EFFECT OF DELAYED CORD CLAMPING ON INFANT IRON STATUS

Abstract

Iron deficiency anemia is highly prevalent globally, and is especially of concern in infants born in developing countries. Breast milk is a poor source of iron, so for the first few months of life, infants primarily rely on iron stores that were built up during pregnancy. The primary objective of this review is to discuss the effects of delayed umbilical cord clamping on the iron status of infants. Primary research articles were found using EBSCO database, PubMed, and the World Health Organization Guideline references. The results indicated that delayed cord clamping improved an infant's hematologic status and decreased iron deficiency anemia during the first few months of infancy. Implementation of delayed cord clamping could decrease the risk of infant iron deficiency anemia in developing countries.

INTRODUCTION

Iron is one of the top nutrients of global concern. According to the World Health Organization (WHO),[1] in 2011, about 115 million children under the age of five were anemic due to iron deficiency. Iron is important for hemoglobin and myoglobin synthesis. These two proteins transport oxygen in the blood and muscles, respectively. Iron deficiency reduces the production of these proteins, resulting in decreased oxygen carrying capacity. Decreased hemoglobin production decreases the production of red blood cells (RBCs), which results in anemia. People who have iron deficiency anemia experience fatigue and decreased immune function.[2] Iron deficiency anemia in infants and children may result in irreversible impairments in growth and cognitive development.[2]

Infants are especially at risk for iron deficiency. The iron content of breast milk is only 0.3-0.5mg/L.[3] For the first sixth months, infants rely on body iron stores, which are built up during pregnancy; however, if the mother does not get sufficient iron during pregnancy, the infant does not store the needed amount.[4] This is a big concern in developing countries where anemia is widespread.[1] The WHO recommends delayed umbilical cord clamping (1-3 minutes after birth) to increase iron stores in the infant.[1] Increasing iron stores using this method could help prevent iron deficiency anemia in the first critical months of growth and development.[1] This solution would be a preferable and cost effective solution in developing countries.[1]

The primary objective of this review is to discuss the effectiveness of delaying umbilical cord clamping to increase the iron stores of infants in developing countries. Peer review journal articles were used to compare traditional early clamping (less than 1 minute after birth) to delayed clamping (more than 1 minute after birth) on infant iron stores and hemoglobin levels. Other maternal and infant health outcomes, including maternal hemorrhage, were also looked at for any contraindications for delayed cord clamping. Increasing iron levels early in infancy through delayed cord clamping would likely prevent early iron deficiency anemia during important periods of growth and development.

METHODS

The journal articles used in this review were found using the databases EBSCO host and PubMed. The terms “iron” and “cord clamping” and “international” resulted in 4 search results. One of these results was used in this review. Some of the other articles used in this review paper came from studies that either cited, or were cited by, the article from the PubMed search results. The WHO recommendations were found on WHO Guidelines for Delayed Umbilical Cord Clamping.[1] The rest of the articles used were referenced by the WHO Guidelines.

RESULTS/DISCUSSION

The use of delayed umbilical cord clamping has been a topic of study for the past half century. In 1969, Yao et al.[5] compared the transfusion of blood from the placenta to the infant in 111 full-term infants. The umbilical cords were clamped at 5, 15, 30, 45, 60, 90, 120, or 180 seconds, or 4, 5, or 6 minutes after birth. Infant blood volume and placental residual blood-volume were measured. Infant flood volume increased with increased delays in cord clamping up to 3 minutes.[5] After 3 minutes, there was no statistically significant increase in infant blood

volume. This suggests that the ideal amount of time between birth and cord clamping to allow or the greatest placental perfusion of blood, and therefore iron, is about 3 minutes.

Another concern for the effectiveness of delayed cord clamping is how the infant should be held before the cord is cut to allow for maximal transfusion. To see if there was any difference in the effectiveness of two different delayed cord clamping methods compared to a control group at two months after birth, Grajeda et al.[6] randomly assigned 88 pregnant mothers in Amatitlan, Guatemala into 3 groups based on clamping time and infant placement. The first group had the cord cut immediately after delivery. The second group had the cord cut when the cord stopped pulsating (about 1 minute after birth), during which time the infant was held at the level of the placenta. The third group also had the cord cut after the cord stopped pulsating, but the baby was held below the level of the placenta. At two months after birth, blood was obtained from 69 of the infants at a follow up visit. The drop-out rate was not significant across groups. There was a significant increase in hematocrit in the delayed groups compared to the early group ($p=0.014$).[6] However, there was no significant difference in hemoglobin or hematocrit between the delayed groups. This shows that delayed cord clamping has a lasting effect at 2 months. The level at which the infant is held during the time between birth and clamping does not seem to have a significant effect on the iron status of the child at 2 months after birth.

Evidence suggests that delayed cord clamping is effective in increasing the iron status of infants born to anemic mothers. Gupta et al.[7], compared the effects of delayed cord clamping on infants born to anemic mothers at 3 months after birth. Fifty-eight infants were randomly assigned to either delayed cord clamping (waiting until the placenta descended into the vagina) or immediate cord clamping. Infant venous blood was collected at 3 months and analyzed for hemoglobin and ferritin levels. Infant ferritin levels were significantly lower in the immediate clamping group ($p<0.001$), while changes in hemoglobin levels compared to at birth were significantly lower in the delayed cord clamping group. These results suggest that even if the mother is anemic, delaying cord clamping can help build-up infant iron stores for the first few months of life. This indicated that delayed clamping may be especially beneficial in countries where infant iron deficiency anemia are increased due to maternal anemia.

While delayed cord clamping has been shown to improve the iron status of infants up to a few months after birth, it is unclear how long these effects last. To determine whether the increased iron stores lasted until 6 months after birth (which is around the time infants begin eating other foods), Chaparro et al.[8] randomly assigned 476 mother-infant pairs in hospitals in Mexico City to either early cord clamping (around 10 seconds) or delayed cord clamping (around 2 minutes). Maternal blood samples were obtained before delivery. A blood sample was collected from the infants at 6 months after birth and analyzed for hemoglobin and hematological profiles. Infants in the delayed cord clamping group had significantly higher levels of mean corpuscular volume ($p=00.1$), mean corpuscular hemoglobin ($p=0.007$) ferritin ($p=0002$), stored iron ($p=0.0003$), and body iron (mg/kg bodyweight) ($p=0003$).[8] Infants in the early cord clamping group had significantly higher levels of iron deficiency ($p=0.05$) and iron deficiency anemia ($p=0.01$).[8] The benefits of delayed cord clamping on iron status were also significantly greater in infants whose mothers had poor iron status compared to mothers with normal iron status. Of infants born to mothers with low ferritin, the delayed cord clamping group had significantly higher levels of infant body iron (mg/kg) ($p=0.008$).[8] This supports the use of delayed cord clamping in infant births to mothers with low iron levels. The positive effect of delaying cord clamping lasted for at least six months.

However, in a different study, delayed cord clamping only helped to prevent iron deficiency up to age 4 months old. Rheehen et al.[9] studied 91 infants delivered to mothers in Mpongwe, Zambia. The mothers were randomly assigned to either delayed cord clamping (average time 305 seconds) or early cord clamping (average time 15 seconds). The infants were followed up at 2, 4, and 6 months, at which time finger prick blood was collected. Over this time period, hemoglobin levels declined in both groups, although the decline at 4 months was greater in the early cord clamping group than the delayed cord clamping group. At 4 months, the early clamping group had marginally higher levels of anemia ($p=0.059$) and iron deficiency anemia ($p=0.054$).[9] However, at 6 months, there was no difference in decreasing rates of hemoglobin, and in both groups, half of the infants were anemic.[9] Several factors may have played a role in the disparity between the results of the studies done by Rheehen at al.[9] and Chaparro et al.,[8] including differences in regional diets (which may have differed in iron content) and the prevalence of malaria in Zambia.

While the evidence listed so far indicates that delayed cord clamping results in increased infant iron stores, there have been concerns about the effect of delayed cord clamping on other maternal-infant outcomes, including hyperbilirubinemia, changes in blood pH, and maternal hemorrhage. In 1972, Saigal et al.[10] found that delayed cord clamping significantly ($p<0.001$) increased the risk of hyperbilirubinemia in premature infants. However, in areas where iron deficiency anemia a large concern, and treatment for infant jaundice is accessible, the benefits of increasing infant iron stores may outweigh the risks of hyperbilirubinemia, especially since it is mainly a concern for preterm infants.[10]

Another concern is that delayed cord clamping might cause dangerous changes in blood pH.[11] The pH of human blood is 7.4, and changes outside of the pH range of 6.8 to7.8 can be fatal.[12] To test how delayed cord clamping changes umbilical cord pH compared to immediate cord clamping, De Paco et al.[11] analyzed the umbilical cord gases of cord clamped at less than 10 seconds after delivery and cords clamped 2 minutes after delivery. They found no significant difference between acid-base and gas analysis of the umbilical vein and artery in early cord clamping and late cord clamping groups, except for an increase in pO2 ($p<0.001$) in the umbilical artery.[11] These results do not indicate that delayed cord clamping is a major risk to changing infant blood pH.

A final concern is that delayed cord clamping may cause increased maternal hemorrhage. To compare the maternal hemorrhage rates between mothers who had immediate cord clamping and mothers who had delayed cord clamping, Ahmad et al.[13] randomly divided 100 women into either early (at one minute) or late (after 1-3 minutes) cord clamping. They found no significant difference in blood loss between mothers in the delayed cord clamping group and the early cord clamping group. Evidence does not suggest that delayed cord clamping increases maternal hemorrhage.

While the evidence in these studies differed in the length at which delayed cord clamping was effective, all studies showed evidence of increased iron levels with the treatment of delayed cord clamping compared to early cord clamping. Importantly, the effects were the greatest on mothers who were anemic compared to mothers who had normal iron levels. This suggests that decreased iron status of the mother at birth does not interfere with the positive effects of delayed cord clamping on the infant. Also, if there is no indication that hyperbilirubemia, changes in pH, or maternal hemorrhage will be a problem in a specific pregnancy, then delayed cord clamping is not contraindicated. These results support the use of delayed cord clamping in developing countries where access to health care may be limited. Delayed cord clamping is a simple method

that may prove very beneficial in increasing iron stores during the first important month of growth and development.

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