Effects of Delayed Cord Clamping on Residual Placental Blood Volume, Hemoglobin and Bilirubin Levels in Term Infants: A Randomized Controlled Trial

Mercer, J. S., Erickson-Owens, D. A., Collins, J., Barcelos, M. O., Parker, A. B., & Padbury, J. F. (2017).

Emily McGregor
Math 1010
Final Presentation
December 17th 2021

Objective:

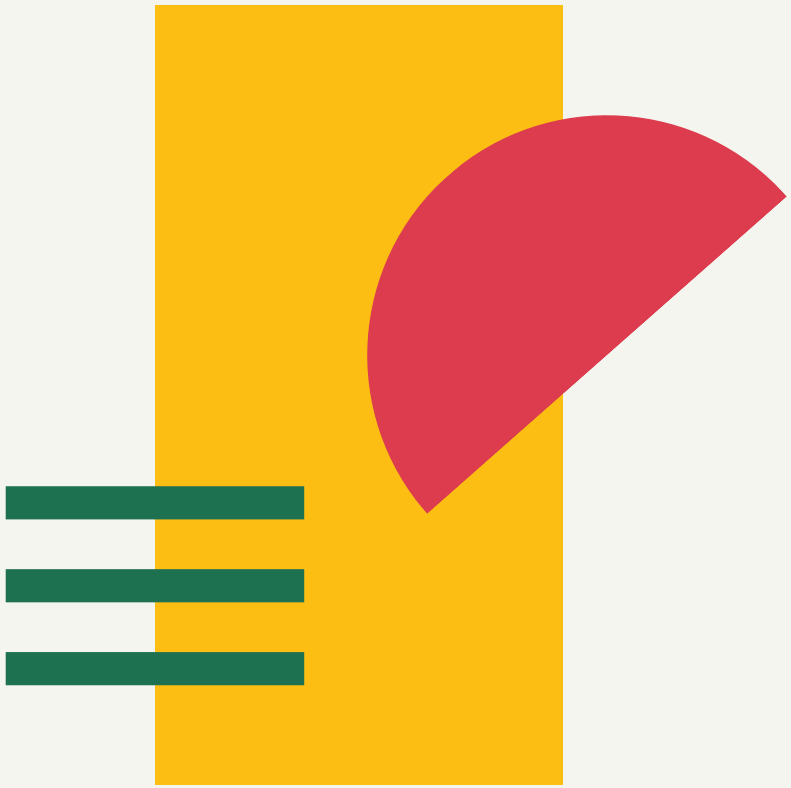
To measure the effects of a five-minute delay (DCC) versus immediate cord clamping (ICC) on residual placental blood volume (RPBV) at birth, and hemoglobin and serum bilirubin at 24 to 48 hours of age.

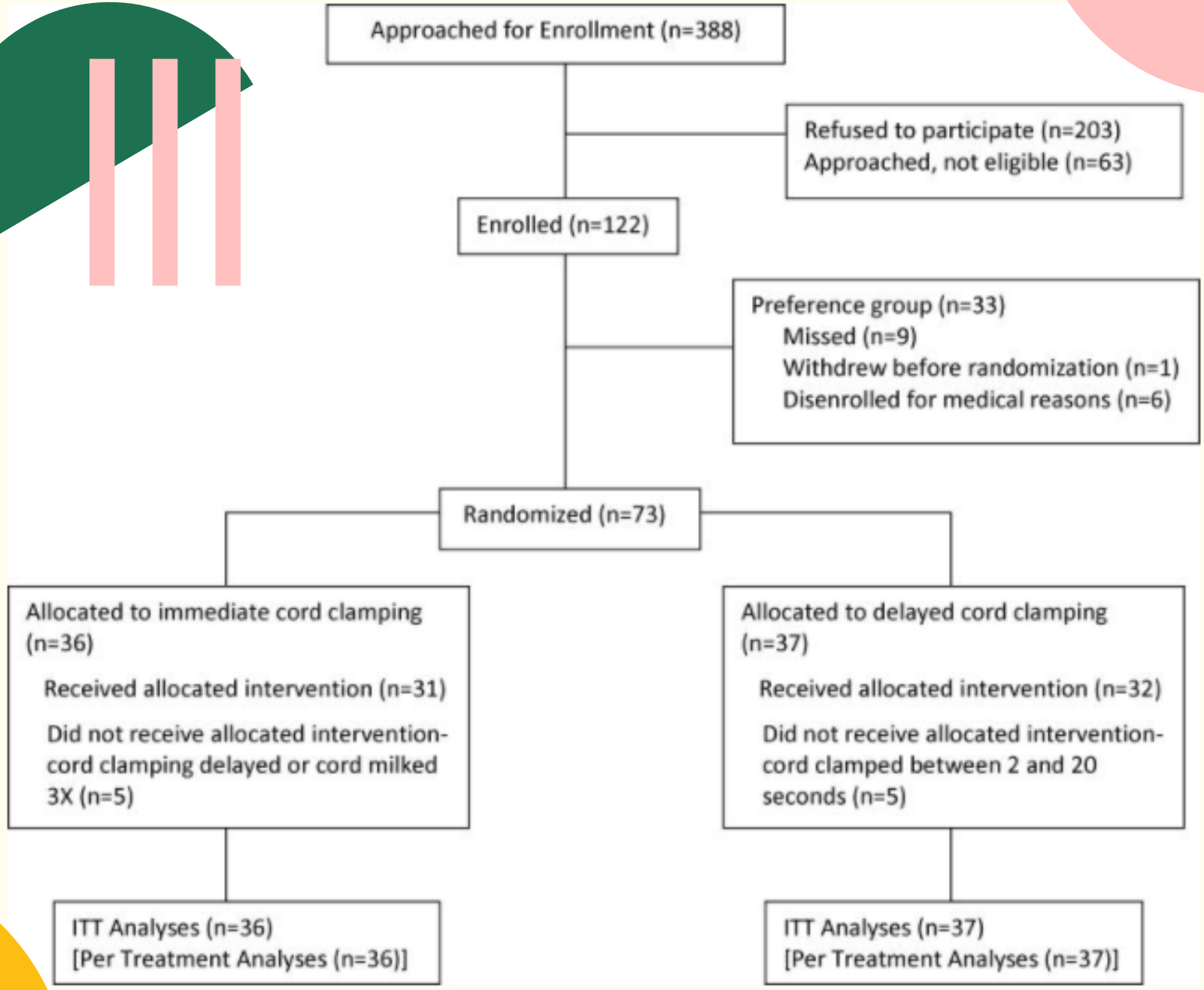
FINAL PROJECT

Hypothosis &Null Hypothosis

Hypothesis: that term infants with DCC of five minutes (or UCM x 5) have lower amounts of RPBV associated with higher hematocrit and hemoglobin at 24 to 48 hours and no increase in jaundice, symptomatic polycythemia, or other adverse effects.

Null: that term infants with DCC of five minutes (or UCM x 5) had equal or lower amounts of RPBV. Or that this was associated with higher hematocrit and hemoglobin at 24 to 48 hours and did have an increase in jaundice, symptomatic polycythemia, or other adverse effects.




Approached for Enrollment (n=388)
Refused to participate (n=203)
Approached, not eligible (n=63)
Enrolled (n=122)
Preference group (n=33)
Missed (n=9)
Withdrew before randomization (n=1)
Disenrolled for medical reasons (n=6)
Randomized (n=73)
Allocated to immediate cord clamping (n=36)
Received allocated intervention (n=31)
Did not receive allocated intervention-cord clamping delayed or cord milked 3X (n=5)
Allocated to delayed cord clamping (n=37)
Received allocated intervention (n=32)
Did not receive allocated intervention-cord clamped between 2 and 20 seconds (n=5)
ITT Analyses (n=36)
[Per Treatment Analyses (n=36)]
ITT Analyses (n=37)
[Per Treatment Analyses (n=37)]

Sampling & Methods

Who was in the study

"In this prospective randomized controlled trial, seventy-three women with term (37 to 41 weeks) singleton fetuses were randomized to DCC (⩾5 minutes; n=37) or ICC (<20 seconds; n=36)."

The study group is small

I was a little shocked to see how small the sample group was. This is a topic that has been well discussed for many years. Out of the total 73 birthing people, 37 babies received the full 5 min DCC and 36 received ICC.

Requirements for study: (more on next slide)

DCC in this study was a full 5 minutes or more, ICC was 20 seconds or less.
The people in this study were birthing in Rhode Island at Women and Infants Hospital.

MATHEMATICS CLASS

Requirements for this study

Women were eligible if they were expecting a healthy singleton pregnancy in the vertex position at term (37-416/7 weeks), had no evidence of medical or obstetrical complications (i.e. hypertension, pre-eclampsia, diabetes, smoking, substance abuse, suspected intrauterine growth restriction), were planning on breastfeeding, spoke English, and were at least 18 years of age.

Looking deeper

had no evidence of medical or obstetrical complications (i.e. hypertension, pre-eclampsia, diabetes, smoking, substance abuse, suspected intrauterine growth restriction), were planning on breastfeeding, spoke English, and were at least 18 years of age. Infants with evidence of intrauterine growth restriction and serious congenital anomalies were excluded. All participants were screened and informed about the study by registered nurses (RNs) who completed the written informed consent with each mother. Doulas were assigned as research assistants (RAs) to each woman to support communication both pre-labor and postpartum and to attend the births, assign randomization, collect the RPBV, conduct two-day hospital visits, and assist with follow-up.

Sampling continued

Enrollment for this prospective randomized controlled trial was conducted from July 2013 to November 2015 at Women and Infants Hospital (WIH) in Providence, Rhode Island after approval by the WIH and the University of Rhode Island Institutional Review Boards. Follow-up for this study is out to 24 months of age and will be finished in November 2017. An independent data safety and monitoring committee reviewed the data after 42 infants were randomly assigned. No concerns were identified.

How the study was conducted:

Materials and Methods:

The RPBV was collected via a blood collection bag and weighed (1 gm = 1mL). The provider inserted the blood bag needle into the umbilical vein when collection was in-utero. Ex-utero collection was done by suspending the placenta and draining into blood bag via needle inserted in the vein. The cord was drained until there was no more blood returned usually about one to two minutes. Blood was collected with the placenta in-utero at vaginal deliveries (n = 54) and ex-utero after cesarean section (n = 19) by necessity.

Results:

Maternal and infant demographics were not different between groups. Mean cord clamping time was 303 ± 121 (DCC) versus 23 ± 59 (ICC) seconds ($p<0.001$) with 10 protocol violations. Cord milking was the proxy for DCC (n = 11) when the provider could not wait. Infants randomized to DCC compared to ICC had significantly less RPBV (20.0 vs 30.8 mL/kg, $p<0.001$), higher hemoglobin levels (19.4 vs 17.8 g/dL, $p=0.002$) at 24 to 48 hours, with no difference in bilirubin levels.

Statistical Analysis

Data analyses included two-sided Pearson's chi-square tests, t-tests, and Wilcoxon rank-sum tests for non-normally distributed variables. Odds ratios and 95% confidence intervals were examined as appropriate. Primary analyses were conducted using intention-to-treat, and sensitivity analyses were conducted using actual treatment in order to assess the robustness of the findings and to examine results of the biologic variables.

shows that there were no significant differences between the DCC and ICC groups with respect to maternal demographics or clinical variables.

Table 1

Maternal Demographics and Clinical Variables at Birth (ITT)

Maternal Characteristics	DCC (n=37)	ICC (n=36)	P value
Age (years)	28.3 ± 5.5	27.2 ± 5	0.35
Primipara	15 (41)	14 (39)	0.89
Maternal education (years)	14 ± 2.7	14 ± 2.6	0.96
Insurance, public	23 (62)	21 (58)	0.74
Hemoglobin at admission (g/dL)	11.6 ± 1	12.0 ± 1	0.14
Lead level at admission (mcg/dL)	1.0 ± 0.4	1.1 ± 0.4	0.76
Ferritin at admission (ng/mL)	23.4 ± 22	16.9 ± 14	0.07
Mode of delivery			
Spontaneous vaginal	27 (73)	25 (69)	0.28
Instrumented vaginal	2 (5)	0 (0)	
Cesarean section	8 (22)	11 (31)	

shows no significant differences between the two groups on the neonatal demographics and clinical variables except for cord clamping time and RPBV. Per protocol, cord-clamping time was significantly longer in the DCC group. Cord clamping time including and excluding those infants who received UCM is noted to assess compliance with the protocol. As expected, RPBV was less in those infants who received DCC or UCM (mean difference of 10.8 mL/kg). Infants delivered by cesarean section had less RPBV than infants born vaginally but this did not reach a level of significance. There were 10 protocol violations. Reasons included 1) the clinical situation of meconium or shoulder dystocia (n=4), 2) the provider preference for the DCC or UCM group (n=2), 3) a misunderstanding between RAs and provider (n=2), and 4) parental request at time of delivery (n=2).

Infant Characteristics	**DCC (n=37)**	**ICC (n=36)**	**P value**
Gestational Age, weeks	39.5 ± 1 (37–41)	39.4 ± 1 (37–41)	0.54
Male: Female	19:18	18:18	0.91
Cord Clamping Time (sec) (includes UCM) Range	192 ± 171 (5–647)	23.1 ± 59 (3–360)	0.001
Cord Clamping Time (sec) (without UCM) Range	303 ± 121 (55–647)	10 ± 6 (3–25)	0.001
Apgar Scores 1 minute, median (range) 5 minutes	8 (2–9) 9 (8–10)	8 (2–9) 9 (5–9)	0.65 0.24
Apgar score ≤7 at 5 min	0 (0)	1 (3)	0.31
Temperature <36.6°C in first 15 minutes	1 (3)	0 (0)	0.32
Birth Weight (g) Range	3584 ± 497 (2455–4410)	3433 ± 454 (2730–4630)	0.18
RPBV (mL/kg) Range	20.0 ± 8.5 (0–36.8)	30.8 ± 9.6 (14.1–65.2)	0.001
Cord blood Hemoglobin (g/dL) Range	14.8 ± 2 (12.0–19.9)	15.2 ± 2 (12–18.9)	0.29
Cord blood Hematocrit (%)Range	44.2 ± 6.3 (24.5–59.2)	45.9 ± 4.7 (36–53)	0.24
Cord blood Ferritin (ng/mL) Range	154.3 ± 115 (16.9–570.4)	134.6 ± 81 (18.1–365.1)	0.42
Protocol Deviations	5 (14)	5 (14)	0.96
Breastfeeding at time of discharge	18 (50)	19 (56)	0.62

Measures of 24 to 48 hour blood values by Intention-to-Treat and Sensitivity Analyses (Actual treatment)

Two Day Values	Intention-to-treat			Actual Treatment		
	DCC (n=37)	ICC (n=36)	P value	DCC (n=37)	ICC (n=36)	P value
Hemoglobin (g/dL), (capillary)	19.4 ± 2 (16.3–25.0)	17.8 ± 2 (14.5–22.5)	0.002	19.5 ± 2.1 (16.3–25)	17.7 ± 1.8 (14.5–22.2)	0.002
Hematocrit (%), (capillary)	58 ± 6.2 (50.3–73.7)	53 ± 5.4 (42.4–63.8)	0.001	58.4 ± 6.2 (50.9–73.7)	52.5 ± 5.2 (42.4–64.4)	0.001
Peak total serum bilirubin (TSB) level, (mg/dL)*	9 ± 3 (1.8–15.3)	8.5 ± 3 (1.7–13.5)	0.50	8.5 ± 3 (1.8–14.9)	9.0 ± 3.2 (1.7–15.3)	0.45
Bilirubin Nomogram High risk zone (≥95%) *(bilitool.org)*	2 (5)	2 (6)	0.95	1 (3)	3 (9)	0.28
Phototherapy (initial hospital stay)	4 (11)	0 (0)	0.04	2 (5)	2 (6)	0.98
Symptomatic Polycythemia	0	0	--	0	0	--
Capillary Hematocrit > 65%	6 (16)	0 (0)	0.01	6 (16)	0 (0)	0.01
Capillary Hematocrit >70%	1 (3)	0 (0)	0.33	1 (3)	0 (0)	0.32
Capillary Hematocrit < 47%	0 (0)	5 (14)	0.02	0 (0)	5 (14)	0.02

Conclusion:

Term infants had early hematological advantage of DCC without increases in hyperbilirubinemia or symptomatic polycythemia.

Reference:

Mercer, J. S., Erickson-Owens, D. A., Collins, J., Barcelos, M. O., Parker, A. B., & Padbury, J. F. (2017). Effects of delayed cord clamping on residual placental blood volume, hemoglobin and bilirubin levels in term infants: a randomized controlled trial. Journal of perinatology : official journal of the California Perinatal Association, 37(3), 260–264. https://doi.org/10.1038/jp.2016.222