Original Article

Immediate and Delayed Cord Clamping in Infants Born Between 24 and 32 Weeks: A Pilot Randomized Controlled Trial

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OBJECTIVE:

This pilot study's aim was to establish feasibility of a protocol for delayed cord clamping (DCC) versus immediate cord clamping (ICC) at preterm birth and to examine its effects on initial blood pressure and other outcomes.

STUDY DESIGN:

A randomized controlled trial recruited 32 infants between 24 and 32 weeks. Immediately before delivery, mothers were randomized to ICC (cord clamped at 5 to 10 seconds) or DCC (30- to 45-second delay in cord clamping) groups.

RESULTS:

Intention-to-treat analyses revealed that the DCC group were more likely to have higher initial mean blood pressures (adjusted OR 3.4) and less likely to be discharged on oxygen (adjusted OR 8.6). DCC group infants had higher initial glucose levels (ICC = 36 mg/dl, DCC = 73.1 mg/dl; p = 0.02).

CONCLUSION:

The research design is feasible. The immediate benefit of improved blood pressure was confirmed and other findings deserve consideration for further study.

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INTRODUCTION

Over the past decade, seven randomized controlled trials documented significant beneficial hematological and circulatory effects of delayed cord clamping (DCC) in low or very low-birth-weight (VLBW) infants.[1–7] The effects include higher mean blood pressure,[1,4,5,7] lower systemic vascular resistance,[4] higher hematocrits,[1,4,7] and a decreased number of transfusions required up to 4 and 6 weeks of age.[1,5,7] Methodological issues have hampered a systematic evaluation of the previous research including the ability to conduct a meta-analysis of the seven studies. The present study expands the extant literature on cord clamping by scrutinizing the feasibility, recruitment strategies, and, most importantly, key outcome variables sensitive to estimating the effect of potential increases in blood volume as a result of delayed cord clamping. Owing to ethical, risk, and methodological issues, there is no direct measure of blood volume. Therefore, manifestations of the effects of increased blood volume include increased early blood pressures and higher hematocrits.[3,8]

An adequate blood volume is essential for a normal circulatory transition after birth.[9] At term, approximately two-thirds of the fetal – placental blood volume (FPBV) is in the fetus.[8,9] In a preterm pregnancy, approximately one half of the FPBV is in the placenta leaving the preterm fetus more vulnerable when the cord is clamped immediately because the infant receives very little placental transfusion.[8,9] During transition from fetal to neonatal life, there is an increase in the circulatory bed as various organs — lung, liver, kidney, etc. — begin to assume the functions sustained by the placenta during fetal life. This increase in circulatory bed or capacity may need additional blood volume that is deprived by immediate cord clamping. The resulting relative hypovolemia leads to decreased blood pressure, poorer perfusion, fewer available nutrients, and may create a subtle hypoxia or hypoxemia that may adversely affect the organs at the cellular level.[9] A delay in cord clamping of 30 to 45 seconds showed increases in both blood volume (11%) and red cell volume (23.5 %) in term infants.[8] More recently, Narenda et al.[3] demonstrated a 22 and 28% increase in blood volume for preterm infants with delayed cord clamping at Cesarean and vaginal births, respectively. Infants with delayed clamping were held lower than the incision or introitus. This additional blood volume could potentially be beneficial for the VLBW infant.

The current pilot study was conducted to assess feasibility of DCC and the study protocol in the authors' institution, and to test

and generate hypotheses in preparation for applying for funding for a larger randomized controlled trial. We tested the primary hypothesis that, for VLBW infants, DCC will result in higher initial mean blood pressure upon arrival in the neonatal intensive care unit (NICU). The secondary hypothesis stated that they would have higher initial hematocrits, less severe clinical acuity reflected by fewer days of ventilation, and fewer days of oxygen use when compared to ICC. This was the first study of DCC to look at outcomes in infants over the entire NICU stay.

METHODS

This is a prospective randomized controlled trial conducted at Women and Infants' Hospital in Providence, Rhode Island. The institutional review boards at Women and Infants' Hospital and the University of Rhode Island approved the study. The experimental procedures followed the ethical standards for human experimentation.[10] Women who presented to the hospital with symptoms indicating that they might deliver before 32 weeks were assessed for eligibility by the research staff. The inclusion criteria were: (1) gestational age between 24 and 31 and 6/7 weeks assessed by the obstetrical team from dating of last menstrual period or ultrasound; (2) singleton pregnancy; (3) the obstetrician agreed to enrollment into the study; and (4) parents gave written consent. Women were excluded if the obstetrician or parents refused consent, if there was intent to withhold or withdraw care, or if the women had diagnoses of placenta previa or abruption, bleeding, or a fetus with a major anomaly.

Subjects
There were 165 eligible mothers during the recruitment period (October 1998 to March 2001), 66 were approached for informed consent; eight refused (5%), and 53 were enrolled (31%). In all, 99 mothers were not approached for consent because the research staff was unavailable or they delivered rapidly after admission. Of the 53 women enrolled, eight were discharged home undelivered (15%) and 13 of the births (24%) were missed due to rapid delivery or unavailability of staff. A total of 32 mothers were randomized into either the delayed or immediate cord clamping group when the birth was imminent.

Study Procedure
The Principal Investigator (PI) or designated research staff screened the mothers for eligibility, informed the parents about the trial, obtained the informed consent, attended all the births, and reviewed the study procedure with staff in the delivery room before the birth. Allocation was concealed from the research staff. The randomization was performed with a system of randomly prepared cards in sealed nontransparent envelopes containing immediate or delayed group assignment and kept on the labor unit. Randomization occurred into either the delayed or immediate cord clamping group when the birth was imminent. The PI or research

staff informed the obstetrician of the infant's grouping at randomization. The research team used a stopwatch to accurately time the cord clamping. For babies in the ICC group, the obstetrician clamped the umbilical cord between 5 and 10 seconds after delivery of the buttocks and transferred the baby to the neonatology staff for routine care of the infant. If the infant was assigned to the delayed clamping group, the obstetrician was instructed to hold the infant in a blanket or towel and lower the baby as much as possible without creating tension on the cord while the infant was still attached to the placental circulation. The goal was for the attendant to hold the infant approximately 10 to 15 in below the mother's introitus at vaginal delivery or 10 to 15 in below the level of the incision at Cesarean section. After delivery of the buttocks, the PI counted out the time elapsed in 10-second intervals to the obstetrician. The cord clamping interval ended at 30 to 45 seconds when the obstetrician placed the first clamp on the umbilical cord. No uterotonics were given before cord clamping. The umbilical cord was then cut and the infant was transferred to the warmer. An additional warming mattress was provided for all babies. No infants appeared so depressed that the obstetrician clamped the cord quickly for resuscitation. In the event that the timing of the cord clamping was less than 30 seconds and the baby was randomized to the DCC group, the infant remained in the DCC group for intent-to-treat analyses and a protocol violation report was completed ($n = 2$, clamping time $= 3$ seconds). It was not possible to mask the trial to the research staff present as they had to inform the team of the randomization and to time the cord clamping interval. The obstetrician had to implement the protocol and the neonatology physicians and nursing staff were needed to be at the delivery for clinical care of the infants. However, the neonatal staff was asked not to record the cord clamping interval in the infant's chart so that this information was not available to staff caring for the infant in the NICU. The subsequent clinical management of the infants was left to the discretion of the neonatologists.

The data were collected at three time points: (1) at birth, (2) after the first 12 hours, and (3) at discharge from the hospital. Data collected at birth included time of cord clamping, sex, Apgar scores, birth weight, and mode of delivery. Data collected in the first 12 hours included body temperature and the initial blood pressure (measured by Dinamap, GE Medical Systems) on admission to the NICU, initial venous hematocrit and glucose level obtained from the first blood drawing when the initial intravenous line was established, mean blood pressures taken over the first 4 hours, number of volume expanders (albumin, saline, plasmanate) used in the first 12 hours, and SNAPPE-II[11] scores. Data collected at discharge by chart review included maximum serum bilirubin level, days on ventilation or oxygen, intraventricular hemorrhage (IVH) by cranial ultrasound, the occurrence of suspected necrotizing enterocolitis (NEC) defined as X-ray ordered to rule out NEC, and oxygen use at 36 weeks and at discharge. Obstetrical gestational age was determined by the

obstetrical team before enrollment and demographic and other data on the mother were collected from the mother's chart at the time of enrollment or after the birth.

Statistical Analyses

Using blood pressure as the primary outcome variable and an expected 10% relative increase by delayed cord clamping ($\alpha = 0.05$, 80% power) we estimated the need for 13 infants in each arm of the study. An additional 20% or six subjects were enrolled to allow for attrition.

Data were analyzed using the intention-to-treat designed as initially planned for the hypotheses.[12,13] Descriptive statistics were computed for the overall sample and subjects according to cord clamping group. The two-sample *t*-test (Student's *t*) was used for analyzing the quantitative variables with normal distribution and Wilcoxon rank-sum test was used where distribution was skewed (e.g. for Apgar scores). In comparisons using Student's *t*, 95% confidence intervals for the mean difference in response provided a range of likely values to assess clinical significance. For nonparametric comparisons, Monte Carlo estimates for the exact *p*-values were used to obtain tests of significance. Differences for categorical variables were tested using χ^2 analyses for the ICC versus DCC comparison. For contingency tables showing expected cell counts < 5, Fisher's exact test was used.

Exploratory analysis using gestational age defined continuously in multivariable models showed that greater efficiency was obtained by specifying gestational age as a categorical factor (24 to 27 versus 28 to 32 weeks). For quantitative outcomes figures of the adjusted mean response by group and age were used to assess the interaction between clamping group and gestational age.

For quantitative outcomes that showed evidence of unadjusted difference, a multivariable regression on the response was used to test the effects of cord clamping status, gestational age, and the interactions between gestational age and clamping group. Tukey–Kramer comparisons for the difference in the (adjusted) least-squares means were used to investigate significant main effects for cord clamping group and the interaction with gestational age. The 95% confidence limits were computed for the adjusted means and their differences and residual plots were used to assess model fit.

For binary outcomes that showed evidence of unadjusted difference, logistic regression was used to test main effects and interactions with gestational age. Adjusted odds ratios were derived for the probability of having low blood pressure, oxygen use at discharge, or suspected NEC. The levels of group status and 95% confidence limits were used to obtain a range of likely values.

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 shows the maternal demographics at enrollment. There were no significant differences in demographic and clinical variables between mothers in the ICC and DCC groups. These included mother's age, insurance status, use of antenatal steroids, use of magnesium sulfate, and hours of ruptured membranes.

Table 2 shows the demographic and clinical characteristics of the study infants. The mean birth weight for the ICC and DCC group of infants was 1005 ± 260 g (mean ± SD) and 1064 ± 291 g, respectively ($p = 0.55$, NS). The other infant characteristics (gestational age, gender, mode of delivery, and Apgar scores) were similar between the two groups. Cord clamping time as per protocol was significantly longer in the DCC group (32 ± 12 versus 6.2 ± 3 seconds, $p < 0.001$). No babies were small for gestational age (SGA) according to the criteria used by Richardson[11] for purposes of the SNAPPE-II™ scoring.

Table 3 shows the clinical outcome data during the first 12 hours of life. Unadjusted group differences were evident for initial mean blood pressure taken upon admission to the nursery (DCC = 35 ± 7.1 versus. 30 ± 4.6 mmHg, $p = 0.02$, 95% CI = 1.04, 9.7). The initial glucose levels drawn immediately after the first intravenous line was established from that site (measured by the hexokinase method, Beckman Coulter, Inc., Brea, CA, USA) was also higher in the DDC group (71 ± 25 versus 53 ± 19 mg/dl, $p = 0.03$, 95% CI = 1.9, 34). All six infants with initial glucose levels below 40 were in the ICC group (OR 2.6, 95% CI 1.5–4.2, $p = 0.007$). No significant differences were found in temperature on admission, initial hematocrit, mean blood pressures over the first 4 hours, use of volume expanders, or SNAPPE-II scores. Figure 1 presents a scatter plot of initial hematocrit levels by seconds of cord clamping time rather than by group. Two infants

Table 1 Maternal Demographics at Recruitment

	Group 1–ICC $n=16$	Group 2–DCC $n=16$	*p*-Value
Mother's age* (years)	24.5±7 (14–40) (median=22)	27.6±8 (16–41) (median=28)	0.25
Insurance[‡]			
Public	11	10	0.90
Private	5	6	
Received antenatal steroids[§]	15 (94%)	15 (94%)	0.98
Received antenatal MgSO₄ [§]	13 (81%)	13 (81%)	>0.99
PROM in hours[¶]	20±36 (0–99) (median=0.63)	20±40 (0–99) (median=0.5)	0.84

Data presented as mean ± standard deviation (range) or *n* (%).
t-Test.
[‡]χ^2.
[§]Fisher's exact test.
[¶]Wilcoxon rank-sum test.

Table 2 Neonatal Characteristics

	Group 1 ICC n=16	Group 2 DCC n=16	p-Value
Birth weight* (g)	1005±260 (640−1570) (median=985)	1064±290 (583−1575) (median=1070)	0.55
Gestational age* (weeks)	27±2.2 (24.3−31) (median=26.4)	28±2 (24.3−31) (median=28.4)	0.28
24 to 27^6 weeks[‡] (No.)	11	6	0.08
28 to 31^6 weeks (No.)	5	10	
Male/female ratio[‡]	6/10	9/7	0.29
Born by Cesarean section[‡]	6 (37.5%)	9 (56%)	0.29
Apgar score means (minutes)[¶]			
1	6 (1−8)	6 (1−9)	0.97
5	7 (4−9)	7 (3−9)	0.68
Cord clamp time* (seconds)	6.2±3 (2−12) (median=5)	32±12 (3−45)[‖] (median=33)	<0.0001

Data presented as mean±standard deviation (range) or *n* (%).
*t-Test.
[‡]χ^2.
[¶]Wilcoxon rank-sum test.
[‖]Two infants were clamped at 3 seconds because of a protocol violation. If not grouped by intent-to-treat protocol, the range for the DCC group would be 30 to 45 seconds and the mean would be 35.5 seconds. All data are analyzed with these two subjects included in the DCC group as appears above.
27^6 and 31^6 indicates 27 weeks and 6 days and 31 weeks and 6 days.

Table 3 Outcomes in the First 12 Hours

	Group 1 ICC n=16	Group 2 DCC n=16	95% Confidence interval	p-Value
Initial mean BP*	30±4.6 (22−38) (median=29.5)	35±7 (27−53) (median=34)	1.04, 9.7	0.017
Initial blood glucose*	53±19 (18−81)	71±25 (41−137)	1.9, 34	0.03
Initial glucose <40 mg/dl[§]				
Yes	6 (38%)	0 (0%)	1.09, 2.3	0.02
No	10 (62%)	16 (100%)		
Temperature on admission to NICU* (°F)	97.4 ±1 (95.4−99.4)	97.3±1 (94.4−100)	0.9, 0.79	0.89
Initial venous hematocrit* (%)	42±9.8 (17−62)	44±10.8 (22−58)	−5.5, 9.5	0.59
Mean of first 4 hours mean blood pressure*	30.7±3.8 (26−37)	33.2±4.3 (26−42)	1.04, 9.7	0.10
Had volume expansion in first 12 hours[¶]	6 (37.5%)	5 (31%)		0.71
SNAPPE-II™ scores[‖]	30+22.6 (0−78) (median=23.5)	24+24 (0−80) (median=15)	18.5, 35	0.30

Data presented as mean±standard deviation (range) or *n* (%).
*t-Test.
[¶]χ^2.
[§]Fisher's exact test; [‖]Wilcoxon rank-sum test.

with immediate cord clamping whose hematocrits were 27.3 and 34 were included in the late group for intention-to-treat analyses due to protocol violations.

Table 4 shows clinical morbidity during the infant's stay in the NICU. Infants in the DCC were found to have fewer incidences of suspected NEC or feeding intolerance (8/16 versus 14/16, $p = 0.02$,
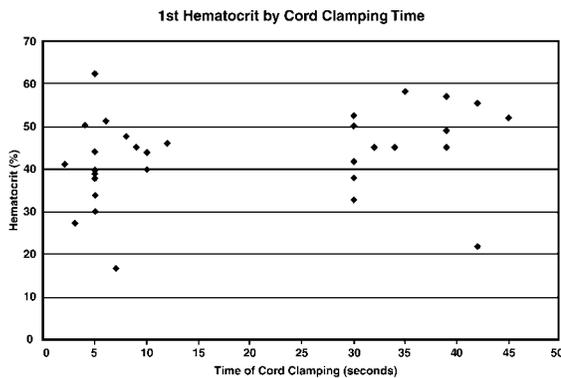
Figure 1. Initial hematocrit by cord clamping time in seconds. Two infants with cord clamping times less than 10 seconds were analyzed in the late group due to protocol violations. Their hematocrits were 27 and 34%.

OR 2.2, 95% CI = 1.2, 4) defined as occurring when the neonatologists ordered an abdominal X-ray to rule out NEC. The incidence of confirmed NEC was similar between the two groups (three infants in the ICC group and one with DCC). There was a trend of fewer babies in the DCC group needing oxygen at 36 weeks for any reason (9/16 or 56% versus 5/16 or 31%, $p = 0.15$). However, more infants in ICC group (7/16, 44% versus 1/16, 6 %, $p < 0.01$) were discharged on oxygen than infants in the DCC group. Those in the ICC group were approximately seven times more likely to be discharged on oxygen compared to those in the DCC group (relative risk = 6.9, 95% CI for the RR = 0.97, 50.5). There were no significant differences in the maximum bilirubin levels, days on ventilation, days needing oxygen, IVH, transfusions, or days hospitalized.

Although there were no significant differences between the groups in birth weight or gestational age, the distribution of these variables was of concern because smaller babies were in the ICC group. Table 5 shows the results of the multivariable regression for initial glucose level testing the effects of cord clamping status, gestational age, and the interaction between gestational age and clamping group. Adjusting for gestational age group revealed that infants older than 28 weeks were more likely to experience

Table 4 Morbidity During NICU Stay

	Group 1 ICC $n=16$	Group 2 DCC $n=16$	*p*-Value
Suspected NEC*	14 (87.5%)	8 (50%)	0.02
Needed O$_2$ at discharge*	7 (44%)	1 (6%)	0.04
Needed O$_2$ at 36 weeks[†]	9 (56%)	5 (31%)	0.15
Maximum serum bilirubin[‡] (mg/dl)	8.1+2.3	8.2+3	0.90
	(5−12.5)	(5−15.3)	
	(median=8.15)	(median=7.15)	
Days on SIMV or HFO[‡]	16.5+16	13+17	0.60
	(0−61)	(0−50)	
	(median=10.5)	(median=2.5)	
Days on oxygen[‡]	51+41	33+36	0.26
	(1−116)	(1−106)	
	(median=50.5)	(median=9)	
Total ml transfused[¶]	62+46	40+44	0.26
	(0−144)	(0−115)	
	(median=59.5)	(median=20)	
IVH[*]	5 (31%)	3 (19%)	0.68
Grade 1	3	1	
Grade 2	2	2	
Days hospitalized[‡]	73+27	56.5+35	0.15
	(19−116)	(8−136)	
	(median=76)	(median=49)	

Data presented as mean± standard deviation (range) or *n* (%).
*Fisher's exact test.
[†]χ^2.
[‡]*t*-Test.
[¶]Wilcoxon rank-Sum test.

Table 5 Multivariable Regression for Initial Glucose with Effects for Clamping Group, Gestational Age Category, and Group-by-Age Interaction (Tukey−Kramer adjustment for multiple comparisons)

Cord clamping group	GA group	n	Glucose mean	Standard error	95% Confidence limits
Delayed*	28−32	10	73.1	6.8	59, 87
Delayed	24−27	6	66.7	8.8	48, 84
Immediate*	28−32	5	36	9.6	16, 55
Immediate	24−27	11	60	6.5	46, 73

*Differences are significant for the infants in the 28- to 32-week group ($p=0.02$; 95% CL 4.9 to 69) but not for infants in the 24- to 27-week group ($p=0.93$; 95% CL 23, 36).

differences in glucose levels with those in the DCC group having higher initial glucose levels (73.1 mg/dl) than those in the ICC group (36 mg/dl, $p = 0.02$, 95% CI $= 4.9$, 69).

Logistic regression analyses used for the binary outcomes of mean blood pressure, suspected NEC, and oxygen use at discharge, showed evidence of unadjusted differences. Cross tabulations between group status and initial mean blood pressure categories (above or below 30 mmHg) showed that infants in the DCC group were four times more likely to have blood pressure over 30 mmHg than infants in the ICC group (OR 4.3, 95% CI $= 0.9$, 21; $p = 0.06$). Adjusting for gestational age group (above or below 28 weeks gestation at birth) slightly diminished the strength of the association but increased efficiency of the estimation (OR 3.4, 95% CI $= 0.6$, 18; $p = 0.1$).

While those in the ICC group were approximately seven times more likely to be discharged on oxygen compared to those in the DCC group, adjusting for gestational age group slightly diminished the effect of the clamping group. However, adjusting for gestational age made the estimation more precise (OR $= 8.6$, 95% CI $= 0.8$, 88.8; $p = 0.07$). Similarly, adjusting for gestational age improved the precision of the association between group membership and suspected NEC. Infants in the ICC group were five times more likely to have an X-ray to rule out NEC (OR 5.1, 95% CI .8, 33.9; $p = 0.09$).

DISCUSSION

The feasibility of the study was determined by several parameters. The first is the safety issue—does this protocol put babies at risk of harm? Three issues related to harm were raised during protocol development: (1) risk for hypothermia, (2) risk for increased hyperbilirubinemia, and (3) effects of delayed intubation. There were no differences between the groups on any variables related to these issues indicating that the protocol did not place the babies at additional risk. Lindner et al.[14] examined the need for immediate intubation for all preterm infants. They reported no increase in morbidity when a selective intubation policy was initiated in which intubation was delayed in VLBW infants for evaluation of need.

A second important issue is the enrollment rate of eligible infants during the study period. Even with only part-time availability of the principal investigator and research assistant, 31%

of the eligible infants were enrolled. Of the 53 women who consented, 13 (24% of 53) did not complete the study protocol because of rapid delivery or unavailability of research staff to attend the birth or they did not give birth prematurely. The number of obstetricians who refused to adhere to the protocol by infants grouping determines a third evaluation of feasibility. This occurred only once in 17 months. A few obstetricians were initially reluctant but agreed to participate after hearing the results of no harm and possible benefit in the other randomized controlled trials on DCC in preterm infants. Cooperation from the nursing staff was very good. Therefore, the willingness of the health professionals to participate in the protocol was almost unanimous. Third, of those randomized to delayed cord clamping, two (6%) did not complete the designated time. These infants were analyzed in their intent-to-treat grouping and this small number does not hamper the evaluation of feasibility for the study. No randomized infants died during the study.

Adjusting for gestational age, infants in the DCC group were three times more likely to have mean BP above 30 mmHg. DCC allows for additional placental transfusion to augment the immediate blood volume of the infant.[9] The finding of higher initial blood pressures is consistent with those found in other trials.[1,4,5,7,15] The higher mean blood pressure is an important physiologic observation because of its potential effect on the improved organ perfusion that may facilitate transition. Hypotension in the newborn has been associated with poor outcomes including cystic leukomalacia,[16] retinopathy of prematurity,[17] and cerebral palsy.[18]

The higher initial blood glucose in the DCC group is an unexpected finding. All glucose levels < 40 mg/dl occurred in the ICC infants and were more likely to occur in those over 28 weeks. The reason for this observation in glucose is difficult to explain. One possible explanation of higher glucose values may be that improved hepatic perfusion supports earlier endogenous glucose production.[19] Red blood cells require a constant supply of glucose to support generation of adenosine triphosphate that in turn supplies the chemical energy needed to maintain membrane integrity.[20] Thus, the higher glucose may be protective for the infant. Callahan et al.[21] reported a protective effect against hypoxic injury to differentiating glial cells from increased glucose availability.

Suspected NEC, as reflected by the physicians ordering abdominal films because of clinical signs of feeding intolerance to rule out NEC, occurred more frequently in the ICC infants. Our speculation on this observation is that initial increase in perfusion, as a result of the higher blood pressure in the DCC babies, may result in better capillary distension and modeling of gastrointestinal mucosa similar to the effect of capillary erection in the lung.[22] Babies who are more stressed by low blood volume may have a double insult: decreased blood flow to the gut as a result of activation of the sympathetic nervous system[23] and hypovolemia.

Several of the infants receiving oxygen at 36 weeks corrected age outgrew the need by the time of discharge. However, the finding that fewer infants with delayed cord clamping were discharged on oxygen was unanticipated. One explanation is that the additional blood received by delayed cord clamping may help to expand the lung capillaries and alveoli causing more initial capillary erection.[22] This increased blood volume and resultant capillary erection may provide structural support to prevent recruitment and de-recruitment with each breath.[22,24,25] Jaykka's[22] work decades ago suggests that forceful ventilation prior to recruitment of the lung by pulmonary perfusion and capillary erection damages the alveoli and causes irregular distension.[24,25]

Another unexpected finding was that the hematocrits were not higher in the DCC infants. Jones, Wardrop, and Holland suggest that there is a poor correlation between blood volume and hematocrit in fragile and sick infants.[26,27] A more likely explanation is that hematocrit was not used as the primary outcome variable in our sample size calculation. The lack of the difference between the two groups may be a result of inadequate sample size.

This pilot study indicates that the design is feasible and the results suggest the need for further studies with a larger sample size stratified by gestational age. If further studies replicate these findings, cost savings from this simple intervention could be substantial.

References

1. Kinmond S, Aitchison TC, Holland BM, et al. Umbilical cord clamping and preterm infants: a randomized trial. BMJ 1993;306:172–5.
2. McDonnell M, Henderson-Smart DJ. Delayed umbilical cord clamping in preterm infants: a feasibility study. J Paediatr Child Health 1997;33:308–10.
3. Narendra A, Beckett C, Aitchison T, et al. Is it possible to promote placental transfusion (PTFx) at preterm delivery? Pediatr Res 1998;44:454 (Abstract).
4. Nelle M, Fischer S, Conze S, Beedgen B, Grischke EM, Linderkamp O. Effects of late cord clamping on circulation in prematures (VLBWI). Pediatr Res 1998;44:454 (Abstract).
5. Rabe H, Wacker A, Hulskamp G, Hornig-Franz I, Jorch G. Late cord clamping benefits extrauterine adaptation. Pediatr Res 1998;44:454 (Abstract).
6. Rabe H, Wacker A, Hulskamp G, et al. A randomised controlled trial of delayed cord clamping in very low birth weight preterm infants. Eur J Pediatr 2000;159(10):775–7.
7. Ibrahim HM, Krouskop RW, Lewis DF, Dhanireddy R. Placental transfusion: umbilical cord clamping and preterm infants. J Perinatol 2000;20:351–4.
8. Yao AC, Moinian M, Lind J. Distribution of blood between the infant and the placenta after birth. Lancet 1969;7626(2):871–3.
9. Waldrop CAJ, Holland BM. The roles and vital importance of placental blood to the newborn infant. J Perinat Med 1995;23:139–43.
10. World Medical Association Recommendations Guiding Physicians in Biomedical Research: Declaration of Helsinki. http://www.wma.net/e/policy/17-c_e.html.
11. Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP-II and SNAPPE-II: simplified newborn illness severity and mortality risk scores. J Pediatr 2001;138(1):92–100.
12. Ebbutt A, Frith L. Practical issues in equivalence trials. Stat Med 1998;17:1691–701.
13. Friedman L, Furberg C, DeMets D. Fundamentals of Clinical Trials. 3rd ed. New York: Springer; 1998.
14. Lindner W, Vobeck S, Hummler H, Pohlandt F. Delivery room management of extremely low birth weigth infants spontaneous breathing or intubation? Pediatrics 1999;103(5):961–7.
15. Oh W, Lind J, Gessner IH. Circulatory and respiratory adaptation to early and late cord clamping in newborn infants. Acta Paediatr Scand 1966;55:17–25.
16. Tsuru A, Mizuguchi M, Takashima S. Cystic leukomalacia in the cerebellar folia of premature infants. Acta Neuropathol (Berl) 1995;94(4):400–2.
17. Arroe M, Peitersen B. Retinopathy of prematurity: review of a seven-year period in a Danish neonatal intensive care unit. Acta Pediatr 1994;83(5):501–5.
18. Murphy D, Hope P, Johnson A. Neonatal risk factors for cerebral palsy in very preterm babies: case control study. BMJ 1997;314(7078):404–8.
19. Polin R, Fox W. Fetal and Neonatal Physiology. 2nd ed. Philadelphia: WB Saunders Company; 1998.
20. Dixon LR. The complete blood count: physiologic basis and clinical usage. J Perinat Neonatal Nurs 1997;11(3):1–18.
21. Callahan DJ, Engle MJ, Volpe JJ. Hypoxic injury to developing glial cells: protective effect of high glucose. Pediatr Res 1990;27(2):186–90.
22. Jaykka S. Capillary erection and the structural appearance of fetal and neonatal lungs. Acta Paediatr 1958;47:484–500.
23. Porges SW. Vagal tone: a physiologic marker of stress vulnerability. Pediatrics 1992;90(3):498–504.
24. Mercer JS, Skovgaard R. Neonatal transitional physiology: a new paradigm. J Perinat Neonatal Nurs 2002;15(4):56–75.
25. Clark R, Slutsky A, Gertsmann D. Lung protective strategies of ventilation in the neonate: what are they? Pediatrics 2000;105(1):112–4.
26. Jones JG, Holland BM, Hudson IR, Wardrop CA. Total circulating red cells versus haematocrit as the primary descriptor of oxygen transport by the blood. Br J Haematol 1990;76(2):288–94.
27. Wardrop CAJ, Holland BM, Jones JG. Consensus on red cell transfusion. BMJ 1995;311:962–3.