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Abstract

The timing of umbilical cord clamping is commonly seen as an innocuous act. Many providers simply cut the cord as soon as they see fit without consideration as to what the impacts of this may be. Early umbilical cord clamping was initially considered a preventative measure for postpartum hemorrhage, but this myth has since been debunked. Now, the practice is still commonly implemented, but for reasons unknown. Delaying the clamping of the umbilical cord is thought to not only provide no risk to the mother but provide benefit to the newborn in relation to their fetal to adult physiologic transition. While this technique may not be beneficial to all neonates, putting it into practice in those who would benefit and implementing it into standard hospital and clinic protocol could prove to have benefit in neonatal health outcomes.

Umbilical Cord Clamping: How Timing Affects Infant Health Outcomes

Introduction

Delayed umbilical cord clamping has shown to have short term benefits for the newborn. Some of these benefits include reduced mortality, increased blood volume, elevated birth hematocrit, and less frequent need for blood transfusion.[22] These results have been seen in both preterm and term infants. While this has all been observed in clinical trials and even deemed adequate by the World Health Organization and multiple gynecologic and obstetric organizations, immediate cord clamping is still proving to be the standard. One hypothesis behind this is that delayed clamping may increase the risk of the newborn developing polycythemia or hyperbilirubinemia or perhaps maternal postpartum hemorrhage.

During the third stage of labor, the umbilical cord is normally clamped and then cut. Early or immediate cord clamping (ICC) is generally done within the first 30 seconds after birth while delayed cord clamping (DCC) is typically completed more than 30 seconds after delivery or once umbilical cord pulsation has ended.[1, 22] In the first few minutes after birth, the umbilical arteries and veins continue to push blood to and from the placenta. The additional blood flow from placenta to newborn is termed placental transfusion and it has been found that by delaying the clamping by 1-3 minutes, a newborn's hemodynamics can be significantly impacted due to increased blood volume and sustained placental respiration.[1, 17]

Throughout the last century, ICC has been the common technique used in the delivery room as it was believed to reduce the risk of maternal postpartum hemorrhaging.[17] Recent studies, however,

have shown that ICC has no true effect on this. More studies are showing that while DCC does not affect postpartum hemorrhage, it may have more beneficial impacts than initially considered.

Valid concerns about adopting DCC universally exist, however. These concerns include possibly delaying timely resuscitation when needed, potential interference with attempts at collecting blood for umbilical blood banking purposes, and potential for possible excessive placental transfusion, putting the newborn at risk for polycythemia. The risk of polycythemia is especially high in newborns born to women with gestational diabetes, severe intrauterine growth restriction, and in those living in high altitudes.[32]

Globally, it is estimated that 3.6 billion people are iron deficient and more than half of them have iron deficiency anemia. The two populations most affected by this are women of reproductive age and children under the age of five in low-income and middle-income countries.[32] Children with iron deficiency anemia have associated neurodevelopmental impairment affecting their cognitive, motor, and behavioral skills.[20, 21] To combat this, food fortification and iron supplementation are used as a form of treatment but with the implementation of delayed umbilical cord clamping (DCC), requirements of these treatments may be deemed unnecessary.[8, 20]

Hyperbilirubinemia is another common concern of the newborn's health. With moderate hyperbilirubinemia, the newborn may experience symptoms of bilirubin-induced neurologic dysfunction, developmental delays, cognitive issues, executive function impairment, along with numerous behavioral and psychiatric conditions.[23] If the hyperbilirubinemia is severe enough, it

can result in the development of kernicterus with signs of hearing loss, upward gaze impairment, or cerebral palsy.[23] Currently, phototherapy and exchange transfusions exist as treatment for this but may require vascular access, additional resources and nursing staff. DCC may be a safe and cost-free alternative to preventing the occurrence of hyperbilirubinemia and the need for exchange transfusion at all.

This review aims to present the evidence in support of DCC becoming the standard practice by obstetricians and gynecologists worldwide. We will compare ICC versus DCC by looking at maternal health outcomes, their use in vaginal and cesarean delivery, as well as their effects on preterm and term infant health outcomes such as cardiopulmonary, hemoglobin, and blood gas results.

Background (Literature Review)

History of umbilical cord clamping

Prior to the World Health Organization (WHO) recognizing that delayed cord clamping has true benefits to the infant, numerous people in history questioned this standard of the time. In 1801, Erasmus Darwin stated "Another thing very injurious to the child, is the tying and cutting of the navel string too soon; which should always be left till the child has not only repeatedly breathed but till all pulsation in the cord ceases. As otherwise the child is much weaker than it ought to be".[13] In 1941, Dr. A.C. Beck wrote "Often the cord is clamped at once...this practice is reprehensible since it deprives the immature infant of considerable blood, which hit otherwise might take up from the placental circulation. Blood in the umbilical cord should be stripped toward the fetus before the umbilical cord is ligated".[21]

In the 1960s, a plan of care termed as “active management of the third stage of labor”, immediate cord clamping was implemented to reduce the risk of maternal blood loss during delivery.[30] Typically, during the third stage, separation of the placenta results in a small amount of blood loss. If uterine contraction does not occur after the birth of the newborn, the mother can expect to have heavy blood loss, putting her at risk of losing her life. The theory was that reducing the time in clamping would reduce the incidence of postpartum hemorrhage. Recent studies have begun to suggest otherwise and instead suggest that early clamping has no true benefits including prevention of postpartum hemorrhage occurrence.[17, 24]

Physiologic Transition from Fetal to Neonate

Once the baby is delivered, the circulatory system must undergo major changes to shift from placental respiration to lung respiration. While this happens, the body undergoes closure of the cardiac fetal shunts, lung expansion, and complete removal of placental circulation.[41]

One of the greatest challenges a newborn must overcome is lung aeration along with the onset of pulmonary gas exchange. While in the womb, the fetus’ lungs are filled with liquid that plays a part in lung growth and development. During delivery, however, this fluid acts as an obstacle for air entry and onset of pulmonary gas exchange. Lung aeration of the newborn is supported heavily by pulmonary gas exchange and is triggered by a decrease in pulmonary vascular resistance, increase in pulmonary blood flow, and umbilical cord clamping, resulting in the transition of fetal circulation to adult.[14]

Physiologic changes of the umbilical cord progress as well. The umbilical vein remains open while the arteries begin to constrict as oxygen saturation increases. This allows the placental blood to flow towards the newborn's circulation.[1, 4, 41] With early umbilical cord clamping, both vessels are constricted at the same time, trapping the placental blood within the placenta. Clamping the umbilical cord early ceases umbilical venous return, resulting in a sudden decrease in both left and right ventricular preload, and further decreases ventricular output.[14, 30, 31] This decrease in cardiac output can have deleterious effects on both systemic perfusion as well as vital organ perfusion.[4] If umbilical cord clamping is delayed, blood volume in the newborn increases, and thus the venous pressure increases, increasing the baby's cardiac preload.[14, 21, 41]

When placental residual blood volume after clamping was measured, it was found that blood continues to flow through the umbilical arteries for approximately 20-25 seconds after delivery, while the umbilical vein continues to flow for up to 3 minutes. The delay in clamping allows for such placental transfusion to the infant. The placental transfusion is most rapid immediately after birth, in the first 15-30 seconds, and progressively slows until completion around 3 minutes.[1, 5, 6, 7, 14]

Health outcomes of early clamping

During gestation, the placenta transports maternal iron to the fetus. In developing countries and areas of the world where maternal iron deficiency anemia is common, fetal iron deficiency anemia is a common occurrence seen in up to 30% of babies.[38] When combined with low birth weight, fetal anemia is related to post-neonatal infant mortality. In the presence of immediate cord clamping, the distribution of blood in the ratio of fetus: placenta is about 2:1. If the infant

were permitted to receive placental transfusion for up to three minutes after delivery, this would result in a greater fetal blood volume.[24, 38] Numerous studies have shown that iron levels at birth significantly predict infant iron status and the probability of anemia later in infancy.[6] A study conducted in Zimbabwe found that the likelihood of anemia at 6, 9, and 12 months of age was three times higher in infants with low fetal iron status' than those with higher iron status'.[6]

At the onset of breathing in the newborn, there is a significant increase in blood flow to the lungs due to the negative pressure that is being created. This blood flow replaces the umbilical venous return, thus increasing cardiac output.[14] With ICC, there may be an increased risk of restricted cardiac output, hypoxia, and cardiac respiratory complications due to this blood flow restriction occurring.[14, 17, 41] It has been found that with DCC in preterm infants, superior vena cava return, as well as right ventricular output were higher when compared to infants who received ICC. This finding suggests that ICC may induce hypovolemia and irregular neonatal hemodynamics with a reduction in cardiovascular function.[39]

A common complication in newborns, especially preterm infants, is cardiovascular compromise. Low blood pressure during the first few days of life results in an elevated risk of intraventricular hemorrhage or bleeding into the brain. This complication can be life-threatening or lead to life-long problems in the newborn. It is hypothesized that early umbilical cord clamping prevents necessary blood transfusion by the placenta, withholding about a third of the neonate's blood volume it could achieve if cord clamping was delayed. [1, 25, 30] This decreased blood volume is what directly contributes to this hypotensive state.

When delayed cord clamping may not be beneficial

Studies on immediate versus delayed cord clamping ensured the safety of the infants by eliminating certain deliveries from study observation for ethical reasons. Deliveries that did not warrant delayed cord clamping included infants with tight nuchal cords (cords wrapped around their necks) and infants that required intervention immediately after delivery such as asphyxiated infants or those in need of immediate resuscitation.[4, 28, 40] The latter group of infants, interestingly, may in fact benefit more from DCC as this would allow further transfusion of blood and oxygen delivery through gas exchange from the placenta.[29]

Methods

Research was conducted to compare the benefits and harms of early versus delayed clamping of the umbilical cord in preterm and term infants. Initial studies on the overall effect of umbilical cord clamping were reviewed. The overall physiology of the umbilical cord was noted, most importantly during and immediately post-delivery of child. Important physiologic factors to note included the transition and re-organization of the cardiovascular system along with pulmonary function, placental blood transfusion, postpartum hemorrhage, and hemoglobin/hematocrit levels. Fetal health outcomes were studied and included the incidence of jaundice, iron deficiency anemia, polycythemia, hyperbilirubinemia, and blood gas results.

Inclusion/Exclusion Criteria

Review of articles included meta-analyses and controlled trials studies of comparing the effects of early versus delayed cord clamping post-childbirth (either vaginally or via cesarean). Preterm and low-birth-weight studies were included in this research review to observe the clinical

deviations various infants endure when it comes to the timing of cord clamping. It was expected that the effect of timing on cord clamping would have differing effects on neonatal outcomes.

All geographical areas were included in this review to observe the differences in umbilical cord clamping technique globally. Umbilical cord clamping is completed in every delivery, so it was deemed beneficial to observe the techniques of various countries and the outcomes of their decisions. Policy and hospital guidelines for various countries were also investigated to observe how different countries are ensuring the implementation of their practices.

Studies and analyses published earlier than the year 2000 were excluded from this review. All journal entries published after this date but prior to 2010 were strictly used as a reference of umbilical cord clamping completed historically and not as evidence for this use of DCC over ICC.

Search Strategy

A literature search was conducted on June 1, 2021, on various electronic databases including Jama, Google Scholar, and PubMed. Text word searched contained “early umbilical cord clamping”, “delayed umbilical cord clamping”, “timing of umbilical cord clamping”, “history of umbilical cord clamping”, “placental transfusion”, “anemia due to umbilical cord clamping”, “cardiovascular transition in neonates”, “maternal health outcomes with umbilical cord clamping” and “fetal health outcomes due to umbilical cord clamping”, “polycythemia in newborns”, “hyperbilirubinemia in newborns”, “jaundice in newborns”, “intraventricular

hemorrhage", "umbilical cord clamping policy", and "umbilical cord milking versus umbilical cord clamping".

Discussion

Defining ICC versus DCC:

Throughout the numerous studies conducted on ICC and DCC, each respective study had different definitions as to how they defined delayed/late cord clamping. Some had direct time intervals set; before 10-15 seconds indicated ICC in, after 30-60 seconds indicated DCC while some studies deemed anything prior to 30 seconds as ICC and any clamping post was DCC. Other studies defined DCC as waiting until the umbilical arterial pulsation ceased.[2, 21, 36] Umbilical cord pulsation occurs continuously in-utero and only briefly after delivery, eventually ceasing as the newborn transitions to more of an adult cardiopulmonary physiology.

As the umbilical cord pulsates, it continues to transfer blood, oxygen, and stem cells from the placenta to the baby until the newborn has fully transitioned to life outside of the uterus physiologically. Once the neonate has transitioned its cardiopulmonary system to that resembling an adult's, the umbilical cord ceases pulsation and the baby can now function without the assistance of the placenta. Immediately after delivery, pulsation is at its peak during the first fifteen to thirty seconds, allowing more adequate blood volume transfer and gas exchange. Many studies used this timing as the indicator of timing for DCC, rather than waiting for complete cessation of pulsation, as transfer between placenta and baby slows down dramatically after this time.

Preterm infants

It was hypothesized that immediate cord clamping in preterm infants would prevent harm from delayed resuscitation, hypothermia, hyperbilirubinemia, and possible polycythemia.[35, 36] This theory has since had evidence produced against it, suggesting that this practice may instead be harmful to the infant. Not only does delaying the time of cord clamping cost nothing more for the hospital, but it may also benefit the preterm infant by allowing increased retrieval of placental blood or by providing proper timing for physiologic transition from fetal to newborn life.[36]

In infants born prior to 37 weeks gestation, systematic reviews of randomized controlled trials have shown improved blood pressure, reduced need for blood transfusion, and decreased incidence of intraventricular hemorrhage in neonates.[36] Reviews of extremely early preterm births (<32 weeks gestation) even showed evidence of decreased mortality when umbilical cord clamping, cord milking, or a combination of both were implemented over immediate cord clamping. A randomized controlled trial in late preterm infants, between 34-36 weeks gestation, showed that waiting even three minutes after birth to clamp the umbilical cord was associated with higher hemoglobin levels at birth and at 10 weeks when compared to infants clamped within 30 seconds.[36]

Not only are effects of DCC seen immediately after birth in preterm infants, but even hours after. At 48 and 100 hours after delivery, a study comparing DCC with ICC found that DCC infants had higher superior vena cava flow than even at the six and 24-hour marks. This finding suggests that the effects of DCC last beyond the immediate postnatal period.[35]

Oxygenation Outcomes:

DCC was observed to improve oxygen saturation in the early transitional period newborns endure as their lungs are not completely active. The findings of Sommers et al. suggest that placental respiration helps to conserve arterial oxygen levels in the chance of pulmonary respiration falling short.[35] In cases where newborns may require resuscitation, these findings suggest prolonging placental respiration to prevent hypoxia or asphyxia.

A study conducted by Andersson et al. found that partial pressure of oxygen (PaO2) was lower in infants who received ICC. They believed this was due to ongoing circulation from the umbilical cord in the DCC group at the time of blood sampling, being that the cord had not been clamped yet.[3] This finding agrees with that of De Paco et al who found that two minutes after DCC, PaCO2 was higher than those with ICC.[11]

Cardiopulmonary Outcomes:

In a study of term infants specifically, infants who endured DCC resulted in higher systolic blood pressure readings within the initial 24 hours after birth.[21] This same group of infants also had higher blood volume, urine output, and effective renal blood flow within the first 12 hours after delivery. A literature review conducted by Mercer et al. found that studies suggested DCC infants showed more cardiopulmonary benefits including increased blood pressure, less need for oxygenation and ventilation, better capillary refill, and greater urine output as well.[27] They suggest this is due to better pulmonary and systemic vasodilation along with elevated RBC flow to the brain.

Intraventricular Hemorrhage Incidence:

Intraventricular hemorrhage is a major complication for infants born prematurely and is a concerning cause of mortality and morbidity. Moderate to severe hemorrhaging can result in posthemorrhagic hydrocephaly, cerebral palsy, and potentially mental retardation but with prompt management of hemodynamics and ventilation of infants experiencing this along with early recognition, morbidity can be lessened. Some studies focused their efforts on identifying if delaying cord clamping can reduce the incidence of this and decrease the probability of occurrence.

In a randomized controlled trial conducted by Mercer et al in 2004 the incidence of intraventricular hemorrhage (IVH) between infants assigned to ICC versus DCC was studied.[26] As IVH is most commonly associated with preterm delivery, women under 32 weeks gestation with preterm labor were allowed in the study. ICC was defined as <10 seconds after birth while DCC was defined as 30-45 seconds after birth. This study found that infants in the DCC group experienced less IVH than those receiving ICC during the first 28 days in the NICU (14% versus 36%). This finding is important as IVH has an association with later incidence of morbidity, mortality, or potential for developmental delays in the child.

Another study focused on 70 preterm infants delivered via cesarean section in Northern Iran.[39] ICC and DCC were defined exactly as Mercer et al had and all infants were routinely examined with ultrasound during their hospitalization to monitor for evidence of IVH. In the ICC group, 11 43% of infants experienced some level of IVH while no IVH was observed in the DCC group of infants. Although this finding was not found to be statistically significant, however, possibly due

to the small sample size, Varij Kazemi et al concluded that delaying cord clamping can be considered a safe method although more studies, preferably with larger sample sizes, are needed to provide more evidence on this.

Blood Volume Outcomes:

Mercer at al observed the effects of DCC on residual placental blood volume as an ethical method to determine neonate blood volume outcomes. Residual placental blood was collected via a collection bag and weighed with the placenta either in utero (vaginal delivery) or ex utero (cesarean section). As hypothesized, residual placental blood volume was less in those who were in the DCC group. Infants delivered via c-section also were found to have less residual placental blood volume than those born vaginally but this finding was not deemed significant.[27]

In a DCC simulation, infant blood volume was increased by 11.7% in comparison to ICC infants. This increase in blood volume attributes to an elevated preload in the DCC infants. The DCC newborns also showed increased stroke volume by 21% when compared to the ICC group. This finding is consistent with findings in a previous study that showed superior vena cava flow and cardiac output to be higher in DCC infants.[35, 41]

Hemoglobin and Iron Outcomes:

Iron deficiency anemia is a public health concern for both mothers and young children across the world. This anemia has associations with delayed growth and neurodevelopment in children, even into their preschool years. Numerous studies focused on how DCC may impact ferritin and total iron stores in the newborn, and how these values may change at follow-up.

Studies have found that delayed umbilical cord clamping has proven to provide elevated hemoglobin levels to infants, whether delivery be via vaginal or cesarean delivery. In the 2018 study on maternal blood loss between immediate vs delayed cord clamping, neonatal hemoglobin levels were higher in the DCC group by 1.7 g/dL.[2] Another randomized controlled study on specifically term, uncomplicated infants provided evidence that DCC would result in higher serum ferritin and less iron deficiency. These same infants from this study were then studied 4 years later and when compared with the ICC group, the DCC children had better fine motor skills and social development than their peers.[21]

Several other trials have studied the effect of cord clamping on hematologic outcomes past infancy as well, at up to six months of age. A review by Hutton and Hassan of randomized controlled trials found that delaying clamping for at least two minutes showed benefit in iron status through six months. These benefits included hemoglobin concentration, ferritin concentration, as well as reduction of anemia risk.[16]

In a study conducted in 2004 by Chaparro et al. in Mexico City, initial iron status was no different between their ICC and DCC infant study groups.[7] Hemoglobin and hematocrit measurements at 7 hours post delivery were significantly elevated in those infants who received DCC. At 6-month follow-up, there was no difference in weight gain or morbidity between the two groups, but the DCC infants had higher mean corpuscular volume, ferritin, body iron and stored iron than those who experienced early clamping. At 6 months, more infants in the ICC group had iron deficiency or iron deficiency anemia than their DCC counterparts. This same

study also found an interaction between the effects of timing of umbilical cord clamping and maternal ferritin. DCC had enhanced effects in infants born to iron-deficient mothers, indicating that this delayed timing of clamping can be more beneficial when implemented in mothers dealing with iron deficiency anemia themselves.

Umbilical Cord Blood Gases:

In the maternal blood loss via cesarian delivery study, umbilical cord arterial blood gases were studied and found the arterial pH to be significantly lower in the infants in the DCC group over those who received ICC.[2] Venous cord gas studies, however, showed no significant difference between the two infant study groups.

A study conducted by De Paco et al. measured umbilical blood acid-base and gas analyses between infants receiving umbilical cord clamping < 10 seconds and others 2 minutes post-delivery.[11] They hypothesized that findings would not be significantly different between the two groups. Their results were synonymous with this, finding that there were no significant differences in the umbilical vein or artery in the ICC and DCC group, except that pO2 of the umbilical artery had a higher mean in the DCC group. They attribute this finding to the fact that the infants began breathing independently while the umbilical cord remained unclamped.

Polycythemia:

A meta-analysis comparing ICC and DCC showed that DCC had an increased risk of polycythemia development (hematocrit > 65%) by 3.8-fold at the 24–48-hour mark post-

delivery. This same study, however, showed that the relative risk of anemia further down the line, around two to three months post-delivery, was reduced by 47% in the DCC group.[21]

Three studies completed in industrialized countries indicated a difference in hematocrit levels in favor of delayed clamping. The change in hematocrit was seen as soon in two to four hours after birth and remained for five days. None of these trials, however, reported clinical manifestations of polycythemia.[38]

A study completed in Iran on ICC versus DCC showed differing results. In their study, there was no significant change in hematocrit between the two groups. This study suggested that placental transfusion did not affect cord blood hematocrit, and thus that placental transfusion does not increase the risk of polycythemia.[18]

A literature review of umbilical cord clamping found that of the plethora of randomized clinical trials between 1980-2000, the studies do not support the notion that DCC has an elevated risk of symptomatic polycythemia, despite showing evidence of elevated hematocrit in DCC groups and preterm infants.[27, 28] In their conducted between 2013 through 2015, it was found that most of their DCC participants (sample size = 37) did not exhibit hemoglobin levels > 65%, the marker for polycythemia, and those that did exceed this amount (6 individuals) remained asymptomatic and did not require treatment of any kind.[28]

Jaundice/Hyperbilirubinemia:

Neonatal jaundice is a common concern for newborns, occurring in roughly 60% of neonates as a physiologic process.[10, 24, 28, 34] This occurs from the breakdown of RBCs and the infant's liver being incapable of metabolizing the particles, as it is too immature at this time. While for many, this is only a physiologic process, for some this can become pathologic (hyperbilirubinemia) and require treatment.

Multiple studies indicated that infants delivered with DCC had a higher relative risk for jaundice immediately after birth and required phototherapy treatment.[21, 24] However, a controlled trial conducted in Germany found that DCC resulted in elevated bilirubin levels in term infants but none of the participants required phototherapy and exchange transfusion.[38] Another study conducted in 2013 looking at randomized controlled trials comparing early versus late cord clamping found that fewer infants in ICC groups required phototherapy for their jaundice compared to those in DCC groups.[24] While this finding may be situational for these trials, the authors concluded that DCC may be more beneficial to the newborn, as long as access to phototherapy treatment is available.

Several risk factors for hyperbilirubinemia in newborns include fetal state of hypoxia from the mother being diabetic or having hypertension or from low birth weight, blood incompatibility such as ABO or Rh-, bilirubin metabolism from delay of meconium elimination or birth trauma, mother's use of medication, or newborn dehydration.[10, 34] In a study conducted in Japan between 2006 and 2014, it was found that hyperbilirubinemia in newborns who underwent DCC was related to a either a genetic factor, birth trauma, or delay in meconium elimination. Their

conclusions were that the elevated bilirubin levels were merely related to bilirubin metabolism issues, with no relation to the timing of umbilical cord clamping.[34]

Maternal health outcomes:

A not commonly considered concern in the timing of umbilical cord clamping is maternal anemia due to blood loss. Of the studies that exist on the topic, nearly all are studying maternal health during vaginal delivery, but few exist on cesarian delivery.

A systematic review of term infants delivered vaginally found no increased risk of maternal postpartum hemorrhage, maternal transfusion incidence, or increased length of the third stage of labor while also finding that there is statistically no change in maternal hemoglobin levels when the umbilical cord is clamped immediately or delayed.[3, 8, 9, 21, 32] Studies hypothesized that due to the increased time spent performing DCC, mothers may experience an increased risk of blood loss from delayed hysterotomy closure or uterine atony but no significant difference was found between DCC and ICC.[32] It is possible, however, that obstetricians were more cognizant of the risk of postpartum hemorrhage as a major complication when conducting DCC and were more attentive in maintaining homeostasis during this procedure than with mothers receiving ICC.

A randomized clinical trial completed in New York City in 2018 screened women with singleton gestations scheduled to undergo cesarian delivery at term, greater than or equal to 37 weeks gestation. Participants who were recruited and consented were randomized to receive either immediate cord clamping (within 15 seconds) or delayed clamping (at 60 seconds) after birth. Hemoglobin levels were measured post-op and found no significant difference between

immediate and delayed clamping indicating no difference in maternal blood loss between techniques in women undergoing cesarian deliveries.[2]

Umbilical Cord Milking:

To create the same positive infant outcomes as DCC but without the extra time needed, some trials have incorporated the study of umbilical cord milking compared to ICC and DCC. One benefit of umbilical cord milking is the reduced concerns for delays in neonatal resuscitation.[17, 21] This method is thought to be even more advantageous especially in the preterm population delivered via cesarean section, but more studies need to be conducted on long-term outcomes.

In a randomized controlled trial of preterm infants born prior to 28 weeks gestation, umbilical cord milking was found to have higher Apgar scores at the one-minute mark, reduced requirement for postnatal transfusion, elevated hemoglobin and blood pressures, and shorter duration of supplemental oxygen requirements when compared to those who had ICC.[15] These same infants who received cord milking had no incidence of polycythemia and no difference in bilirubin levels in those with ICC.

Another randomized controlled trial on premature infants delivered at 24 to 33 weeks gestation studied the difference between umbilical cord milking to DCC at 30 seconds after birth. In this study, there were no differences in Apgar scores, blood pressures, hemoglobin levels, transfusion necessity, and morbidity and mortality between the two techniques.[31] A study of 39 participants compared umbilical cord milking with DCC at 30 seconds in children at two and three and a half years of age. In this study, they found that those who received umbilical cord milking showed

better neurodevelopmental outcomes, with higher language and cognitive scores. Due to the small sample size, however, these results may be skewed.[19] A different study looked at cord milking with DCC at 30 seconds as well and found improved motor scores in children 18-22 months old who received cord milking alone.[28]

Conclusion

Although the World Health Organization, the American Academy of Pediatrics, and The American College of Obstetricians and Gynecologists have all recommended that delayed cord clamping beyond 60 seconds is beneficial to the infant's immediate health, many hospitals have not established clinical guidelines to direct this practice in the hospital/clinic setting.[8, 9, 17, 22, 28, 40] In hospitals that have acquired this as protocol, DCC is still only used in about 50% of cases, with differing shifts showing differing adherence. A study by Nelin et al in 2011 found that when observing a hospital in Kathmandu, Nepal that was working to implement DCC as the norm, night shift deliveries more often delayed cord clamping. These infants were 5.6 times more likely to receive DCC than ICC.[28] In Saudi Arabia, there is no established definition as to what the timing should be for umbilical cord clamping in the policies and procedures within their local hospitals.[17] Many of their local obstetricians report the existence of umbilical cord clamping guidelines but these may not be written and are simply verbal agreements between them and their clinical staff. These findings suggest that while DCC is commonly accepted as the technique of choice with many obstetricians and gynecologists worldwide, there needs to be uniform guidelines established that directly reflect the WHO recommendations.[22]

A study published in 2020 aimed at interviewing Australia's health professionals to view their perspectives on cord clamp timing. One provider stated, "*I think we need to do some more research on what the effects are of early cord clamping because really that is the intervention…I think instead of talking about the benefits of DCC, talking about the risks of ECC…reframing that deferred clamping as being normal*".[29] This quote highlights the fact that ICC is the riskier option. Most studies conducted have been highlighting the benefits of DCC rather than informing on the setbacks of ICC and why this should not be common practice in the delivery room unless needed as a form of intervention.

More than five percent of newborns globally require breathing assistance immediately after delivery. This complication takes the lives of more than 800,000 newborns each year. It is common practice to forego DCC for ICC, to be able to rapidly move baby to a resuscitation chamber and provide better life outcomes for it. While not many studies have been conducted on this matter, it is theorized that delaying clamping may benefit these children more by increasing the blood flow from the placenta to the newborn, allowing more oxygenation.[4]

From the research conducted, it was found that DCC benefits the newborn in numerous ways without inhibiting or imposing new risks. Polycythemia and hyperbilirubinemia have been the main cause of concern for DCC and that this delay may cause more harm than good in the short-term. While these are valid concerns and may happen, studies have found that their occurrence has no correlation with timing of umbilical cord clamping and are due to other physiologic processes of the infant at birth. With delaying cord clamping, we are providing the infant to receive a higher volume of blood, allowing their cardiopulmonary transition to occur fully, and

elevating their hematocrit and hemoglobin levels, all without increasing the risk of mortality to the baby or mother. The question arises is this better than umbilical cord milking at birth. Recent studies have suggested that yes, this may prove to have more beneficial long-term effects for neurodevelopment and motor skills years later, but more studies need to be conducted to confirm that this method can be used safely in preterm and term infants with longer follow-up time.

While the world is now beginning to accept that DCC is the better option in terms of when to clamp the healthy newborn, policies need to be implemented with guidelines on what exactly constitutes “delayed” as well as when this method should perhaps not be utilized. Rather than being a verbal agreement between clinical staff that this method is preferred, it needs to become a part of the written guidelines within hospital systems to further ensure the implementation is educated and adhered to.

References

[1]Alzaree F, Elbohoty A, Abdellatif M. Early Versus Delayed Umbilical Cord Clamping on Physiologic Anemia of the Term Newborn Infant. *Open Access Macedonian Journal of Medical Sciences*. 2018;6(8):1399-1404. doi:10.3889/oamjms.2018.286

[2]Ananth CV, Arditi B, Mauney L, et al. Effect of Delayed Versus Immediate Umbilical Cord Clamping on Maternal Blood Loss in Term Cesarean Delivery: A Randomized Clinical Trial. *Obstetric Anesthesia Digest*. 2019;40(3):113-114. doi:10.1097/01.aoa.0000689384.11179.85

[3]Andersson O, Hellström-Westas L, Andersson D, Clausen J, Domellöf M. Effects of delayed compared with early umbilical cord clamping on maternal postpartum hemorrhage and cord blood gas sampling: a randomized trial. *Acta Obstetricia et Gynecologica Scandinavica*. 2012;92(5):567-574. doi:10.1111/j.1600-0412.2012.01530.x

[4]Blank DA, Badurdeen S, Omar F Kamlin C, et al. Baby-directed umbilical cord clamping: A feasibility study. *Resuscitation*. 2018;131:1-7. doi:10.1016/j.resuscitation.2018.07.020

[5]Boere I, Roest AAW, Wallace E, et al. Umbilical Blood Flow Patterns Directly After Birth Before Delayed Cord Clamping. *Archives of Disease in Childhood*. 2014;99(Suppl 2). doi:10.1136/archdischild-2014-307384.614

[6]Chaparro CM. Timing of umbilical cord clamping: effect on iron endowment of the newborn and later iron status. *Nutrition Reviews*. 2011;69. doi:10.1111/j.1753-4887.2011.00430.x

[7]Chaparro, C., Neufeld, L., Tena Alavez, G., Eguia-Líz Cedillo, R. and Dewey, K., 2006. Effect of timing of umbilical cord clamping on iron status in Mexican infants: a randomised controlled trial. *The Lancet*, 367(9527), pp.1997-2004.

[8]Committee Opinion No. 684: Delayed Umbilical Cord Clamping After Birth. *Obstetrics & Gynecology*. 2017;129(1). doi:10.1097/aog.0000000000001860

[9]Committee Opinion No. 814; Delayed Umbilical Cord Clamping After Birth. ACOG. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2020/12/delayed-umbilical-cord-clamping-after-birth. Published December 2020. Accessed June 30, 2021.

[10]Dennery PA, Seidman DS, Stevenson DA. Neonatal Hyperbilirubinemia. *Drug Therapy*. February 2001. doi:10.32388/5btibi

[11]De Paco C, Florido J, Garrido MC, Prados S, Navarrete L. Umbilical cord blood acid–base and gas analysis after early versus delayed cord clamping in neonates at term. *Archives of Gynecology and Obstetrics*. 2010;283(5):1011-1014. doi:10.1007/s00404-010-1516-z

[12]Downey CL, Bewley S. Historical perspectives on umbilical cord clamping and neonatal transition. *Journal of the Royal Society of Medicine*. 2012;105(8):325-329. doi:10.1258/jrsm.2012.110316

[13]Hooper, S.B., Binder-Heschl, C., Polglase, G.R. *et al.* The timing of umbilical cord clamping at birth: physiological considerations. *Maternal health, Neonatology and Perinatology.* 2016. doi:10.1186/s40748-016-0032-y

[14]Hooper SB, Polglase GR, te Pas AB. A physiological approach to the timing of umbilical cord clamping at birth. *Archives of Disease in Childhood - Fetal and Neonatal Edition*. 2014;100(4). doi:10.1136/archdischild-2013-305703

[15]Hosono S, Mugishima H, Fujita H, et al. Umbilical cord milking reduces the need for red cell transfusions and improves neonatal adaptation in infants born at less than 29 weeks' gestation: a randomised controlled trial. *Archives of Disease in Childhood - Fetal and Neonatal Edition*. 2008;93(1). doi:10.1136/adc.2006.108902

[16]Hutton EK, Hassan ES. Late vs Early Clamping of the Umbilical Cord in Full-term Neonates. *JAMA*. 2007;297(11):1241. doi:10.1001/jama.297.11.1241

[17]Ibrahim NO, Sukkarieh HH, Bustami RT, Alshammari EA, Alasmari LY, Al-Kadri HM. Current umbilical cord clamping practices and attitudes of obstetricians and midwives toward delayed cord clamping in Saudi Arabia. *Annals of Saudi Medicine*. 2017;37(3):216-224. doi:10.5144/0256-4947.2017.216

[18]Jahazi A, Kordi M, Mirbehbahani NB, Mazloom SR. The effect of early and late umbilical cord clamping on neonatal hematocrit. *Journal of Perinatology*. 2008;28(8):523-525. doi:10.1038/jp.2008.55

[19]Katheria A, Garey D, Truong G, et al. A Randomized Clinical Trial of Umbilical Cord Milking vs Delayed Cord Clamping in Preterm Infants: Neurodevelopmental Outcomes at 22-26 Months of Corrected Age. *The Journal of Pediatrics*. 2018;194:76-80. doi:10.1016/j.jpeds.2017.10.037

[20]KC A, Rana N, Målqvist M, Jarawka Ranneberg L, Subedi K, Andersson O. Effects of Delayed Umbilical Cord Clamping vs Early Clamping on Anemia in Infants at 8 and 12 Months. *JAMA Pediatrics*. 2017;171(3):264. doi:10.1001/jamapediatrics.2016.3971

[21]Kresch M. Management of the Third Stage of Labor: How Delayed Umbilical Cord Clamping Can Affect Neonatal Outcome. *American Journal of Perinatology*. 2017;34(14):1375-1381. doi:10.1055/s-0037-1603733

[22]Madhavanprabhakaran GK, Wittmann AL, Vaidyanathan G, Aldughaishi T, Thomas DS. Knowledge and Practice of Umbilical Cord Clamping among Maternity Care Providers. Journal of Midwifery and Reproductive Health. 2018; 6(3): 1320-1327. doi: 10.22038/JMRH.2018.23553.1252

[23]McAdams RM. Delayed cord clamping in red blood cell alloimmunization: safe, effective, and free? *Translational Pediatrics*. 2016;5(2):100-103. doi:10.21037/tp.2016.04.02

[24]McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Evidence-Based Child Health: A Cochrane Review Journal*. 2014;9(2):303-397. doi:10.1002/ebch.1971

[25]Mercer JS. Current Best Evidence: A Review of the Literature On Umbilical Cord Clamping. *Journal of Midwifery & Women's Health*. 2001;46(6):402-412. doi:10.1016/s1526-9523(01)00196-9

[26]Mercer JS, Vohr BR, McGrath MM, Padbury JF, Wallach M, Oh W. Delayed Cord Clamping in Very Preterm Infants Reduces the Incidence of Intraventricular Hemorrhage and Late-Onset Sepsis: A randomized, controlled trial. *PEDIATRICS*. 2006;117(4):1235-1242. doi:10.1542/peds.2005-1706

[27]Mercer JS, Erickson-Owens DA, Collins J, Barcelos MO, Parker AB, Padbury JF. Effects of delayed cord clamping on residual placental blood volume, hemoglobin and bilirubin levels in term infants: a randomized controlled trial. *Journal of Perinatology*. 2016;37(3):260-264. doi:10.1038/jp.2016.222

[28]Nelin V, KC A, Andersson O, Rana N, Målqvist M. Factors associated with timing of umbilical cord clamping in tertiary hospital of Nepal. *BMC Research Notes*. 2018;11(1). doi:10.1186/s13104-018-3198-8

[29]Peberdy L, Young J, Massey D, Kearney L. Maternity health professionals' perspectives of cord clamp timing, cord blood banking and cord blood donation: a qualitative study. *BMC Pregnancy and Childbirth*. 2020;20(1). doi:10.1186/s12884-020-03102-8

[30]Rabe H, Gyte GML, Díaz-Rossello JL, Duley L. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database of Systematic Reviews*. 2019. doi:10.1002/14651858.cd003248.pub4

[31]Rabe H, Jewison A, Fernandez Alvarez R, et al. Milking Compared With Delayed Cord Clamping to Increase Placental Transfusion in Preterm Neonates. *Obstetrics & Gynecology*. 2011;117(2):205-211. doi:10.1097/aog.0b013e3181fe46ff

[32]Ruangkit C, Leon M, Hassen K, Baker K, Poeltler D, Katheria A. Maternal bleeding complications following early versus delayed umbilical cord clamping in multiple pregnancies. *BMC Pregnancy and Childbirth*. 2018;18(1). doi:10.1186/s12884-018-1781-6

[33]Raju TNK, Singhal N. Optimal Timing for Clamping the Umbilical Cord After Birth. *Clinics in Perinatology*. 2012;39(4):889-900. doi:10.1016/j.clp.2012.09.006

[34]Shinohara E, Kataoka Y. Prevalence and risk factors for hyperbilirubinemia among newborns from a low-risk birth setting using delayed cord clamping in Japan. *Japan Journal of Nursing Science*. 2020;18(1). doi:10.1111/jjns.12372

[35]Sommers R, Stonestreet BS, Oh W, et al. Hemodynamic Effects of Delayed Cord Clamping in Premature Infants. *PEDIATRICS*. 2012;129(3). doi:10.1542/peds.2011-2550

[36]Tarnow-Mordi W, Morris J, Kirby A, et al. Delayed versus Immediate Cord Clamping in Preterm Infants. *The New England Journal of Medicine*. 2017;2017(377). doi:10.1056/NEJMoa1711281

[37]Ultee CA, van der Deure J, Swart J, Lasham C, van Baar AL. Delayed cord clamping in preterm infants delivered at 34 36 weeks' gestation: a randomised controlled trial. *Archives of Disease in Childhood - Fetal and Neonatal Edition*. 2008;93(1). doi:10.1136/adc.2006.100354

[38]van Rheenen P, Brabin BJ. Late umbilical cord-clamping as an intervention for reducing iron deficiency anaemia in term infants in developing and industrialised countries: a systematic review. *Annals of Tropical Paediatrics*. 2004;24(1):3-16. doi:10.1179/027249304225013286

[39]Varij Kazemi M, Akbarianrad Z, Zahedpasha Y, Mehraein R, Haghshenas Mojaveri M. Effects of delayed cord clamping on intraventricular hemorrhage in preterm infants. *Iranian Journal of Pediatrics*. 2017;27(5). doi:10.5812/ijp.6570

[40]WHO. Guideline: Delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes. Geneva: World Health Organization; 2014

[41]Yigit MB, Kowalski WJ, Hutchon DJR, Pekkan K. Transition from fetal to neonatal circulation: Modeling the effect of umbilical cord clamping. *Journal of Biomechanics*. 2015;48(9):1662-1670. doi:10.1016/j.jbiomech.2015.02.040

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