

Abstracts LB 1-2

LB 1 Premature Infants Receiving Cord Milking or Delayed Cord Clamping: A Randomized Controlled Non-inferiority Trial



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OBJECTIVE: Umbilical cord milking (UCM) might be an alternative to delayed cord clamping (DCC) to provide additional blood to pre-term infants without delaying resuscitation. There are limited safety data with UCM in extremely premature infants.

STUDY DESIGN: Multi-national, randomized controlled non-inferiority trial enrolled preterm infants of 23-31 weeks gestation. Infants were randomized to either UCM (4 times) or DCC (at least 60 seconds) stratified by mode of delivery and gestational age, lower gestational age (GA) strata: 23 -27 weeks and higher GA strata: 28 - 31 weeks gestation. Exclusions - major congenital anomalies, severe placental abruption, trans-placental incisions, cord prolapse, hydrops, bleeding accreta, monochorionic multiples, fetal or maternal risk for severe compromise at delivery, and families unlikely to return for 24-month neuro-developmental testing. Contingent on local IRBs, consent was obtained either before or after delivery. The composite primary outcome included severe intraventricular hemorrhage (IVH) or death in the entire group (23-31 weeks). Severe IVH was defined as grade 3 or higher. We planned to enroll 1500 infants (750 per group) to achieve 90% power to demonstrate non-inferiority with a 1% non-inferiority margin based on a 1-sided 95% confidence interval.

RESULTS: 474 infants were enrolled from June 2017 through August 2018. 19/238 (8%) of infants randomized to DCC died or developed severe IVH, compared to 28/236 (12%) randomized to UCM (p=0.16). There was no difference in death between the two groups. However, the incidence of severe IVH was higher in the lower GA strata in the UCM group (22% vs 4%, p=0.0007). Following an interim assessment, the DSMB recommended stopping recruitment based on the safety outcome of increased severe IVH in infants randomized to UCM in the lower GA strata. In this strata there were no differences in maternal and delivery characteristics (Table 1). The neonatal outcomes for the lower strata are presented in Table 2.

CONCLUSION: In extremely premature infants, there was an increased risk of severe IVH after exposure to UCM. Centers practicing UCM should consider discontinuing this practice in infants 23-27 weeks gestation.

Table 1. Maternal and Delivery Characteristics of infants 23-27 wks GA	DCC (N=89)	UCM (N=93)	p-value
Maternal Age, years	30.3 (5.5)	30.2 (5.5)	0.92
Gestational Age, weeks	25.6 (1.3)	25.9 (1.5)	0.09
Birth Weight, grams	791 (178)	839 (239)	0.12
Cesarean Section	59 (67%)	66 (71%)	0.50
Female	44 (49%)	42 (45%)	0.56
Maternal Diabetes	13 (15%)	8 (9%)	0.17
Maternal Chorioamnionitis	44 (49%)	36 (39%)	0.17
PIH/Pre-eclampsia	12 (13%)	23 (25%)	0.06
Labor or uterotonics before delivery	61 (69%)	59 (63%)	0.47
Duration of rupture of membranes, hours	122.4 (285)	105.2 (287)	0.69
Steroids given before delivery	74 (83%)	80 (86%)	0.96
General anesthesia	14 (16%)	14 (15%)	0.82
Antenatal magnesium	62 (70%)	68 (73%)	0.83

Data are presented as mean (SD) or (percentage). UCM, umbilical cord milking. DCC, delayed cord clamping.

Table 2 Delivery Room and Neonatal Outcomes (infants: 23-27 wks GA)	DCC (N=89)	UCM (N=93)	p-value
Time of cord clamp, seconds	56.7 (16.4)	21.1 (13.8)	<0.0001
Crying or breathing before cord clamping	68 (76%)	48 (52%)	0.0007
Admission temperature, °C	36.8 (0.7)	36.8 (0.6)	0.998
Apgar score, 1 min: Median (Q1-Q3)	5.0 (2, 6)	4.0 (3, 7)	0.47
Apgar score, 5 min: Median (Q1-Q3)	7.0 (6, 8)	7.0 (5, 8)	0.91
Needed Positive Pressure Ventilation	77 (87%)	79 (85%)	0.899
Intubation in delivery room	54 (61%)	53 (57%)	0.67
Hemoglobin at 4 hours of life, g/dL	15 (2.4)	15 (2.8)	0.86
Urine output first 24h, mL/kg per h	4.0 (1.5)	4.5 (1.3)	0.025
Peak bilirubin, mg/dL	7.1 (1.9)	7.3 (2.0)	0.70
Retinopathy necessitating surgery	16 (18%)	6 (6%)	0.045
Necrotizing enterocolitis	6 (7%)	4 (4%)	0.75
Spontaneous intestinal perforation	4 (4%)	1 (1%)	0.37
Oxygen at 36 wk corrected	23 (26%)	20 (22%)	0.97
Any IVH	27(30%)	25 (27%)	0.61
Severe IVH	4 (4%)	20 (22%)	0.0007
Death	12 (13%)	14 (15%)	0.76
Severe IVH or Death	16/89 (18%)	26/93 (28%)	0.11

Data are presented as mean (SD) or count (percentage) unless otherwise stated. UCM, umbilical cord milking. DCC, delayed cord clamping. IVH, intraventricular hemorrhage.