

Effect of Timing of Umbilical Cord Clamping on Neonatal Jaundice in Preterm Newborns between Gestational Age 32-36 Weeks: An Observational Study

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Abstract: *There is concern regarding safety of delayed cord clamping in preterm newborns. Thus, Aa hospital based prospective, observational study on vaginally delivered stable babies between 32 to 36 weeks gestation born to mothers with no apparent co-morbid illness and complications was done. Timing of cord clamping was noted and 100 newborns subjected to DCC (>30sec till 180sec) or ECC (<30sec) at birth were enrolled. Primary objective was to compare hyperbilirubinemia and need of requirement of phototherapy in the study groups in first week of life. Secondary outcomes included, hematocrit and ferritin levels at 6 weeks postnatal age. Mean peak bilirubin levels in ECC and DCC group were 11.3mg/dl and 12.57mg/dl respectively (p>0.001). Results showed no increased risk of hyperbilirubinemia in DCC group. Mean Hct at 6weeks in ECC and DCC group was 30.47% and 38.17% respectively (p<0.001); significantly higher in DCC group. DCC performed in moderate to late preterm infants showed no increased risk of hyperbilirubinemia or need /duration of phototherapy in respect to timing of cord clamping. DCC benefits moderate to late preterms with no significant adverse effects and helps in building iron stores in infants and preventing anemia at 6 weeks. The ability to provide delayed umbilical cord clamping may vary among institutions and settings. The ability to provide delayed umbilical cord clamping may vary among institutions and settings. The ability to provide delayed umbilical cord clamping may vary among institutions and settings. Results showed no increased risk of hyperbilirubinemia in DCC group. Mean Hct at 6weeks in ECC and DCC group was 30.47% and 38.17% respectively (p<0.001).*

Keywords: Preterm; Neonates; Polycythemia; Hyperbilirubinemia; Clamping

1. Introduction

One essential goal of neonatal critical care is to deliver adequate oxygen to baby to meet tissue demand. Increasing fetal hemoglobin (Hb) by placental transfusion is an extremely effective method of enhancing oxygen content in arteries, increasing cardiac output and improving oxygen delivery. Immediate cord clamping (ICC) results in approximately 30% of fetoplacental blood volume remaining in the placenta, whereas DCC reduces residual fetoplacental blood volume to 20% by 60 s and to 13% by 3–5 min.

Every year, an estimated 15 million babies are born preterm worldwide and incidence of preterm babies born in India is 3.5 million. Moderate to late preterm babies (32–36 weeks of gestation) are at risk of various short-term morbidities such as respiratory distress, apnea, hyperbilirubinemia, feeding difficulties, requiring admission directly to neonatal intensive care unit for observation and may require critical care support. The timing for performing the clamping of the umbilical cord at preterm birth in different healthcare setting are variable¹. In preterm births, most studies define ECC as the clamping of the umbilical cord immediately after

delivery (within 15 to 30 seconds), while DCC is usually anytime beyond 30 seconds after delivery.^{2,3,4}

Despite the evidences favoring placental-to-newborn transfusion strategies over immediate cord clamping (ICC) at birth in both terms and preterms, implementation of DCC or UCM to improve outcomes and reduce risks in newborns has not been widespread.^{5,6} The ability to provide delayed umbilical cord clamping may vary among institutions and settings as theoretical concerns like hyperbilirubinemia, polycythemia and delayed resuscitation due to delayed cord clamping results in a liberal exclusion clause within their policy. Hence, the present study was conducted to determine effects, feasibility of DCC in preterms being followed in our institute and its effect on serum bilirubin levels in first week of life.

2. Material and Methods

Study design: A hospital based prospective observational study from Nov 2017- March 2019.

Participants: All mothers who presented to labor room of our tertiary care unit with gestation 32–36 weeks by LMP or

by first trimester ultrasound (if LMP was not known) who were likely to deliver by vaginal delivery were screened for eligibility and approached for consent. Neonates with congenital malformations , newborns requiring resuscitation, babies with cyanosis, respiratory distress requiring admission, birth asphyxia/birth trauma, maternal morbidities and complications like abruptio placentae, cord prolapse ,multiple pregnancy were excluded.

Methods

An informed and valid consent was taken from one of the parents and the stable newborns born by vaginal delivery between 32 to 36 weeks were included. Baseline demographic information and clinical details were obtained .The observation of cord clamping timing was done by an independent observer not involved in the care of mother; using a digital stop watch from the time of complete expulsion of baby till the cord is clamped by the obstetric health care provider. No active intervention was done during the course of study. Obstetric practice in the labor room was observed and the stable babies were allocated in one of the two groups: ECC group (at or within 30 seconds of birth) and DCC group (> 30 sec till 180 seconds).

Sample size was calculated using Kelsey's formula. 100 newborns (ECC=44 and DCC=56) were enrolled. The infants were monitored as per standard NICU protocols. Infants were monitored every twelve hours and anytime if significant clinical jaundice was noted till one week of life, it was confirmed by serum bilirubin levels.

Hyperbilirubinemia was defined and managed according to NICE guidelines (UK) in gestation <34 weeks newborn and acc. to American Academy of Pediatrics (AAP) guidelines⁷ if gestation ≥35 weeks. Secondary outcomes included haematological parameters like haematocrit and ferritin levels at 6 weeks, babies requiring red blood cell transfusions, morbidities such as IVH, NEC, Sepsis, BPD, NICU stays. Morbidities were defined according to standard definitions. Polycythemia was defined as a venous haematocrit of >65%⁸. Excluding 27 among the 100 enrolled infants (who lost to follow-up :not responding to telephone calls, changed phone numbers), haematocrit and ferritin levels were sent at 6 weeks of life. Completed data was collected and analysed.

3. Results

The baseline demographic and clinical characteristics of the subjects in study groups were compared and they showed statistically insignificant difference (Table 1). Most of the women went into spontaneous labor in the study groups. In ECC group the mean maternal Hb, was 10.12± 1.61g/dl and in DCC was 10.58±1.66g/dl. The mean gestational age in ECC group was 33.80 weeks and 34.41 weeks, comparable in the two groups. The mean time of cord clamping in ECC group was 22.86±4.65 seconds and DCC group was 42.41±9.28 seconds. Mean birth weight between the groups was ECC=1809.34 grams and DCC=1832.46 grams.

The primary outcome variables are shown in Table 2 and Figure 1. Mean peak bilirubin levels in ECC and DCC group

showed no significant difference in respect to timing of cord clamping. On comparing the primary outcome variables within the study groups, incidence of NNH was 13.6% babies in ECC and 25% babies in DCC group, which was statistically not significant in respect to timing of cord clamping. Out of total babies with NNH in each group, 50% in ECC group and 35.7% babies in DCC group required phototherapy as an intervention. None of them required DVET as an intervention for NNH.

Table 1: Demographic variables in study groups

Variable	ECC (n=44)	DCC (n=56)	p value
Maternal Hb. mean± SD (gm/dl)	10.12± 1.61	10.58 ±1.66	0.169
Gender			
Male (%)	72.7	44.6	0.025
Female (%)	27.3	55.4	
Birth weight (mean± SD) (grams)	1809.34±343.81	1832.46±305.72	0.728
Gestational age (mean± SD) (weeks)	33.80±1.4	34.41±1.3	0.06
APGAR score			
At 1 min (median± IQR)	7±1	8±1	0.214
At 5 min (median± IQR)	8±1	9±1	0.021

Table 2: Primary outcome variables in the study groups

Variable	ECC (n=44)	DCC (n=56)	p value
Newborns with NNH (n (%))	6(13.6%)	14(25%)	0.086
Newborns with NNH requiring PT (n (%))	3(50%)	5(35.7%)	1.000
Mean peak bilirubin levels (mg/dl)	11.3±1.84	12.57±3.35	0.409
Mean phototherapy hours (hrs)	24.67±11.01	29.20±17.86	0.763

Newborns were followed up till 6 weeks of life and hematological parameters were assessed at 6 weeks to evaluate the effects of delayed cord clamping. Mean Hct at 6 weeks in ECC and DCC group was 30.47% and 38.17% respectively, which was significantly higher in DCC group (p<0.05). In the ECC and DCC groups, mean ferritin levels at 6 weeks of age were 154.32±46.9 ng/ml and 183.4±54.2 ng/ml which was statistically significant.

Secondary outcomes like IVH, NEC, sepsis, BPD were also included and compared in the study groups. None of the study subjects in ECC or DCC group had NEC, IVH or BPD. Culture-positive sepsis was found in 3 out of 44 babies in ECC and 1 in DCC group, with no statistical significance.

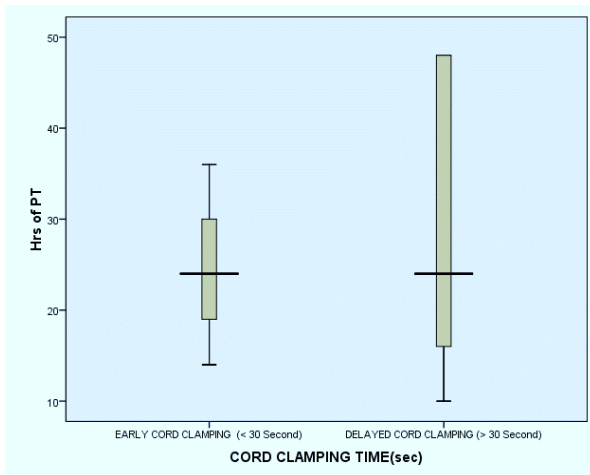


Figure 1: Distribution of mean phototherapy hours in ECC and DCC groups

Table 3: Tabulated secondary outcome variables data in the study groups

Variable	ECC (n=44)	DCC (n=56)	p value
Hb at 6weeks (gm/dl)	10.18±1.13	9.4-14.8	0.000
Hct at 6weeks(%)	30.47±3.3	38.17±4.7	0.000
Ferritin at 6weeks(ng/ml)	154.32±46.9	183.4±54.2	0.038
Culture-positive sepsis , n(%)	3(6.8%)	1(1.8%)	0.317
Red blood cell transfusions, n(%)	0	1(1.8%)	0.140
Intraventricular Hemorrhage, n(%)	0	0	-
Necrotising Enterocolitis, n(%)	0	0	-
Bronchopulmonary dysplasia, n(%)	0	0	-

4. Discussion

This shows no significant difference in hyperbilirubinemia between two study groups in respect to association with delayed cord clamping. Higher requirement of phototherapy in ECC group can be explained by factors like inadequate feeding, cephalhematoma, etc. There was no case of haemolytic disease of newborn due to ABO/Rh incompatibility in ECC group. Mean peak bilirubin levels of babies with NNH in their first week of life in ECC and DCC group were 11.3±1.8mg/dl and 12.57±3.4mg/dl respectively, which was statistically insignificant (p)

We observed no significant difference in hyperbilirubinemia between two study groups in respect to timing of umbilical cord clamping. The present study results are comparable with study results by Chirulovu et al⁹, which showed mean bilirubin levels of 8.76±2.01mg/dl and 9.51±2.22gm/dl in historic cohort and DCC cohort respectively at 48hrs of life. In the meta-analysis done by Hutton et al¹⁰ including 8 trials, there was no significant difference in mean serum bilirubin levels within the first 24 hours of life^{11,12}. Higher requirement of phototherapy in ECC group can be explained by factors like inadequate feeding, cephalhematoma, etc.

Mean peak bilirubin levels of babies with NNH in their first week of life in ECC and DCC group were 11.3±1.8mg/dl and 12.57±3.4mg/dl respectively, which was statistically insignificant (p=0.409). Dicky et al¹³ and Chiruvolu et al¹⁴ showed similar results with no significant increase in incidence of jaundice and requirement of phototherapy in

ECC and DCC groups as well as length of hospital stay and need for admission to NICU.

Mean ferritin levels at 6 weeks of age in ECC and DCC group were 154.32±46.9 ng/ml and 183.4±54.2 ng/ml. Similar to our study, Ranjit et al¹⁵ studied the mean serum ferritin between ECC and DCC groups and the results were significantly higher in the infants randomized to DCC group.

DCC performed in moderate to late preterm infants was associated with increased haematocrit and better circulatory stability at birth. Few potential disadvantages like polycythemia and jaundice were not associated with delayed cord clamping and there was no increased incidence and duration of requirement of phototherapy for hyperbilirubinemia in DCC groups. In present study, the higher requirement of phototherapy in ECC group can be explained by factors like prematurity, inadequate feeding, cephalhematoma, etc.

There was statistically significant increase in hematocrit levels in infants at 6 weeks of life. A significant difference in ferritin levels was seen in DCC group in the way that DCC helps in building iron stores in infants and decreases need for blood cell transfusions. Confounding factors like poor socioeconomic status, lack of awareness, poor compliance of mothers to seek healthcare and visits for follow-up were a few factors which could have affected the final outcomes.

The present study adds to the growing body of knowledge on the benefits of DCC in preterm infants especially from a developing country like India. Delayed cord clamping of the umbilical cord is a physiologic and inexpensive means of enhancing hematological status and preventing anaemia at 6 weeks, also it is likely to have an important impact on all preterm newborns who do not require resuscitation at birth. Placental transfusion should always be considered at every delivery as it can have a marked impact on the outcomes of newborns and adopt a team-based approach to ensure that it's a routine practice.

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