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Original Research Article

A Randomized Comparative Clinical Assessment of the Role of Delayed Cord Clamping in Improving the Outcome in Preterm Babies

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Abstract

Aim: The aim of our study was 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 randomized, controlled trial was conducted at Department of pediatrics, Sri Krishna Medical college and Hospital, Muzaffarpur, Bihar, India for the period of one year.

Results: 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 poly- or oligohydramnios. 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 weeks in the ICC group compared with 34.1 weeks in the DCC group; mean birth weight was 2250 g in the ICC cohort compared with 2325 g in the DCC cohort. Male infants represented 35% in DCC group, compared to 38% in the ICC group. Red blood cell transfusion need in the first week of life was significantly lower in the DCC cohort compared with the ICC, although the use of pressor 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.

Conclusion: DCC, as performed in our institution, was associated with significant reduction in IVH and early red blood cell transfusions. DCC in preterm infants appears to be safe, feasible, and effective with no adverse consequences.

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

Introduction

Before the mid-1950s, the term early clamping was defined as umbilical cord clamping within 1 min of birth, and late clamping was defined as cord clamping more than 5 minutes after birth. [1,2] In obstetrics, it is usual practice to clamp and cut the umbilical cord in the first few seconds to minutes after the delivery of the infant. Waiting a longer period to clamp the umbilical cord has been shown to allow more blood from the placental circulation to enter the neonatal circulation; this is known as placental auto-transfusion. A delay of 30 to 45 seconds in cord clamping of preterm infants results in an 8% to 24% increase in blood volume (2–16 mL/kg after cesarean birth and 10–28 mL/kg after vaginal birth). [3] Immediate cord clamping (ICC) may deprive the VLBW infant of essential blood volume and create a state of potential circulatory compromise resulting in hypotension [4,5] and poor perfusion of tissues. [6,7] But recently several systematic reviews have suggested that clamping the umbilical cord in all births should be delayed for at least 30–60 seconds, with the infant maintained at or below the level of the placenta because of the associated neonatal benefits, including increased blood volume, reduced need for blood transfusion, decreased incidence of intracranial hemorrhage in preterm infants, and lower frequency of iron deficiency anemia in term infants. [8-10]

WHO recommendations 2012, based on several randomized controlled studies, for basic newborn resuscitation are, in newly born babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than 1 min after birth. [6]

The aim of our study was to compare between immediate and delayed cord clamping in preterm infants less than 37 weeks, and its effect on the outcomes of such babies.

Materials and Methods

This randomized, controlled trial was conducted at Department of Pediatrics, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India for the period of one year. During the prospective study period, after implementation of DCC protocol 80 infants were born at less than 37 weeks' gestation. After excluding multiple gestation infants, DCC was performed on all of the 79 eligible infants per pre specified protocol (DCC). During the retrospective study period, 80 infants were born at less than 37 weeks' gestation, all of these infants received immediate umbilical cord clamping (ICC) after birth.

An independent data safety and monitoring committee consisting of a maternal-fetal medicine obstetrician, a neonatologist, a nurse physiologist, and a nurse statistician reviewed the data after 14 and again after 50 patients were randomly assigned. The primary outcome variable was BPD and the secondary outcome variables were SNEC, IVH, LOS, and ROP. Other outcome variables included: Apgar scores, temperature on arrival in the NICU, the highest serum bilirubin level, initial and hourly blood pressures for 4 hours, initial hematocrit, and need for blood transfusion during the infant's hospital stay.

Inclusion criteria: All women admitted between 24 and 31.6 weeks' gestation with preterm labor. The gestational age assessment using last menstrual period and/or early pregnancy ultrasound was used to establish eligibility for the study.

Exclusion criteria: Obstetrician's refusal to participate, major congenital anomalies or multiple gestations, intent to withhold care, severe maternal illnesses, or placenta abruption or previa.

Women had to be admitted to the hospital at least 2 hours before delivery to allow time for enrollment. Once a potential subject was identified, approval of the attending obstetrician was obtained, the mother was approached, and written informed consent was obtained.

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, 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, (intensive phototherapy defined as irradiance in the blue-green spectrum of at least 30 μW/cm2 per nm).

For all tests of significance, p-values less than 0.05 were considered statistically significant and were used as evidence against the null hypothesis of no difference between DCC and ICC participants. All statistical methods were performed using the SAS software system (Release 8.2, SAS Institute, Inc., Cary, NC, USA).

Results

Table 1: Maternal demographic and clinical data

Maternal Data	DCC n=80	ICC n=80	P value
Maternal age, mean (SD)	26.3(6.7)	26.2(5.4)	.8
Artificial reproductive therapy, n (%)	2 (2.5)	1 (1.25)	.8
Number of CS, n (%)	48 (60)	52 (65%)	.9
Chorioamnionitis, n (%)	1 (1.25)	1 (1.25)	.8
Gestational DM, n (%)	3 (3.75)	5 (6.25%)	.66
Pre-eclampsia, n (%)	1 (1.25)	3 (3.75)	.7
Poly or oligohydramnios, n (%)	5 (6.25)	7 (8.75)	.9
Ante-natal steroid, n (%)	68 (85)	74 (92.5)	.5
Mg sulfate	1 (1.25)	2 (2.5)	.8

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 poly- or oligohydramnios. Overall antenatal steroid administration and maternal magnesium exposure were similar between the groups.

Table 2: Infants' Demographic and Clinical Characteristics after delivery

Infants Data	DCC 80	ICC 80	P value
Gestational age wk, mean (SD)	34.2(2.2)	34.6(2)	0.3
Birth Weight age, mean (SD)	1325(365)	1250(429)	0.4
Sex			
Male, n (%)	36 (45%)	38 (47.5%)	0.5
Female, n (%)	44(55%)	42(52.5%)	0.7
Apgar Score at 1min, median (range)	8 (3-9)	8 (3-9)	0.7
Apgar Score at 5min, median(range)	9 (4-9)	9 (5-9)	0.7
Admission Temperature, mean (SD)	36.8 (2.3)	36.7 (2.2)	0.5
Initial blood glucose, mean (SD)	73 (28.1)	51s(18)	0.03
Initial mean blood pressure, mean (SD)	29(4.8)	33(6)	0.1
Intubation in the delivery room, n (%)	3 (3.75%)	7 (8.75%)	0.03
PH, mean (SD)	7.3 (0.06)	7.3 (0.07)	0.6
PCO2 mmHg, mean (SD)	47 (13.2)	46.3 (11.6)	0.7
PO2 mm Hg, mean (SD)	55 (28)	60.3(20.4)	0.8

There were no significant differences in baseline neonatal characteristics between the two groups. Mean gestational age was 34 weeks in the ICC group compared with 34.1 weeks in the DCC group; mean birth weight was 2250 g in the ICC cohort compared with 2325 g in the DCC cohort. Male infants represented 35% in DCC group, compared to 38% 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.

Table 3: Infant morbidity during NICU stay

Infants Morbidity	DCC 80	ICC 80	P value
Blood transfusion after 1 wk of birth, n (%)	24(30)	36(45)	0.02
Pressor Support or Corticosteroid, n (%)	42(52.5)	46 (57.5)	0.9
Phototherapy, n (%)	52 (65)	40 (50)	0.03
RDS-use of surfactant n (%)	44 (55)	64 (80)	0.02
Assisted Ventilation, n (%)	52 (65)	66 (82.5)	0.03
Days on oxygen, mean ± SD	45 (14.3)	49 (16.7)	0.3
IVH, n(%)	16 (20)	24 (30)	0.01
Suspected NEC, n (%)	8 (10)	16(20)	0.01

Red blood cell transfusion need in the first week of life was significantly lower in the DCC cohort compared with the ICC, although the use of pressor 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 extrauterine life. Number of preterm with suspected NEC (necrotizing enterocolitis) or feeding intolerance were, significantly lower in the DCC compared to ICC group.

Discussion

In obstetrics, it is usual practice to clamp and cut the umbilical cord in the first few seconds to minutes after the delivery of the infant. Anyone who has participated in this practice has noted that there is still blood left in the umbilical cord vessels that represents a portion of the fetal circulation. Waiting a longer period to clamp the umbilical cord has been shown to allow more blood from the placental circulation to enter the neonatal circulation; this is known as placental auto-transfusion.

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. [11-15] 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 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. [16,17] Our observed reduction in the incidence of RDS and surfactant administration adds evidence to the recommendation of DCC for decreased incidence of RDS. [18,19]

In our study, preterm babies who needed blood transfusion were lower in the DCC group compared to ICC group, 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. [20,21] 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. [22,23]

In our study, the number of babies who needed phototherapy in the DCC group were significantly higher than ICC group. One analysis found a very slight (2%) 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. [24,25] In agreement with other studies, our study showed significantly lower number of pt with IVH and suspected NEC 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). [25,26] 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. ICC [immediate cord clamping] leaves nearly one-third of these critical cells in the placenta. Stem cells may also "help to repair any brain damage the baby might have suffered during a difficult birth," [27,28,29]

Conclusion

DCC, as performed in our institution, was associated with significant reduction in incidence of IVH. DCC in preterm infants appears to be safe, feasible, and effective with no adverse consequences. Our study demonstrates that implementation of the DCC process with standardized protocol in preterm infants is feasible and effective with improved outcomes. In conclusion, we have implemented DCC process successfully in a large delivery hospital. 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.

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