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Review article in

Serum zinc changes in term neonates with hyperbilirubinemia after phototherapy

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Abstract

Neonatal jaundice is the most common cause of admission of newborns. It may be physiological and mostly self limited but may be dangerous because of the potential bilirubin toxicity of the brain. It is treated by ultraviolet phototherapy incubator. In this papers we reviewed literature to ident the relationship between the serum zinc and serum bilirubin and the phototherapy. We found that the serum zinc is inversely proportionated to serum bilirubin and its significantly increased after phototherapy for the same cause. Zinc supplements have no role in prevention of jaundice but can decrease the need for phototherapy.

Keywords: zinc, bilirubin, phototherapy

Introduction

One of the most prevalent clinical symptoms in newborn newborns is jaundice. In babies, jaundice appears as a yellow discoloration of the skin and sclera, indicating a high serum bilirubin level that causes bilirubin to accumulate in the tissues, including the skin and mucous membranes. In neonates with pale skin tones, jaundice is estimated to be noticeable at bilirubin levels of roughly 90mmol/litre. The diagnosis of jaundice is more difficult in babies with dark skin tones, but the sclerae are always white, and visual assessment of jaundice requires a thorough examination of the eyes (1). Neonatal jaundice is a common physiologic condition that occurs during the first few weeks following birth. It is a physical feature associated with numerous probable etiologies, rather than a single disease. Pathophysiology is thought to be the cause of severe newborn jaundice (2).

Because bilirubin can be harmful to the central nervous system, it's critical to diagnose neonatal jaundice early and treat it properly,

especially when bilirubin levels in physiological ranges can cause lasting neuronal damage (3). In the first week of life, 60 percent of term and 80 percent of preterm infants develop jaundice, and 10% of breastfed children stay jaundiced until they are one month old. In England, jaundice was the most prevalent reason for term newborns being admitted from their homes to neonatal facilities (4Breastfed newborns are more prone to develop jaundice within the first week of life, which is assumed to be due to an intensified physiological jaundice induced by a decreased caloric intake and increased enterohepatic bilirubin circulation. Breastfed infants can also develop prolonged unconjugated jaundice that lasts longer than a week. The mechanism underlying this later "breast milk jaundice condition" is still unknown. Blood group incompatibility (rhesus or ABO issues), various causes of haemolysis, sepsis, bruising, and metabolic abnormalities are all non-physiological causes. Rare causes of newborn jaundice include Gilbert's and Crigler–Najjar syndromes (5). Indirect bilirubin deposits in the neuron membrane cause persistent neuronal damage. The primary goal of diagnosing and treating neonatal hyperbilirubinemia is to prevent bilirubin encephalopathy and its chronic sequelae. Phototherapy and blood exchange transfusion are two treatments for unconjugated hyperbilirubinemia in newborns that are both costly, time-consuming, and possibly dangerous. To reduce increased serum bilirubin, new therapeutic techniques appear to be required. Reduced unconjugated bilirubin levels can be prevented by inhibiting enterohepatic circulation, which is one of the prospective therapy for preventing bilirubin neurotoxicity (6-8).

In this short review, we will discuss the changes in serum Zinc before and after the phototherapy and the modern use of Zinc compounds in treatment of hyperbillirubinemia.

Literature review

Because zinc is a critical trace element for normal operation, it is linked to severe inadequacies when it is lacking. Zinc is essential for a variety of biological processes, including nucleic acid metabolism, immunological function, protein synthesis, and cell function preservation. It is a cofactor in the creation of over 200 enzymes, including metalloproteinases, phosphatases, and oxide-reducatases (25). Several materials have been employed to prevent intestinal bilirubin absorption, such as laxatives and oral agar. Oral zinc salts at normal body temperatures have also been demonstrated to be beneficial.

Because they deposit unconjugated bilirubin, pH lowers the maximum bilirubin serum (26).

According to a recent study (9) the serum zinc levels of infants with jaundice were lower than those of neonates without jaundice. In diverse animal species and humans, zinc deficiency during pregnancy causes numerous difficulties for the fetus, including structural deformities, intrauterine growth retardation (IUGR), premature birth, and SGA. Zinc deficiency is thought to affect nearly half of all women of reproductive age. Low maternal serum zinc levels, low transferred zinc to the fetus, and an increased risk of developmental abnormalities have all been linked in studies. Many proteins include zinc, which has structural and enzymatic functions. Changes in the activity of proteins in the embryo may account for some of the teratogenic effects of zinc deficiency (10). During the third trimester, the level of serum zinc in the embryo rises, accumulating particularly in the fetal liver. There is also an increase in fetal metallothionein levels. The reason for these shifts is still unknown.

Zinc supplementation throughout pregnancy may be beneficial for immune system growth and maturation. Zinc deficiency may cause congenital malformations. There was a link between maternal serum zinc levels and the occurrence of low birth weight babies (11). Hypozincemia may alter the erythrocyte membrane by preventing lipid depolarization of cell membranes. It could lead to insufficient production of a variety of enzymes involved in bilirubin metabolism, Hypozincemia may also cause structural defects in the erythrocyte membranes, resulting in hemolysis (12).

According to the study, serum zinc levels in neonates with non-hemolytic hyperbilirubinemia (103.336.56 ug/dl) were significantly lower than in healthy neonates without jaundice (128.62 40.83 ug/dl), and zinc deficiency in jaundiced neonates (25.3 percent) was statistically significantly higher than in healthy neonates (6.7 percent). There was no significant link between blood zinc levels and other characteristics such as maternal age, parity, feeding pattern, gender, or weight, however there was a link with maternal zinc intake during pregnancy (13). Phototherapy is a safe and effective treatment option for newborn pathology. Zinc salts can shorten the duration of phototherapy by causing unconjugated bilirubin to precipitate in the gut. Zinc and bilirubin levels are adversely associated in infants with significant hyperbilirubinemia, according to one cohort research.

Additionally, phototherapy resulted in a substantial increase in the number of newborns with potentially hazardous zinc levels (zinc >200 gm/dl) among those with severe hyperbilirubinemia, while there was no significant change among those with mild to moderate hyperbilirubinemia (6).

The mean serum calcium, copper, and magnesium levels were significantly higher in newborns with hyperbilirubinemia, whereas the mean serum zinc level was significantly lower; these levels were modified after phototherapy, according to a recent study. Total bilirubin, direct bilirubin, calcium, and magnesium all showed statistically significant decreases. However, there is a difference between zinc and copper. After phototherapy, there was a statistically significant rise (23). According to a new study, there was no statistically significant difference in mean zinc levels before and after phototherapy. There was no statistically significant difference in total serum bilirubin (TSB) levels at admission and after 12 hours, but statistically significant changes were found after 24 hours and at discharge. The majority of infants with hyperbilirubinemia, on the other hand, were zinc deficient (14).

Another study, on the other hand, discovered a link between phototherapy and serum zinc. Regardless of the severity of hyperbilirubinemia, phototherapy generates a considerable increase in serum zinc levels. It may, however, cause zinc poisoning. After phototherapy, the blood bilirubin level dropped considerably to 8.47 1.36 mg/dl. After phototherapy, serum zinc levels increased considerably, reaching 75.45 14.94 mcg/mL. The difference in serum zinc levels between the control and study groups was highly statistically significant, with the case group being greater than the control group (15).

El mazary et al. found that neonates with indirect hyperbilirubinemia had significantly higher copper and magnesium serum levels and significantly lower zinc serum levels than healthy neonates, which were unrelated to maternal serum levels. Intensive phototherapy had little effect on their levels, but exchange transfusion raised them to levels comparable to those of healthy newborns (16).

Phototherapy was linked to a highly statistically significant increase in blood zinc levels in neonates with severe hyperbilirubinemia (TSB 18 mg/dL) in another study conducted in Egypt. The serum zinc level increased statistically substantially following phototherapy in patients with mild-to-moderate hyperbilirubinemia, reaching 129.17 mcg/mL in mild-to-moderate hyperbilirubinemia and 187.37 mcg/mL in severe hyperbilirubinemia, according to the study (17).

In infants with severe jaundice, Saravanan et colleagues discovered a substantial inverse link between zinc and bilirubin levels. In infants with severe jaundice, phototherapy was linked to a considerable increase in serum zinc levels, but not in those with mild-moderate jaundice. Furthermore, phototherapy resulted in a substantial rise in the number of newborns with potentially toxic zinc levels (Zn>200) among those with severe jaundice, while no change was seen among those with mild-moderate jaundice (18). Because the chemical structure of bilirubin has the potential to chelate with metal ions, such as zinc, the mechanism could explain the observed relationship between zinc and bilirubin levels investigated previously as in vitro studies showing that zinc salts precipitate unconjugated bilirubin at physiological pH. Because zinc salts produce a decrease in blood unconjugated bilirubin but an increase in fecal bilirubin excretion, in vivo investigations have shown that they can impede the enterohepatic circulation of unconjugated bilirubin by precipitating it in the colon (19). Although zinc has long been thought to be a harmless element, recent research has revealed that free ionic zinc can cause significant damage to neurons (20). Zinc salts have recently been recommended for lowering bilirubin levels in neonates, preventing neonatal jaundice, and lowering bilirubin levels in neonates (21).

When compared to a control group, zinc levels were found to be substantially related with higher TSB in another investigation.

When compared to the control group, the zinc level in cases was considerably lower. Phototherapy was linked to a considerable increase in serum zinc levels in infants with severe hyperbilirubinemia. All cases were divided into two groups based on their baseline TSB levels: moderate hyperbilirubinemia (TSB18 mg/dL) and severe hyperbilirubinemia (TSB18 mg/dL). Zinc levels increased significantly in both subgroups following phototherapy. The level of zinc in the blood had a strong negative connection with TSB (22). Oral zinc treatment reduces blood bilirubin levels in rats, according to animal research. Zinc salts can deposit unconjugated bilirubin, and zinc sulfate inhibits bilirubin enterohepatic circulation in hamsters. One to six hours after treatment, zinc (4 mol/kg) significantly reduced carbon monoxide (CO) and bilirubin levels. The hemoxygenase enzymes are inhibited by zinc salts and other metals such as strontium, which may help to prevent jaundice (24). And this relation may explain the negative correlation between the serum zinc levels and the total serum bilirubin level in term neonates.

According to old hypothesises, the use of zinc supplements could prevent the incidence of neonatal hyperbilirubinemia, it was postulated that Zinc salts have the ability to limit bilirubin circulation in the intestine, most likely via precipitating unconjugated bilirubin in the colon. but, the results of number of studies contradicts with that assumption.

A recent study found that giving a zinc supplement (10 mg/daily zinc sulfate) to a baby within the first week of life does not diminish hyperbilirubinemia or postpone the onset of jaundice. The zinc group gained higher weight between the third and seventh days of life, and there were no side effects recorded in the zinc group. In comparison to the

placebo group, the zinc group had fewer admissions and phototherapy sessions (27).

Another meta-analysis backs up the previous findings. They also discovered that zinc sulfate does not lower TSB levels and has no effect on newborn jaundice. Zinc sulfate, on the other hand, significantly shortens the time of phototherapy. Phototherapy for neonatal jaundice should be used with prudence (28).

Conclusion

According to the literature that we reviewed above, the phototherapy affect and increase the levels of serum zinc by decreasing the levels of bilirubin in blood. And also there is no effect for the zinc supplements on the incidence nor treatment of neonatal jaundice but may decrease the need for phototherapy so the use of zinc supplement is recommended in neonatal period.

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