAR score of 0-3, 53.1% had score of 4-6 and 34.4% had score of 7-10 whereas in control group more neonates had score of 0-3 21.6%, 43.2% had score of 4-6 and 35.1% neonates had score of 7-10. Among the intervention group, 28.1% required off support at 48 hours and in control group 13.2% required off support at 48 hours. In the present study, 52.6% required noninvasive ventilation, 39.5 % required mechanical ventilation and 7.9% did not required support in group whereas in Intervention group 56.3% required noninvasi--vse ventilation and 40.6% neonates required mechanical vent--ilation. Among the intervention group, 26.7% showed abnor--mal MRI and in control group 64.7% showed abnormal MRI

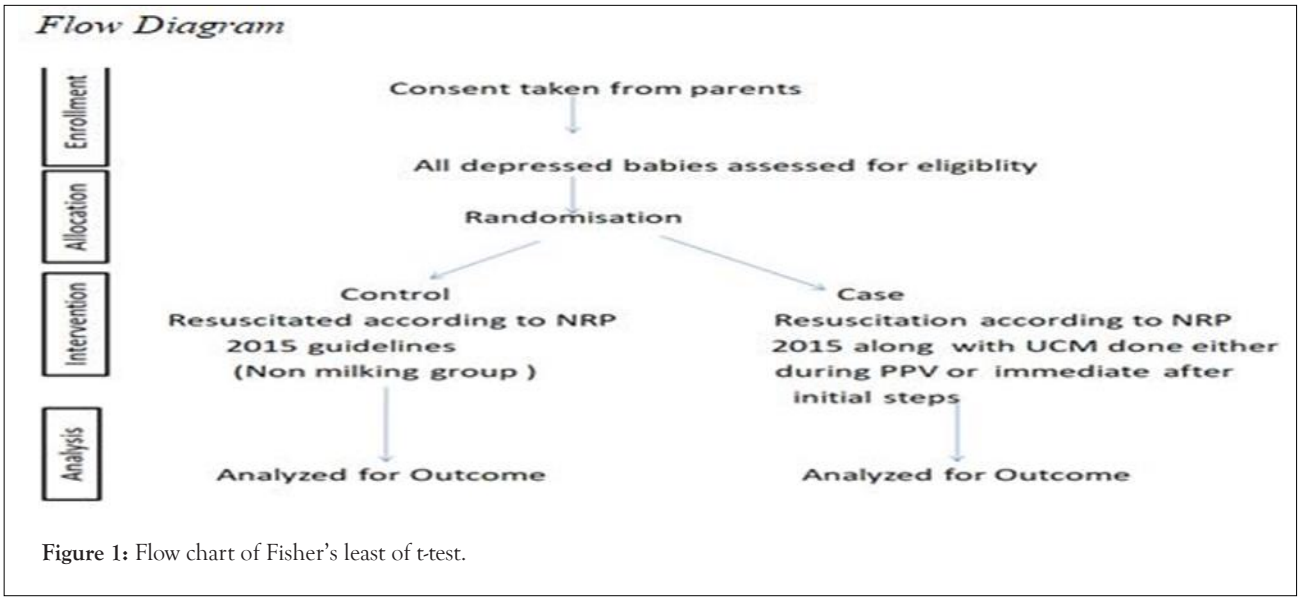

Figure 1: Flow chart of Fisher's least of t-test.

Table 1: Baseline characteristics.

Demographics	Control group (n=38)	Intervention group (n=32)	Total (n=70)
Gestational age			
34-34 weeks+6 days	4	6	10
37-38 weeks+6 days	16	19	35
39-40 weeks+6 days	16	9	25
Birth weight			
≤ 2.5	11	8	19
>2.5	27	24	51
Sex			
Male	22	20	42
Female	16	12	28
Maternal history of pregnancy induced hypertension			
Yes	3	3	6
No	35	29	64
Type of delivery			
Spontaneous delivery	19	10	29
Caesarean section	11	18	29
Vacuum delivery	8	4	12

Table 2: Primary and secondary outcomes.

Variables	Category	Milking of cord				P value
		Not done(control)		Done (case)		
		n=38	Percentage	n=32	Percentage	
Primary outcomes						
HIE	No HIE to Mild HIE	17	44.70%	17	53.10%	0.484
	Moderate to severe HIE	21	55.30%	15	46.90%	
Secondary outcomes						
APGAR at 5'	0-3	8	21.60%	4	12.50%	0.556
	4-6	16	43.20%	17	53.10%	
	7-10	13	35.10%	11	34.40%	
Off support at 48hrs	No	33	86.80%	23	71.90%	0.119
	Yes	5	13.20%	9	28.10%	
NIMV/IMV	Off support	3	7.90%	1	3.10%	0.691
	NIMV	20	52.60%	18	56.30%	
	IMV	15	39.50%	13	40.60%	
MRI	Normal	6	35.30%	11	73.30%	0.031
	Abnormal	11	64.70%	4	26.70%	

DISCUSSION

There are no recent clinical evident trails to emphasize the importance of placental transfusion in neonatal outcomes and the role of each component of placental transfusion believed in the past by the WHO for the active management of the third stage of labour concepts were changed. Hence, the practice of immediate cord clamping was excluded by the WHO guidelines in 2012, and cord traction was defined as optional [12-15]. Placental transfusion is the transfer of placental blood to neonate during the first few minutes of life [16]. This procedure helps in reducing rates of mortality in asphyxiated neonates and prevent iron deficiency anaemia in term neonates [17,18].

Placental transfusion conducts through DCC or UCM, may also acts as an important procedure for ensuring better neonate outcome without a stormy course of NICU stay. DCC and UCM both helps in increasing arterial oxygen content, maintain haemodynamic stability and can be also done in low-resource settings. Cord clamping time, uterine contractions, umbilical blood flow, breathing, and gravity all play a central role in determining placental transfusion effectiveness [16].

DCC provides a passive transfer of placental blood, at a slow rate meanwhile UCM is an active stripping of blood through the umbilical cord to the neonate, as a faster method [3].

According to RCOG article, 2015, UCM is an alternative to DCC in case of preterm births, but it needs to be further investigated in order to evaluate associated benefits and risks so that it can be performed worldwide [19].

There is a need for larger randomized trials on UCM to be conducted in developing countries and has insufficient knowledge to prove its neonatal outcome. Moreover, there is no standardization on DCC method and its optimal time to do, despite of time is being essential for passive placental transfusion. As it is common practice is to give a depressed newborn to the neonatologist as soon as possible after birth considering the safety of depressed neonates who requires resuscitation in first golden minute.

According to Italian recommendations in case of ceaseran term newborns, if DCC cannot be performed, UCM may be considered as an alternative procedure with the purpose of increasing haemoglobin levels in postnatal period and iron reserves in the following weeks [22].

In fact, UCM is believed to be a simple procedure that can be safely performed in a matter of seconds also by obstetricians, with no time. Furthermore, this method may also be very useful in cases of neonatal asphyxia, helping in the crucial importance of neonatal outcomes. UCM may be a feasible procedure can be done in depressed neonates along with resuscitation, it will not cause any resuscitation delays or harm in depressed newborns compared to ICC [10, 21].

A previous study concluded in their retrospective analysis that neonates with acidosis, who had received UCM and needed resuscitation and ongoing respiratory support were fewer in number than those who received ICC [21]. There are ongoing cited studies evaluating haematological parameters such as haemoglobin, haematocrit, and ferritin which can prove that there is significantly higher UCM results compared to ICC groups at different times from the delivery [18,22-24]. Inspite

studies evaluating UCM outcomes, a standardized procedure for milking is needed and it should be followed internationally. McAdams's is the only study evaluating different outcomes between different UCM procedures, showing that I-UC promotes a larger transfusion of blood volume to newborns at birth than C-UCM [24]. Even if published data on UCM enlightens pos--itive effects of encouraging, stating that UCM may be the most effective method to provide placental transfusions and UCM received depressed neonates would have lesser NICU stormy course.

The implementation of procedure could also be associated with clinically approved UCM guidelines availability, knowledge of UCM in short and long term neonatal outcomes, and requires friendly cooperation within the delivery team.

CONCLUSION

It is concluded that there is insufficient knowledge and inappropriate practice to conduct placental transfusion within in the limits and its benefits leads to a world wide variation in the managing of cord clamping. It would be useful if UCM practice is standardized in all depressed neonates at birth, included in third stage of labour management and its guidelines to spread knowledge among professionals through educational programs and conferences.

LIMITATIONS

Since this being a pilot study smaller sample size, co-morbidities could not be separated, long term outcome not assessed, chance error because of lack of blinded randomization could affected outcome.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, et al. Part 13: Neonatal resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18):S543-560.
2. Upadhyay A, Gothwal S, Parihar R, Garg A, Gupta A, Chawla D, et al. Effect of umbilical cord milking in term and near term infants: Randomized control trial. Am J Obstet Gynecol. 2013;208(2):120e1-120e6.
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. Jaiswal P, Upadhyay A, Gothwal S, Singh D, Dubey K, Garg A, et al. Comparison of two types of intervention to enhance placental redistribution in term infants: Randomized control trial. Eur J Pediatr. 2015;174(9):1159-1167.
5. Aziz K, Henry C, Escobedo MB, Hoover AV, Kamath-Rayne BD, Kapadia VS, et al. Part 5: Neonatal resuscitation 2020 American heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Pediatrics. 2021;147(1):e2020038505E.
6. Carroll PD. Umbilical cord blood—an untapped resource: Strategies to decrease early red blood cell transfusions and improve neonatal outcomes. Clin Perinatol. 2015;42(3):541-56.
7. Jiun L. Autologous umbilical cord blood cells for newborn infants with hypoxic-ischemic encephalopathy. Cell Organ Transplantology. 2013;1(1):27-8.
8. Aridas JD, McDonald CA, Paton MC, Yawno T, Sutherland AE, Nitsos I, et al. Cord blood mononuclear cells prevent neuronal apoptosis in response to perinatal asphyxia in the newborn lamb. J Physiol Paris. 2016;594(5):1421-35.
9. Bhatt S, Polglase GR, Wallace EM, Te Pas AB, Hooper SB. Ventilation before umbilical cord clamping improves the physiological transition at birth. Front Pediatr. 2014;2:113.
10. Vicki Taylor. Video presentation: On correctumbilical cord 'milking' technique. Australian Placental Transfusion, West Mead Hospital, Sydney, Australia
11. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. Lancet Glob Health. 2014;2(6):e323-33.
12. World Health Organization. WHO recommendations for the prevention and treatment of postpartum haemorrhage. 2012.
13. American College of Obstetricians and Gynecologists. ACOG practice bulletin: Clinical management guidelines for obstetrician-gynecologists number 76, October 2006: Postpartum hemorrhage. Obstet Gynecol. 2006;108(4):1039-47.
14. Katheria AC, Lakshminrusimha S, Rabe H, McAdams R, Mercer JS. Placental transfusion: A review. J Perinatol. 2017;37(2):105-11.
15. Palethorpe RJ, Farrar D, Duley L. Alternative positions for the baby at birth before clamping the umbilical cord. Cochrane Database Syst Rev. 2010(10).
16. Agarwal S, Jaiswal V, Singh D, Jaiswal P, Garg A, Upadhyay A. 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.
17. Alzaree F, Ahmed Elbohoty MA. Early versus delayed umbilical cord clamping on physiologic anemia of the term newborn infant. Open Access Maced J Med. Sci. 2018;6(8):1399.
18. Duley LM, Weeks AD, Hey EN. Clamping of the umbilical cord and placental transfusion.2015.

19. Perrone B, Ghirardello S. Placental transfusion strategies in Italy: A nationwide survey of tertiary-care delivery wards. Am J Perinatol. 2017;34(07):722-8.

20. Jaiswal P, Upadhyay A, Gothwal S, Chaudhary H, Tandon A. Comparison of umbilical cord milking and delayed cord clamping on cerebral blood flow in term neonates. Indian J Pediatr. 2015;82(10):890-5.

21. Katheria A, Mercer J, Brown M, Rich W, Baker K, Harbert MJ, et al. Umbilical cord milking at birth for term newborns with acidosis: Neonatal outcomes. J Perinatol. 2018;38(3):240-4.

22. Erickson-Owens DA, Mercer JS, Oh W. Umbilical cord milking in term infants delivered by cesarean section: A randomized controlled trial. J Perinatol. 2012;32(8):580-4.

23. Bora R, Akhtar SS, Venkatasubramaniam A, Wolfson J, Rao R. Effect of 40-cm segment umbilical cord milking on hemoglobin and serum ferritin at 6 months of age in full-term infants of anemic and non-anemic mothers. J Perinatol. 2015;35(10):832-6.

24. McAdams RM, Fay E, Delaney S. Whole blood volumes associated with milking intact and cut umbilical cords in term newborns. J Perinatol. 2018;38(3):245-50.