Review Article

Delayed Umbilical Cord Clamping: A Boon for an Infant

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ABSTRACT

Delayed cord clamping (Clamping of umbilical cord after cessation of cord pulsations) is proved to be effective in increasing neonatal blood volume thereby, iron status and prevents infant anemia in term infants. It improves hemodynamic stability, reduces incidence of intraventricular hemorrhage, late onset sepsis in very low birth weight babies. Also, protects infants in malaria-endemic area. A brief delay in clamping the umbilical cord results in a placental transfusion that supplies the infant with millions of stem cells. Delayed cord clamping reduces the blood lead concentration in lead exposed infants. The following article shows evidence based benefits of delayed cord clamping to the newborn, and during its journey till infancy. It is the simple, cost-free, and effective intervention, and is a great privilege for infant.

Keywords: delayed cord clamping, infant anemia, intraventricular hemorrhage, late onset sepsis, stem cell, blood lead concentration

INTRODUCTION

Timing of umbilical cord clamping is the issue of controversy since past. Few obstetricians still practise immediate cord clamping as it was once thought to be necessary to prevent maternal postpartum hemorrhage but this has been repeatedly shown to be false. It is now widely accepted that delayed umbilical cord clamping is most beneficial to the infant without incurring any risk to the mother. [¹] Allowing placental transfusion of blood to run to completion before clamping the umbilical cord can provide the infant with an additional 15–20 mL of blood volume, increasing its total blood volume by an estimated 30%. [¹]

In 2007, the Pan American Health Organization (PAHO) released the following updated recommendations for the timing of umbilical cord clamping: “The optimal time to clamp the umbilical cord for all infants regardless of gestational age or fetal weight is when the circulation in the cord has ceased, and the cord is flat and pulseless (approximately 3 minutes after birth). After cord pulsations have ceased (approximately 3 minutes after delivery), clamp and cut the cord following strict hygienic techniques”. [¹]

COMPARATIVE STUDIES BY VARIOUS AUTHORS

Author Strauss et al, in 2008 did partially blind RCT, in < 36 weeks estimated gestational age. Study was early cord clamping (n=60) within 15 sec. delayed
(n=4) 1 minute late, results were, circulating RBC vol/mass increased and Hct values were higher after delayed clamping. Hutton and Hassan, 2007, 15 RCTs, full-term infants.

Early = immediately after birth; delayed = minimum of 2 min., found improved hematologic status over 2 to 6 months with delayed clamping. McDonald and Middleton, 2008, 11 RCTs, full-term infants. Early = within 60 sec; delayed = > 1 min after birth or when cord pulsation ceased. No difference in rates of PPH, increase in neonatal Hgb/Hct; increase in jaundice. A more "liberal" approach to delaying clamping in healthy term infants. Jahazi et al., 2008, Healthy, full-term vaginally born neonates; delayed, n = 34; early, n = 30. Early = 30 sec; delayed = 3 min. No increase in Hct noted; significantly increased ENBV, Potential benefit should be considered by providers. [2] (EGA = estimated gestational age; ENBV = estimated neonatal blood volume; Hct = hematocrit; Hgb = hemoglobin; PCV = packed cell volume; PPH = postpartum hemorrhage; RBC = red blood cell; RCT = randomized controlled trial) [2]

BENEFITS OF DELAYED CORD CLAMPING
In premature infants by improving hemodynamic stability:

Delayed cord clamping (DCC) shows significant placental transfusion in term and premature infants, amounting 10% to 15% additional blood volume in premature infants, which may provide beneficial effects during the transition from fetal to neonatal life. Immediate cord clamping (ICC) deprives the premature infant of this potential additional blood volume, which could result in hypovolemia and hypotension, leading to serious morbidities, such as periventricular or intraventricular hemorrhage (P/IVH) and periventricular leukomalacia. Premature infants exposed to DCC have higher superior vena cava (SVC) blood flow during the first 4 days of life when compared with infants exposed to ICC. Increased SVC blood flow in preterm infants may attenuate P/IVH rates by facilitating a more efficient cerebral vascular regulation in the presence of pathophysiological events, such as hypoxia and hypercapnia. [3]

The study was performed between May 2009 and July 2010 at Women & Infants Hospital of Rhode Island, reported, infants exposed to DCC exhibited higher SVC blood flow over the course of the study compared with the infants exposed to ICC after controlling for gestational age and birth weight (ANOVA: Groups, P = .003). Infants exposed to DCC had higher RVO (right ventricular output) and right ventricle stroke volumes (RV-SV) than infants exposed to ICC at 48 hours of life (ANOVA: Interactions, P = .003, Fisher least significant difference, P = .04). Infants exposed to DCC trended to have higher RV-SV over the course of the study (ANOVA: Groups, P = .1). [3]

In Very Low Birth Weight (VLBW) Infants by Reducing Incidence of Intraventricular Hemorrhage & Late-Onset Sepsis

The benefits of delayed cord clamping (DCC) in VLBW infants include higher blood pressure, higher hematocrit levels, more optimal oxygen transport and higher red blood cell flow, fewer days on oxygen and ventilation, fewer transfusions, and lower rates of intraventricular hemorrhage (IVH). Also, less suspected necrotizing enterocolitis (SNEC), and lower incidence of bronchopulmonary dysplasia (BPD) due to additional red blood cells obtained by delayed cord clamping. DCC offers protection against Late onset sepsis (LOS), and retinopathy of prematurity (ROP). [4]
The randomized, controlled trial was conducted between August 2003 and December 2004 at Women and Infants' Hospital of Rhode Island by Judith S. Mercer, Betty R. Vohr, Margaret M. McGrath, in infants in ICC (immediate cord clamping) and DCC weighed 1151 and 1175 g, and mean gestational ages were 28.2 and 28.3 weeks, respectively. Study shows that infants in the DCC group had less IVH (five [14%] vs 13 [36%]; \( P = .03 \)) during the first 28 days in the NICU. Infants in the DCC group were less likely to have blood culture-proven sepsis during the NICU stay (3% vs 22%; \( P = .03 \)). There were no adverse events or deaths in the DCC group.\(^4\)

The IVH rate was >3 times higher in the ICC group (odds ratio [OR]: 3.5, 95% confidence interval [CI] 1.1–11.1). A similar study for LOS adjusted for gestational age showed that infants in the DCC group were less likely to have sepsis (OR: 0.10, 95% CI: 0.01–0.84).\(^4\)

**In Full-Term Neonates Improves Iron Status At Birth:**

Delaying clamping of the umbilical cord for at least 2 minutes after birth consistently improves both the short- and long-term hematologic and iron status of full-term infants. Placental transfusion associated with late cord clamping shows consistently higher hematocrit levels within normal physiologic range and improvement in markers of iron status over the first months of life without having a significant impact on the absolute values of bilirubin and plasma viscosity during the first week of life.\(^5\)

Eileen K. Hutton Eman S. Hassan compared the potential benefits and harms of late vs early clamping of the umbilical cord in term infants. Among the 15 studies, a total of 1912 newborns underwent a trial of late (n=1001) or early (n=911) clamping of the umbilical cord.\(^5\)

**Mean Hematocrit:** Mean neonatal hematocrit measured in capillary or venous blood samples collected from the newborns at around 6 hours after birth was higher for those allocated to late vs early cord clamping (2 trials, 494 infants) 32.37 (WMD, 4.16%; 95% CI, 0.83% to 7.49%).\(^5\)

**Mean Hemoglobin Level:** At 7 hours after birth, the mean neonatal haemoglobin level measured in capillary blood was higher in newborns with late cord clamping (1 trial, 354 infants) (WMD, 0.60 g/dL; 95% CI, 0.11 to 1.09).\(^5\)

**Blood Volume and Plasma and Blood Viscosity:** Blood volume during the first 2 to 4 hours of life was higher in infants who had late cord clamping (2 trials, 60 infants) (WMD, 9.07 mL/kg; 95% CI, 5.81 to 12.32).\(^5\)

**Bilirubin Level:** There was no significant difference in mean serum bilirubin levels within the first 24 hours of life (2 trials, 163 infants) (WMD, 3.81 mmol/L; 95% CI, -17.55 to 25.18).\(^5\)

**Iron Status:** Iron status was assessed in terms of mean ferritin level and stored iron level. Ferritin levels at ages 2 to 3 months were higher for infants allocated to late vs early cord clamping (2 trials, 144 infants) (WMD,17.89 µg/L; 95% CI, 16.58 to 19.21)\(^\)\(^5\)

At 4 months age by preventing Infant anemia:

In term infants born after normal pregnancies, delaying clamping of the umbilical cord had significant effects on iron status at 4 months with higher serum ferritin concentration, less iron deficiency, and similar effects on all measured indicators of iron status. Delayed clamping also reduced the prevalence of neonatal anaemia at 2 days of age without increasing the rate of respiratory symptoms or need for phototherapy.\(^\)\(^6\)

Two meta-analysis of clamping study conducted by Ola Andersson , Lena
Hellström-Westas, Dan Andersson showed that four months post partum, at a mean (SD) age of 121 (5) days, 350 children (92%) returned for assessment. There was 29% difference in ferritin concentrations, and the geometric mean serum ferritin concentration was 45% (95% confidence interval 23% to 71%) higher in the delayed cord clamping group (117 µg/L with delayed clamping v 81 µg/L with early clamping, P<0.001).

Iron deficiency was significantly more prevalent in the early clamping group.

The measured amount of blood retained in the placenta was 37% (24% to 48%) lower in the delayed cord clamping group (geometric mean volume 25 mL v 39 mL, P<0.001). Results suggest that delayed cord clamping also benefits infant health in regions with a relatively low prevalence of iron deficiency and should be considered as standard care for full term deliveries after uncomplicated pregnancies. [6]

**In Term Infants Living In Malaria-Endemic Area:**

DCC (Delayed Cord Clamping) could help improve the haematological status of term infants living in a malaria-endemic region at 4 months of age. However, the beneficial haematological effect disappeared by 6 months. It can possibly be explained by two pathophysiological mechanisms. Either the infants out-grow their iron stores, or the infants suffer increased loss of iron via the gastrointestinal tract during episodes of diarrhoea or during the feeding of whole cow’s milk. [7]

Patrick van Rheenen, Lette de Moor, Sanne Eschbach, Hannah de Grooth and Bernard Brabin performed a randomised controlled trial in a highly malarious rural area of Zambia to assess whether DCC is effective in reducing anaemia in term infants up to the age of 6 months, and is associated with complications in infants and mothers.

The study showed mean increase in PCV on the first day postpartum was significantly higher in newborns from the DCC group (0.13 vs. 0.07; P < 0.001). By 4 months more infants in the control group had Hb levels below 2 SD cut-off level and were classified as having iron deficiency anaemia than those with delayed clamping, but the differences were marginally significant (odds ratio 0.3, 95% CI 0.1; 1.0) [7]

**BENEFITS TO NEWBORN BY PROVIDING Stem Cells:**

In addition to red blood cells, fetal blood contains large numbers of highly activated hematopoietic stem cells along with endothelial cell precursors, mesenchymal progenitors, and multipotent/pluripotent lineage stem cells many of which are lost to the infant with ICC (immediate cord clamping). The concentration of stem cells is much higher in the blood of premature infants compared with full-term infants. [8] Tolosa et al argue that “artificial loss of stem cells birth could predispose infants to diseases such as chronic lung disease, asthma, diabetes, cerebral palsy, infection, and neoplasm.” [9] The authors of this article suggest the hypothesis that a newborn should obtain his or her full allotment of available stem cells at birth and this can be facilitated by placental transfusion (DCC or by milking the cord). If the labor and birth was in anyway traumatic for the infant, it is possible that the stem cells may assist with healing.

**REDUCES BLOOD LEAD CONCENTRATION IN INFANTS WITH HIGHER LEAD EXPOSURE:**

Iron deficiency (ID) & Elevated Blood Lead levels (EBL) disproportionately affect infants and children and are
negatively and independently associated with neurodevelopmental impairment.\textsuperscript{[10,11]} ID & EBL often overlap in population they affect because of shared risk factors including low socioeconomic status, urban or inner city residence and poor nutrition. The relationship between lead and iron has been better elucidated with the discovery of Gastrointestinal iron transporter, divalent metal transporter 1 (DMT1) which also transport lead. Iron deficiency increases DMT1 expression resulting in greater absorption of both iron and lead. Maternal and cord blood lead levels are generally similar indicating that lead is readily transferred to the fetus via placenta during pregnancy. Delayed cord clamping (DCC) significantly improves infant iron status which is important in preventing lead absorption.\textsuperscript{[12]}

**SUMMARY**

Evidence based study of this article shows that Delayed cord clamping (DCC) is a boon for an infant without any maternal deterioration. DCC improves hemodynamic stability in premature infants thereby reducing incidence of P/IVH and long term sepsis in very low birth weight babies requiring NICU admission. Study also shows that DCC causes significant reduction in incidence of infant anemia which is a leading cause of infant mortality in developing countries. Infant Mortality in malaria-endemic area is very high, DCC protects infant from lethal consequences of malaria as it is effective in preventing infant anemia. Stem cells which have incredible potential of healing are transferred to infant in maximum quantity with delay in clamping of cord. This protects the premature and low immunity infants from infections and trauma during birth. DCC also found to be beneficial in reducing the blood lead concentrations in infants with higher lead exposure by increasing the iron concentration. Thus, the trend of immediate cord clamping should be changed and obstetricians must follow DCC and bless the newborn with gift of immunity!

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