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Original Research Article

Assessment of Cord Clamping in Preterm Infants Less Than 37 Weeks and its Impact on the Outcomes

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Abstract

Aim: The aim of our study is to compare between immediate and delayed cord clamping in preterm infants less than 37 weeks, and its effect on the outcomes of such babies. **Methods:** This study was conducted at Department of Pediatrics, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India for 11 months. The total number of babies included in the study was 200 preterm, where the protocol of DCC was applied on 100 preterm. All infants born at less than 37 weeks' gestation were eligible for DCC and Eligible infants were left attached to the placenta for 45 seconds after birth. Neonatal process and outcome data were collected until discharge. **Results**: Mean gestational age was 34.3 weeks in the ICC group compared with 34.1 weeks in the DCC group; mean birth weight was 2330 g in the ICC cohort compared with 2415 g in the DCC cohort. Male infants represented 48 (48%) in DCC group, compared to 47 (47%) in the ICC group. There were no significant differences in 1 and 5-minute Apgar scores, admission temperature or Ph, PCO2, PO2 done at birth from the umbilical cord. Phototherapy in first week of life was significantly higher in the DCC, but none of the infants in either groups received intensive phototherapy or exchange transfusion. Incidence of RDS and surfactant administration was significantly lower in the DCC cohort. Our study showed significantly lower number of pt with IVH 22 suspected NEC 8% in DCC group. In our study, the number of babies who needed phototherapy in the DCC group (73%) was significantly higher than ICC group (51%). One analysis found a very slight (3%) increase in jaundice among babies who received delayed cord clamping. **Conclusion:** The DCC, as performed in our hospital, was associated with a significant reduction in IVH and early red blood cell transfusion. Further clinical studies are needed to optimize the timing and technique of DCC and to report the impact of this potentially valuable procedure on long term neuro developmental outcomes of the preterm infants.

Keywords: Delaying Umbilical Cord Clamping, Preterm Infant, Intra Ventricular Hemorrhage.

Introduction

In an active management strategy, the umbilical cord is usually clamped shortly following birth of the infant. This is generally carried out in the first 30 seconds after birth, regardless of whether the cord pulsation has ceased[1]. Late cord clamping, or delayed clamping, a physiological approach, involves clamping the umbilical cord when cord pulsation has ceased. However, definitions of what constitutes early and late cord clamping vary[2,3]. This placental transfusion can provide the infant with an additional 30% more blood volume and up to 60% more red blood cells[1]. The amount of blood returned to the infant also depends on when the cord is clamped and at what level the infant is held (Above or below the mother's abdomen) prior to clamping[4]. Early cord clamping may increase the likelihood of feto-maternal transfusion (The amount of blood that is forced back across the placental barrier into the maternal circulation), as a larger volume of blood remains in the placenta. This would have been considered a potential issue prior to the introduction of Rh D immunoglobulin prophylaxis, since early clamping of the cord was considered to increase the risk. The potential benefits of delayed cord clamping have been identified and they involve less intraventricular haemorrhage, less need for blood transfusion, improvement in the blood pressure and cerebral oxygenation in low birth weight neonates[5,6]. Increasing iron stores in infants through delayed cord clamping may be particularly beneficial in resource-poor settings where severe anaemia is common[7]. There is a concern that delayed cord clamping could result in polycythaemia and hyper bilirubinaemia[8]. It is vital to keep in mind that there are some situations in which it is advisable to perform early cord clamping[9]. For instance, infants with hydrops are already overloaded with fluid and may not tolerate additional volume; during foetal distress there is also a greater than normal transfer of blood from the placenta to the foetus prior to delivery; infants at risk for polycythaemia, such as infants of diabetic mothers or severely growth restricted infants, severely asphyxiated infants, and in cases where resuscitative efforts need to be initiated without delay, early cord clamping may be warranted[9,10]. The delayed cord clamping has obvious haematological benefits both in term and preterm infants as observed in many previous studies. The term infants with delayed cord clamping had higher haemoglobin, haematocrit and ferritin levels at the age of 2 months[11]. Further various expert committees including World Health Organization (WHO), American Academy of Paediatrics, and one of the studies have stressed on prevention of anaemia during first six weeks of life for normal physical and cognitive development and therefore a strong reason to delay cord clamping[12]. The aim of our study is to compare between immediate and delayed cord clamping in preterm infants less than 37 weeks, and its effect on the outcomes of such babies.

Material and methods

This study was conducted in the Department of Pediatrics, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India for 10 months. The total number of babies included in the study was 200 preterm, where the protocol of DCC was applied on 100 preterm. With approval by the institutional review board, prospective and retrospective data were extracted from maternal and neonatal electronic medical records.

Methodology

The study period for the historic cohort was also one year. Collected data included maternal demographics, obstetric complications, any antenatal steroid and

magnesium use, and other labor and delivery variables. Neonatal data included gestational age, birth weight, sex, and post-delivery data variables such as Apgar scores, resuscitation data, and the infant's temperature upon admission to the neonatal intensive care unit. Other clinical variables included treatment with phototherapy.

All infants born at less than 37 weeks' gestation were eligible for DCC, unless they met the following exclusion criteria: severe maternal illness that prompted immediate delivery, placental causes (abruption or previa) or fetal causes (multiple gestation, major congenital anomalies, severe growth restriction, or hydrops fetalis). After birth, the infant was left unstimulated, attached at or slightly below the level of placenta for 45 seconds. The cord was then clamped and cut, and the neonatal team initiated resuscitation efforts. Apgar timing was initiated at the time of birth when the infant was delivered completely. We placed the baby at or below the level of the placenta as feasible. Because most of the preterm deliveries in our institution were cesarean sections, it was a challenge getting the baby truly below the level of the placenta. Because good evidence is emerging in more mature infants, the optimal timing and positioning in a very preterm infant still must be explored. A large percentage of deliveries did not receive DCC because of our predefined narrow eligibility criteria. The DCC being beneficial or harmful in this higher risk excluded infants (such as multiple gestations, growth restricted, and other vulnerable preterm groups) must be explored carefully in the future.

Results

During the prospective study period, after implementation of DCC protocol 100 infants were born at less than 37 weeks' gestation. After excluding multiple gestation infants, DCC was performed on all of the 100 eligible infants per pre specified protocol (DCC). During the retrospective study period, 100 infants were born at less than 37 weeks' gestation, all of these infants received immediate umbilical cord clamping (ICC) after birth. There were no significant differences in maternal characteristics. Artificial reproductive therapy and cesarean delivery numbers were not different between the groups. Similarly, there were no differences in other maternal variables such as chorioamnionitis, gestational hypertension or diabetes mellitus, preeclampsia, or polyoroligohydramnios. Overall antenatal steroid administration and maternal magnesium exposure were similar between the groups. There were no significant differences in baseline neonatal characteristics between the two groups. Mean gestational age was 34.3 weeks in the ICC group compared with 34.1 weeks in the DCC group; mean birth weight was 2330 g in the ICC cohort compared with 2415 g in the DCC cohort. Male infants represented 48 (48%) in DCC group, compared to 47 (47%) in the ICC group. There were no significant differences in 1- and 5-minute Apgar scores, admission temperature or Ph, PCO2, PO2 done at birth from the umbilical cord. However, significantly fewer infants in the DCC cohort were intubated in the delivery room compared with the ICC cohort. Significant differences in glucose levels with those in the DCC group having higher initial glucose levels than those in the ICC group. Red blood cell transfusion needs in the first week of life was significantly lower in the DCC cohort compared with the ICC, although the use of presser support or corticosteroids was not different. Phototherapy in first week of life was significantly higher in the DCC, but none of the infants in either groups received intensive phototherapy or exchange transfusion. Incidence of RDS and surfactant administration was significantly lower in the DCC cohort. A significant reduction was noted in the incidence of IVH in the DCC group compared with the ICC group. After adjustment for gestational age,

an association was found between the incidence of IVH and DCC, with IVH significantly lower in the DCC group compared with the ICC group. Also, we found that, despite delaying resuscitation briefly, Apgar scores, other resuscitation variables, and mean admission temperature were not different between the DCC and ICC control groups. Additionally, a significantly lower number of infants in the DCC group were intubated in the delivery room. More infants were breathing spontaneously after DCC, which contributes to the success of non-mechanical ventilation. This supports the general hypothesis that DCC at birth decreases the need for resuscitation by promoting a more physiologic transition to extra uterine life. Number of preterm with suspected NEC (necrotizing enterocolitis) or feeding intolerance were, significantly lower in the DCC compared to ICC group.

Table 1: Maternal demographic and clinical data

Maternal Data	**DCC n= 100**	**%**	**ICC n= 100**	**%**	**P value**
Maternal age, mean (SD)	26.3(7.6)		26.2(6.3)		0.71
Artificial reproductive therapy	3	3	3	3	0.71
Number of CS	63	63	65	65	0.82
Chorioamnionitis	3	3	3	3	0.82
Gestational DM	6	6	9	9	0.76
Pre-eclampsia	3	3	5	5	0.63
Poly or oligohydramnios	7	7	11	11	0.89
Ante-natal steroid	88	88	80	80	0.56
Mg sulphate	3	3	4	4	0.73

Table 2: Infants' Demographic and Clinical Characteristics after delivery

Infants Data	**DCC 100**	**ICC 100**	**P value**
Gestational age (wk), mean (SD)	34.3(3.2)	34.1 (3.1)	0.33
Birth Weight (gm), mean (SD)	2330 (341)	2415 (369)	0.44
Sex			
Male, n (%)	48 (48)	47 (47%)	0.55
Female, n (%)	52 (52%)	53 (53%)	0.72
Apgar Score at 1min, median (range)	8(3-11)	8 (3-11)	0.73
Apgar Score at 5min, median(range)	8 (4-11)	8 (4-11)	0.74
Admission Temperature, mean (SD)	35.2 (2.2)	35.2 (2.2)	0.59
Initial blood glucose, mean (SD)	68(28.1)	48(15.2)	0.031
Initial mean blood pressure, mean (SD)	27(4.1)	30(5.5)	0.13
Intubation in the delivery room, n (%)	5(5)	7 (7.88)	0.035
PH, mean (SD)	7.3 (0.06)	7.3 (0.07)	0.67
PCO2 mmHg, mean (SD)	45(12.8)	46.1 (11.2)	0.79
PO2 mm Hg, mean (SD)	56(27)	60.1(19.2)	0.8

Table 3: Infant morbidity during NICU stay

Infants Morbidity	DCC n= 100	%	ICC n=100	%	P value
Blood transfusion after 1 wk of birth	37	37	52	52	0.022
Pressor Support or Corticosteroid	62	62	59	59	0.98
Phototherapy	73	73	51	51	0.036
RDS-use of surfactant	61	61	84	84	0.027
Assisted Ventilation	63	63	86	86	0.035
Days on oxygen, mean ± SD	46 (12.9		47 (14.1)		0.37
IVH	22	22	28	28	0.015
Suspected NEC	8	8	19	19	0.015

Discussion

Our study agreed with other studies about delayed cord clamping in preterm infants. Many obstetricians and neonatologists share the same concern regarding DCC in preterm infants, which are adverse outcomes that result from delaying the resuscitation in these infants[13-17]. We found that, despite delaying resuscitation briefly, Apgar scores, other resuscitation parameters, and mean admission temperature were not different between the DCC and control group. Additionally, a significantly lower number 5/100 (5%) of infants in the DCC were intubated in the delivery room. More infants were breathing spontaneously after DCC, which contributes to the success of non-mechanical ventilation. This supports the general hypotheses that DCC at birth decrease the need for resuscitation by promoting a more physiologic transition to extra uterine life[18,19]. Our observed reduction in the incidence of RDS and surfactant administration adds evidence to the recommendation of DCC for decreased incidence of RDS[20,21].

In our study, preterm babies who needed blood transfusion were lower (37%) in the DCC group compared to ICC group (52%), this was in agreement with physiologic studies in preterm infants, which have shown that a transfer from the placenta of approximately 80 mL of blood occurs by 1 minute after birth, reaching approximately 100 mL at 3 minutes after birth. This additional blood can supply extra iron, amounting to 40–50 mg/kg of body weight. This extra iron, combined with body iron (approximately 75 mg/kg of body weight) present at birth in a preterm newborn, may help prevent iron deficiency during the first year of life[22,23].

According to Mark Sloan, M.D., whether a baby "is premature or full term, approximately one-third of its total blood volume resides in the placenta. This is equal to the volume of blood that will be needed to fully perfuse the fetal lungs, liver, and kidneys at birth. In addition to the benefits that come with adequate iron stores babies whose cords are clamped at 2 to 3 minutes—and thus, who have an increased total blood volume compared with their immediately-clamped peers—have a smoother cardiopulmonary transition at birth[24,25]. Another potential benefit of delayed cord clamping is to ensure that the baby can receive the complete retinue of clotting factors." In other words, the increased volume of blood will naturally increase blood platelet levels, which are needed for normal blood clotting[26,27]. In our study, the number of babies who needed phototherapy in the DCC group (73%) were significantly higher than ICC group (51%). One analysis found a very slight (3%) increase in jaundice among babies who received delayed cord clamping. However, according to the Thinking Midwife, "The only studies available involve the

administration of an artificial oxytocic (syntocinon or syntometrine) in the 'delayed clamping' group IV syntocinon is associated with jaundice. Therefore, it could be the oxytocic making a difference here– not the clamping. Other studies found "that the difference between early and late cord clamping for clinical jaundice did not reach statistical significance. Another concern sometimes mentioned is polycythemia, or blood that is too thick to properly oxygenate tissues. Researchers also looked at this issue and did not find anything statistically significant[28,29]. Our study showed significantly lower number of patients with IVH 22 suspected NEC 8% in DCC group. There is growing evidence that enhanced placental transfusion by delaying umbilical cord clamping (DCC) in preterm infants may improve hemodynamic stability after birth and decrease the incidence of major neonatal morbidities, such as intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC)[29,30]. Delayed clamping also results in an infusion of "stem cells, which play an essential role in the development of the immune, respiratory, cardiovascular, and central nervous systems, among many other functions. The concentration of stem cells in fetal blood is higher than at any other time of life.

Conclusion

The present study concluded that the DCC, as performed in our hospital, was associated with a significant reduction in IVH and early red blood cell transfusion. Further clinical studies are needed to optimize the timing and technique of DCC and to report the impact of this potentially valuable procedure on long term neuro developmental outcomes of the preterm infants.

Reference

1. McDonald S. Physiology and management of the third stage of labour. In: Fraser D, Cooper M, eds. Myles textbook for midwives. 14th edn. Edinburgh: Churchill Livingstone 2003.
2. Ladipo OA. Management of third stage of labour, with particular reference to reduction of feto-maternal transfusion. British Medical Journal 1972;1(5802):721-3.
3. Prendiville W, Elbourne D. Care during the third stage of labour. In: Chalmers I, Enkin M, Keirse MJNC, eds. Effective care in pregnancy and childbirth. Oxford: Oxford University Press 1989: p. 1145-69.
4. Yao AC, Lind J. Placental transfusion. American Journal of Diseases of Children 1974;127(1):128-41.
5. Mercer JS, McGrath MM, Hensman A, et al. Immediate cord clamping in infants born between 24 & 32 weeks: a pilot randomized controlled trial. Journal of Perinatology 2003;23(6):466-72.
6. Baezinger O, Stolkin F, Keel M, et al. The influence of the timing of cord clamping on postnatal cerebral oxygenation in preterm neonates: a randomized, controlled trial. Pediatrics 2007;119(3):455-9.
7. McDonald S. Management of the third stage of labor. Journal of Midwifery and Women's Health 2007;52(3):254-61.
8. Ultee CA, Van der Deure J, Swart J, et al. Delayed cord clamping in preterm infants at 34-36 weeks' gestation: a randomised controlled trial. Archives of Disease in Childhood Fetal and Neonatal Edition 2008;93(1):F20-F3.
9. Blackburn ST. Maternal, fetal & neonatal physiology: a clinical perspective. 3rd edn. Missouri: Saunders Elsevier 2007: p. 247-8.
10. Rabe H, Reynolds G, Diaz-Rossello J. Early versus delayed umbilical cord clamping in preterm infants. Cochrane Database Systematic Review 2004;(4):CD003248.

11. Geethanath RM, Ramji S, Thirupuram S, et al. Effect of timing of cord clamping on the iron status of infants at 3 months. Ind Pediatr 1997;34(2):103-6.
12. World Health Organization. Care in normal birth: report of the technical working group meeting on normal birth. Geneva: WHO, Maternal Health and Safe Motherhood Program, 1996.
13. Jelin AC, Kupperman M, Erickson K, Clyman R, Schulkin J. Obstetrician's attitudes and beliefs regarding umbilical cord clamping. J Matern Fetal Neonatal Med. 2014; 27(14): 1457–1461.
14. Farrar D, Tuffnell D, Airey R, Duley L. Care during the third stage of labour: a postal survey of UK midwives and obstetricians. BMC Pregnancy Childbirth. 2010; 10-23.
15. Ononeze AB, Hutchon DJ. Attitude of obstetricians towards delayed cord clamping: a questionnaire-based study. J Obstet Gynaecol. 2009; 29(3): 223–224.
16. Reynolds GJ. Beyond sweetness and warmth: transition of the preterm infant. Arch Dis Child Fetal Neonatal Ed. 2008; 93(1): F2–F3.
17. Bell EF. Increasing the placental transfusion for preterm infants. Obstet Gynecol. 2011; 117(2): 203–204.
18. Redmond D, Isana S, Ingall D. Relation of onset of respiration to placental transfusion. Lancet. 1965; 285(7380): 283–285.
19. Kjeldsen J. Pedersen J. Relation of residual placental blood volume to onset of respiration and respiratory distress syndrome in infants of diabetic and non-diabetic mothers. Lancet. 1967; 289(7483): 180–184.
20. Bound JP, Harvey PW, Bagshaw HB. Prevention of pulmonary syndrome of the newborn. Lancet. 1962; 280(7249): 1200–1203.
21. Usher RH, Saigal S, O'Neill A, Surainder Y, Chua LB. Estimation of red blood cell volume in premature infants with and without respiratory distress syndrome. Biol Neonate. 1975; 26(3-4): 241–248.
22. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114(1): 297–316.
23. Bell MJ, Ternberg JL, Feigin RD. et al. Neonatal necrotizing enterocolitis: therapeutic decisions based upon clinical staging. Ann Surg. 1978; 187(1):1–7.
24. Sommers R, Stonestreet BS, Oh W, et al. Hemodynamic effects of delayed cord clamping in premature infants. Pediatrics. 2012; 129(3): e667–e672.
25. Rabe H, Diaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database Syst Rev. 2012; 15(8): CD003248.
26. Ehrenkranz RA, Walsh MC, Vohr BR. et al. Validation of the National Institutes of Health consensus definition of bronchopulmonary dysplasia. Pediatrics. 2005; 116(6): 1353–1360. doi: 10.1542/peds.2005-0249.
27. Raju TN, Singhal N. Optimal timing for clamping the umbilical cord after birth. Clin Perinatol. 2012; 39(1): 889–900.
28. An International Committee for the Classification of Retinopathy of Prematurity. The international classification of retinopathy of prematurity revisited. Arch Ophthalmol. 2005; 123(7): 991–999.
29. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with

birth weights less than 1500 gm. J Pediatr. 1978; 92(4): 529–534.
30. Bolisetty S, Dhawan A, Abdel-Latif M, Bajuk B, Stack J, Lui K. Intraventricular hemorrhage and neurodevelopmental outcomes in extreme preterm infants. Pediatrics. 2014; 133(1): 55–6.