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Effect of delayed cord clamping on very preterm twins

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ABSTRACT

Background: The very preterm infants of twin births may particularly benefit from delayed cord clamping (DCC) as the likelihood of unfavorable outcome is greater compared to singletons. Unfortunately, there is paucity of available information regarding safety and efficacy of DCC in this group.
Objective: To report the clinical consequences of delayed cord clamping (DCC) in very preterm twins, born between $23^{0/7}$ and $31^{6/7}$ weeks gestation.
Study design: In this pre and post intervention retrospective cohort study, we compared 30 very preterm infants born from 15 twin deliveries during historic study period to 32 very preterm infants born from 16 twin deliveries during DCC study period. During historic study period (August 19, 2013 to January 31, 2015), infants included were eligible to receive DCC, but their cords were immediately clamped. DCC study period (February 1, 2015 to January 31, 2017) included infants who had DCC performed for 60 s after birth.
Results: The Apgar scores and other resuscitation variables were similar between both groups. After adjusting for gestational age and mode of delivery, significantly fewer infants in the DCC cohort needed red blood cell (RBC) transfusions in first week of life compared to the historic cohort (15.6% vs. 43.3%; $P = 0.03$). Death and other major neonatal outcomes were similar between both groups.
Conclusion: DCC in very preterm twins was safe, feasible and not associated with any adverse neonatal outcomes compared to early cord clamping. DCC was associated with a significant reduction in early RBC transfusions.

1. Introduction

There is published evidence that enhanced placental transfusion by delaying umbilical cord clamping is beneficial in very preterm infants. This includes improved hemodynamic stability after birth resulting in decreased need for early red blood cell (RBC) transfusions, and lower incidence of major neonatal morbidities, such as intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC) [1–6]. Unfortunately, there is paucity of information available on the effect of delayed cord clamping (DCC) on very preterm infants of twin births, as they were excluded from many of the clinical trials [7]. These higher risk premature infants may particularly benefit from DCC, as the likelihood of unfavorable outcome is greater compared to singletons born at similar gestation [8,9]. However, there are concerns regarding safety and efficacy of DCC in this group. The 2017 American College of Obstetricians and Gynecologists (ACOG) committee opinion no. 684 did not make a recommendation for or against DCC in twin gestations, due to insufficient evidence [10].

In our institution, we started performing DCC on twin births starting February 1, 2015. The objective of this cohort study is to report the clinical consequences of DCC in very preterm twin gestations, born between $23^{0/7}$ and $31^{6/7}$ weeks. We hypothesized that DCC for 60 s in these infants would not compromise initial resuscitation and would not be associated with any adverse effects compared to a similar historic cohort with early cord clamping.

2. Methods

The DCC quality improvement (QI) process was implemented in our hospital on very preterm singleton infants, starting August 19, 2013. It was extended to include twin gestations starting February 1, 2015. All infants of twin births born between $23^{0/7}$ and $31^{6/7}$ weeks gestation were eligible for DCC, unless they met one of the following exclusion criteria: severe maternal illness that prompted immediate delivery, placental causes (abruption or previa) or fetal causes (major congenital anomalies or hydrops fetalis). After birth, the first twin was left

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attached at or slightly below the level of the placenta for 60 s by calling the time every 15 s (15, 30, 45, 60). The cord was then clamped and cut, and the infant was handed over to the neonatal team to initiate the resuscitation efforts. The same DCC process was repeated for second twin. Apgar timing was initiated at the time of birth when infant was delivered completely. Cord milking was not performed in either group.

With approval from the local institutional review board, we performed a pre and post intervention retrospective cohort study. The historic study period included 15 twin deliveries from August 19, 2013 to January 31, 2015. DCC study period included 16 twin deliveries from February 1, 2015 to January 31, 2017. Collected data included maternal demographics, obstetric complications, antenatal steroid and magnesium use. Neonatal data included gestational age, birth weight, gender, Apgar scores, temperature on admission to the neonatal intensive care unit (NICU) and hematocrit at birth (obtained in the NICU within first 1 h of life). Other clinical variables included phototherapy, RBC transfusion, inotropic and steroid therapy in the first one week of life. RBCs were transfused for symptomatic anemia associated with hematocrit < 40%. Additional outcome variables included incidence of respiratory distress syndrome (RDS), surfactant therapy, patent ductus arteriosus needing therapy, culture positive sepsis and hospital length of stay (LOS). Surfactant was administered via endotracheal tube if oxygen requirement exceeded 30% in the first 24 h of life. We also recorded incidence of major neonatal outcomes such as death, IVH, bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), and NEC Bell's stage ≥2 [11]. IVH was graded 1to 4 based on the criteria developed by Papile et al. who defined grades 3 and 4 as severe IVH [12]. White matter injury, such as periventricular leukomalacia and porencephaly also were documented. Diagnosis of BPD was made at 36 weeks post-menstrual age if there was any supplemental oxygen requirement [13]. Any operative interventions for NEC or ROP were also documented [14].

Maternal data were compared between the historic and DCC cohorts with the use of the Student *t*-test for continuous variables, and chi-squared or Fisher exact test for categorical variables. Due to correlation between the twin's observations, Generalized Linear Mixed Models (GLMMs) were utilized to evaluate the neonatal outcomes between the two groups adjusting for gestational age and mode of delivery. A probability value < 0.05 was considered to be the threshold of statistical significance. Statistical analyses were performed with JMP (version 13.2) and SAS Enterprise Guide software (version 7.1; SAS Institute Inc., Cary, NC).

3. Results

During the historic study period, out of 22 very preterm twin deliveries, 15 were eligible for DCC (68%) resulting in a historic cohort of 30 very preterm infants of twin births. These infants were eligible to receive DCC, but their cords were immediately clamped as they were born prior to DCC implementation in twin gestations. The 7 deliveries were ineligible for DCC due to placental causes. During the DCC study period, out of 21 twin deliveries, 16 received DCC (76%) resulting in the DCC cohort of 32 infants. These infants had DCC performed for 60 s after birth. DCC was not performed in 5 deliveries due to placental causes.

There were no significant differences in the maternal demographics (Table 1). The incidence of pregnancy with assisted reproductive technology was similar in both groups. The type of twin gestation did not differ between both groups, with majority being dichorionic. Antenatal steroid and magnesium therapy were similar between both groups. There were no differences in the incidence of other obstetric complications, such as hypertensive disorders of pregnancy, diabetes and chorioamnionitis. However, the incidence of cesarean section was significantly higher in DCC cohort compared to historic cohort (87.5% vs. 46.7%; $P = 0.04$). Postpartum hemorrhage was not reported in either group.

Table 1
Maternal characteristics.

	Historic cohort ($n = 15$)	DCC cohort ($n = 16$)	*P*
Maternal age, years[a]	26.5 ± 6.1	29.3 ± 5.1	0.19
Maternal race, n (%)			0.58
White	6 (40)	9 (56.3)	
Black	5 (33.3)	3 (18.7)	
Other	4 (26.7)	4 (25)	
Hypertensive disorders of pregnancy, n (%)	2 (13.3)	4 (25)	0.65
Maternal diabetes, n (%)	0 (0)	1 (6.3)	0.99
Assisted reproductive technology, n (%)	4 (26.7)	3 (18.7)	0.69
Twin gestation type, n (%)			0.99
Dichorionic	14 (93.3)	15 (93.7)	
Monochorionic	1 (6.7)	1 (6.3)	
Antenatal steroids, n (%)	13 (86.7)	14 (87.5)	0.99
Maternal magnesium, n (%)	14 (93.3)	16 (100)	0.49
Chorioamnionitis, n (%)	0 (0)	1 (6.3)	0.99
Rupture of membranes > 18 h, n (%)	2 (13.3)	5 (31.3)	0.38
Cesarean section, n (%)	7 (46.7)	14 (87.5)	0.04

[a] Data are given as mean ± SD.

Table 2
Neonatal characteristics.

	Historic cohort ($n = 30$)	DCC cohort ($n = 32$)	*P*
IUGR, n (%)	5 (16.7)	8 (25)	0.74
Gestation, weeks[a,b]	27.5 ± 2.6 29.7 (25.3–29.6)	28.6 ± 2.6 29.7 (26.5–30.3)	0.33
Birth weight, grams[a,b]	1023.8 ± 311 1035 (700–1213)	1187.8 ± 367 1220 (965–1455)	0.17
Male, n (%)	19 (63.3)	17 (53.1)	0.75
Apgar score, n[b]			
1 min	5 (1–8)	7 (1–9)	0.16
5 min	8 (4–9)	9 (6–9)	0.43
Intubation in DR, n (%)	11 (36.7)	7 (21.9)	0.78
Admission temperature, F[a,b]	98.1 ± 0.9 98 (97.4–98.5)	98.1 ± 1.2 98 (97.2–99.1)	0.90
Hematocrit at birth, %[a,b]	44.7 ± 7.0 43.2 (39.2–48.6)	48 ± 6.4 48.1 (42.4–51.9)	0.30

IUGR: Intrauterine growth restriction; DR: delivery room.
[a] Data are given as mean ± SD.
[b] Data are given as median (range).

There were no significant differences in neonatal characteristics, such as gestational age, birth weight, gender or incidence of intrauterine growth restriction between both groups (Table 2). The 1 and 5 min Apgar scores were similar between both cohorts. Similarly, the NICU admission temperature and the hematocrit at birth did not differ between both groups. After adjusting for gestational age and mode of delivery, significantly fewer infants in the DCC cohort needed RBC transfusions in first week of life compared to the historic cohort (15.6% vs. 43.3%; $P = 0.03$). The need for inotropes, steroids or phototherapy in the first one week of life did not differ between the groups. Fewer infants in the DCC cohort received surfactant therapy for RDS compared to historic cohort (43.8% vs. 80%; $P = 0.04$). Major neonatal outcomes, such as death, IVH, severe IVH, PVL, BPD, ROP and NEC were similar between both groups (Table 3). Median RBC transfusions during the entire hospital stay and median LOS were not significantly different between the groups.

4. Discussion

There is little information with regard to the safety and efficacy of DCC in twins making it one of the major gaps in evidence [7]. In the recently published statement, ACOG could not recommend for or against DCC in multiple gestations as there is lack of sufficient evidence [10]. The current study shows that DCC is safe, feasible, and not