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Review Article

Placental transfusion

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ABSTRACT

Cord clamping denotes a landmark period of transition from fetus to neonate. Recently, delayed cord clamping has been advocated by most international organizations based on available scientific evidence. Delayed cord clamping reduces iron deficiency in term neonates and intraventricular hemorrhage, necrotizing enterocolitis, need for blood transfusion in preterm's compared to early cord clamping. Recently, the focus has shifted to umbilical cord milking as an alternate strategy to have delayed cord clamping, especially in neonates needing resuscitation. Long-term follow-up data from these trials are limited.

1. Introduction

The umbilical cord acts as a conduit between the fetus and placenta, delivering blood supply to the fetus. Umbilical cord clamping (UCC) signifies a landmark period during which the newborn transforms into an independent entity. Much interest has recently focused on the appropriate timing of UCC, particularly on the risks and benefits of delaying cord clamping for a set period of time after birth. Debate on appropriate timing of UCC following birth has been ongoing for several decades (even centuries), yet the ideal time still remains unknown. Practice of cord clamping is undergoing shift from early to delayed cord clamping in preterm and term infant born appropriate for gestational age.

2. Changing practice of UCC after birth

Most mammals in the animal kingdom wait until expulsion of placenta to sever umbilical cord from newborn after delivery. Over two centuries ago, Erasmus Darwin noted the importance of not clamping the umbilical cord too soon after delivery to ensure the well being of both mother and infant. Approximately one century later, starting in the early 1900s, obstetric practices shifted from delayed umbilical cord clamping (DCC) (i.e. 2–3 min after birth or at the end of cord pulsations), which was the standard practice at the time, toward early umbilical cord clamping (ECC) (i.e. 10–15 s after birth). It is believed that the practice of immediate cord clamping was an unintended addition to active management of third stage of labor to prevent postpartum hemorrhage though it has no physiologic

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rationale.[1] However, in the recent years, after strong scientific evidence, timing of cord clamping has shifted from early to delayed cord clamping. No consensus exists about the definitions for early and delayed cord clamping for either term or preterm births. ECC is usually defined as clamping within 60 s with time for DCC from 1 to 3 min.[2]

3. Physiological rationale

Umbilical cord serves as a conduit between the fetus and placenta with umbilical vein carrying oxygenated blood from placenta to fetus and artery carrying blood from fetus to placenta. UCC causes a profound reduction in venous return and ventricular preload because the umbilical circulation receives a large proportion of combined ventricular output in the fetus. Consequently, both right and left ventricular output decreases (by as much as 50% in lambs)[3] and remains low until the lungs are aerated and pulmonary blood flow increases. Consequently, during the period between UCC and ventilation onset, when cardiac output is compromised, the infant is at significant risk of hypoxic/ischemic brain injury. With onset of ventilation, pulmonary vascular resistance decreases, causing increased right and left ventricular output. With onset of ventilation, pulmonary vascular resistance decreases, causing increased right and left ventricular output. These large swings in cardiac output and arterial pressure increase the risk of perinatal brain injury[4] but can be avoided by delayed cord clamping. DCC until after ventilation onset maintains ventricular preload and stabilizes cardiovascular function during the transition period, which also provide an alternative explanation for the lower risk of cerebral hemorrhage.[5]

4. Hematological effects of cord clamping

The time at which umbilical cord is clamped has profound effects on infant's blood volume at birth and subsequently, the contribution of hemoglobin iron to newborn total body iron. For a cord clamping delay of approximately 2–3 min in a full-term infant, about 25–35 ml blood per kg body weight is provided to infant from placental circulation.[6] Assuming a hemoglobin concentration of roughly 170 g/L at birth, and an iron concentration in hemoglobin of approximately 3.4 mg/g, roughly, a 3 kg infant would receive 46–60 mg of iron as hemoglobin from this placental transfusion. As newborn requires approximately 0.7 mg of iron per day for growth and development, maintenance of hemoglobin, myoglobin, and enzyme levels, 46–60 mg would be equivalent to roughly 1–3 months' worth of infant's iron requirements.[7] Although evidence is scarce, the relative contribution in blood volume and red cell mass following delayed cord clamping may be greater than for those born at term, as higher proportion of intrauterine blood volume is sequestered in placenta. Nevertheless, for preterm births, placental transfusion may take longer, and may be incomplete if cord is clamped within 30–90 s.[8]

5. Outcomes in term babies

Several randomized controlled trials have compared effects of delayed and early cord clamping in term babies. Timing of early clamping has been mostly within 10 s or as soon as possible in various trials. However, there is wide variation in time of delayed cord clamping varying from stoppage of cord pulsations to 60–180 s after delivery. Most studies have evaluated neonatal outcomes, i.e. incidence of hyperviscosity and its complications, along with effect on iron stores at varying ages ranging from 2 to 6 months. Only one study has evaluated long-term neurodevelopmental outcome. Neurodevelopment assessment was done by Ages and Stages Questionnaire (ASQ) in the trial by Andersson et al.[9] At 4 and 12 months of age, the total scores from the Ages and Stages Questionnaire (ASQ) did not differ between groups.[10] At 4 years of age, there was no difference in the Wechsler Preschool and Primary Scale of Intelligence between the groups, with fewer children in the DCC group having results below the cutoff in the ASQ fine-motor domain (11.0% vs 3.7%; $P = .02$) and the Movement ABC bicycle-trail task (12.9% vs 3.8%; $P = .02$).[11] Results from the major trials are summarized in the table below.

Study	Intervention	Neonatal hematological outcome	Hematological outcomes at follow-up
Grajeda et al.[12] $n = 69$	Group 1-ECC (immediate) Group 2 – after stoppage of cord pulsation, infant at level of placenta Group 3 – same as above, infant below placenta	No difference in Hct Higher polycythemia in Group 3 vs Group 1 and 2	Higher Hb at 2 months in Group 2 and 3 vs Group 1 Ferritin at 2 months – no difference
Gupta et al.[13] $n = 102$	ECC – immediately DCC – after descent of placenta in vagina		Higher ferritin and Hb at 3 months in DCC
Chaparo et al.[14] $n = 476$	ECC – 10 s DCC – 2 min	Higher Hb in DCC Clinical jaundice and polycythemia – no difference	Higher ferritin at 6 months in DCC group Increased iron deficiency anemia in ECC (4% vs 0%)