The Study of the effect of serum zinc level in the mothers and Neonates on neonatal jaundice in al-diwanyia

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الخلاصة
الخلفية العلمية
ان للزنك دوراً طبياً في النمو و التطور الجنيني خلال فترة الحمل و كذلك في مرحلة نمو الطفل , فضلاً عن دوره الاساسي في الاحساس والتذوق والشم.
اظهرت الدراسات التي اشتملت على الحيوانات والمراهقين والمولودين بأوزان منخفضة ان اعطاء املاح الزنك يقلل مستوى البلروبين في مصل الدم ويعتقد ان السبب في ذلك يعود لتسببه في تقليل مستوى سريان دخول البلروبين للكبد.
الهدف
دراسة تأثير مستوى الزنك في مصل الدم للمواليد الجدد والامهات على مرض اليرقان في حديثي الولادة.
المرضى وطرق العمل
شملت هذه الدراسة (130) وليد مع امهاتهم واجريت في مستشفى الحسين للأطفال في الديوانية واستمرت هذه الدراسة من مايس الى تشرين الاول 2016 .(130) وليد مع امهاتهم , (65) منهم ادخلو الى المستشفى بسبب اليرقان الولادي (65) وليد من الاصحاء . اجريت للمواليد الفحوصات : مستوى البليروبين الكلي في الدم , الهيموتوكرت وزمرت الدم ومستوى الزنك في الدم للأمهات والمواليد .
النتائج
كان مستوى الزنك في مصل المصابين باليرقان في حديثي الولادة اقل معنوياً ($P<0.05$) بالمقارنة مع غير المصابين.
109 من اصل 130 ام يمتلكون مستوى الزنك في المصل بنسبة قليلة.
بالمقارنة , قلة الزنك كان مرتفعاً في الامهات في كلا المجموعتين .
لم يكن هناك فرقاً معنوياً في معدل مستوى الزنك في مصل الدم عند اخذ فترة الحمل بنظر الاعتبار ($P>0.05$)
الاستنتاج
اظهرت الدراسة ان مستوى الزنك في دم المواليد المصابين باليرقان الولادي هو اقل من المواليد الاصحاء .
الكلمات المفتاحية
اليرقان في حديثي الولادة , الزنك في مصل الدم.

Abstract
Background :
Zinc has a role in normal growth and development during pregnancy, childhood, and is needed for the proper sense of taste and smell. Studies on animals, adolescents and low birth weight neonates showed that oral zinc salt intake decreased serum bilirubin level, probably through inhibition of the bilirubin enterohepatic circulation.
Objective :
To study the effect of serum zinc level of the newborn and their mothers on neonatal jaundice.
Patient and methods
A case control study included a total 130, 65 with jaundice and 65 healthy neonates with their mothers. The study was carried out from May to October 2016 at

ALhussein hospital for children in Al-Diwanyia city. For all neonates serum zinc, total serum bilirubin, hematocrit, blood group typing and Rhesus were carried out. Serum zinc for the mothers also was measured .

Results :

Serum zinc in jaundiced neonates was significantly lower than non jaundiced neonates (P<0.05). One hundred and nine mothers out of 130 mothers have low serum zinc. In multipara, zinc deficiency was more frequent in the mothers of both groups and P value (0.69).There was no significant difference was in mean serum zinc level when gestational age was taken into consideration (full term versus pre-term) (P>0.05).

Conclusions :

This study showed that serum concentration of zinc in neonates with jaundice was significantly lower than that in healthy control.

Key words: neonatal jaundice, serum zinc

Introduction

Hyperbilirubinemia is one of the main clinical conditions that are seen in daily pediatric practice (1). Hyperbilirubinemia in the neonate is frequently seen at the first week of poastnatal life (2, 3). The rate of hyperbilirubinemia in neonates is in the range of 8% to 11%. The definition of hyperbilirubinemia resides on the level of total serum bilirubin (TSB) which is considered at $> 95^{th}$ percentile for age (4, 5).

Idiopathic neonatal jaundice is frequently seen in 60 to 80 % of well being infant (6). The clinical sign of neonal jaundice is seen in the form of yellowish discoloration of skin and sclera and this makes the parents anxious to seek medical advice (7). Referring to National Neonatal-Perinatal Database (NNPD) the rate of house live-births neonatal jaundice is around 3.3%, whereas for extramural admissions it is approximately 22.1% (8). First of all for neonatal jaundice is to involve the face then it will spread to the rest of the body as a reflection to rise in serum TSB (8).

Although Bilirubin plays an important role as antioxidant (9-11), high concentrations are harmful to the neonate and may cause neurologic and behavioral abnormalities (Neurotoxicity or Kernicterus) (12-14).

The rate of neonates that require management for development of jaundice is in the range of 5 to 10% (15).

Neonatal jaundice may be associated with different parameters such as gestational age, birth weight, early membranes rupture, maternal infections or other illness throghout pregnancy, possessing varaible sources of origin, hence being of different kinds (16).

A lot of kinds of Bilirubinemia have been registered in neonates such as pathological jaundice, physiological jaundice, breastfeeding or breast milk jaundice and hemolytic jaundice divided into three subtypes due to ABO blood group incompatibility Rh factor incompatibility, and Jaundice related Glucose-6-phosphate dehydrogenase (G6PD) deficiency (17). permanent neuronal damage may results from aggregations of indirect bilirubin in the neuron membrane. Protection against bilirubin encephalopathy and its long term complications is the main aim of diagnosing and managing neonatal hyperbilirubinemia (18). Therapeutic strategies for neonatal unconjugated hyperbilirubinemia, such as phototherapy and blood exchange transfusion are of high cost, needing long time and carry potential risks (19, 20). Recent therapeutic modalities appear to be essential to reduce high serum bilirubin. One of the promising modes for getting rid of bilirubin neurotoxicity is through

decreasing the unconjugated bilirubin concentration by preventing enterohepatic circulation (21). Zinc salts have the ability to prevent enterohepatic circulation of bilirubin possibly by precipitating unconjugated bilirubin in the GIT (22). Hence, a lot of clinical studies have assessed the effects of zinc adminstration on hyperbilirubinemia in neonates subjected to phototherapy (23-26).

Free zinc concentration inside the cell is lower than that outside the cell, which produces electrochemical gradient that pushes zinc inward. An high intracellular zinc level carry toxic hazards (27). Sobieszczanska et al. (28) proposed that decreasing extracellular zinc by chelating substances in energetically inadequate cells, may inhibit the influx of this element and its associated toxic hazards. For that reason, "Zinc is essentially a 'Two-edged sword' that may both induce injury and protect neuronal cells from injury" (29).

The bilirubin chemical structure has the ability to chelate metal ions, including zinc (30). Hence, reduction of bilirubin by phototherapy

could cause a rise in serum zinc concentrations. So further zinc administration may results in zinc toxicity.

So the aim of the present study was to evaluate the effect of serum zinc level of the newborn and their mothers on neonatal jaundice.

Patients and Methods

The present case control study involves a total of one hundred and thirty neonates with their mothers . They were attending the ALhussein hospital for children in Al-Diwanyia city. The data was collected from May 2016 to October 2016. Sixty five neonates are presented with jaundice (study group) and another sixty five healthy neonate with no jaundice (control group). In the study group, the age of neonates ranged between 2 to 10 days. In control group the neonates are of comparable age and sex as in study group, they were selected from healthy neonates attending the hospital for vaccination. The following investigations were done for all neonates, including determination of total serum bilirubin concentration, hematocrit for the baby, blood group typing and Rh and serum zinc concentration of the mother and her baby. A full history was taken from their close family members including, the age of the mothers, economic state , previous baby with jaundice, parity, maternal medical diseases during pregnancy, residence, the age and gender of baby, the gestational age of the baby(preterm, term) , type of feeding (breast versus formula feeding), birth weight (normal is $\geq$ 2.5 kg , low < 2.5 kg). The onset of jaundice classified as (second-third day and fourth day-one week). The mothers age are grouped into two groups; less than 20 years and more than 20 years

In this study we exclude neonate with sepsis, and any critical illness (asphyxia, RDS, major anomalies). Inclusion criteria: Live neonates from the age of (2-10) days who admitted to the hospital for jaundice and the control data was the same age and gender.

The way of samples taking were by heal prick for total serum bilirubin, hematocrit , and blood group and Rh . Samples were collected by nursing staff and transferred immediately to hospital laboratory. The total serum bilirubin was done by using Bilrubin Meter [APEL] Japan. Serum bilirubin regarded as hyperbilirubinemia if total serum bilirubin is more than 12 mg / dl in term infant and more than 10 mg /dl in preterm infants. Another sample from a peripheral vein from the baby and the mother sent for serum zinc measurement to private laboratory (Albelad laboratory), where the sample were analyzed by automated method by spectrophotometer . Serum zinc normal reference range is (60 -120 Mcg / dl for individuals 0-10 years , and 66-110 Mcg/dl for individuals older than 10 years).

The data were entered in the data base and analyzed using the statistical package for the social sciences software SPSS program (version 22 for windows 7) with statistical significance of p–value <0.05,values less than 0.01 were considered to be highly significant.

Results

The demographic characteristics of the study sample are shown in table 1. Serum zinc level was classified into normal and low and was correlated with neonatal jaundice, gestational age, breast feeding, and parity of mother and the results were shown in table 2. There was significant association between neonatal jaundice and zinc deficiency

(P<0.05). In addition, there was significant association between bottle feeding and zinc deficiency (P<0.05). No significant association was encountered between neonatal jaundice and gestational age and also between neonatal jaundice and parity (P>0.05)

Table 1: Demographic characteristics of the study sample

Characteristics		**n**	**%**
Jaundice	Positive	65	50
	Negative	65	50
Gender	male	49	37.6
	Female	81	62.4
Residency	Urban	86	66.1
	Rural	44	33.9
Birth weight	Normal	105	80.7
	Low	25	19.3
Mother age	< 20 years	24	18.4
	≥ 20 years	106	81.6
Parity	Primi	33	25.3
	Multi	97	74.7

Table 2: Serum zinc level

Characterstic		**Study group N=65**		**Control group N=65**		**p-value**
		Normal zinc	**Low zinc**	**Normal zinc**	**Low zinc**	
Neonate	**All neonate**	18	47	36	29	0.001*
	Preterm	3	3	3	5	0.639
	Full term	27	32	27	30	0.862
	Brest feeding	24	30	18	17	0.519
	Bottle feeding	2	9	17	13	0.028*

Mother	**All mothers**	9	56	12	53	0.369
	Primipara mothers	3	17	2	6	0.532
	Multipara mothers	5	40	5	52	0.693
	Mothers with preterm baby	3	3	2	6	0.333
	Mother with full term baby	8	51	6	51	0.616

***significant at p<0.05**

Discussion

The current study showed that the serum zinc level of neonates with jaundice was lower than that of the neonates without jaundice. In 2 previous studies in Iran, they found that the serum zinc level of the neonates with jaundice was lower than that of those without jaundice (31, 32. Another study in Iraq (Baghdad) also found a positive correlation between serum zinc and neonatal jaundice ,they found that serum level of bilirubin was lower in jaundiced neonate than healthy control group (33). A similar study in Iraq (Babylon) on physiological changes in infantile hyperbilirubinemia showed that serum level was lower in jaundiced group than control group (34). There are several studies about the use of zinc in the treatment and prevention of neonatal hypebilirubinemia.

In a study in India, they administer a zinc solution orally 5 mg twice daily by the mother for 7 days to jaundiced group and placebo for another jaundiced group. They found that there is a decrease in mean duration of phototherapy by 21.3 hours (35). The prophylactic effect of zinc in neonatal hyperbilirubinemia was studied in Indonesia, they found that serum bilirubin was comparable in both zinc and placebo group at day of discharge and day 5 after birth (36). Zinc is very important co-factors for a lot of enzyme systems and has an important role in the synthesis of nucleic acids (37,38). Zinc prevents the lipid depolarization of the cell membranes and zinc deficiency may modulate the erythrocyte membrane. It may result in deficient synthesis of enzymes that play a role in the bilirubin metabolism (39), Hypozincemia may also cause structural defects in the red cells membranes, resulting in hemolysis (40).

In our study, of the whole study groups,109 mothers have low serum zinc level. This may be associated with poor nutritional status and many pregnant women receiving iron therapy during pregnancy without zinc supplement and the iron is known to interfere with zinc absorption in the bowel, this is supported by the results of 2 studies that report a reduction in plasma zinc level in pregnant women given high (164–395 mg/d) or moderate (60 mg/d) doses of iron (41,42). Besides various inhibiting factors in vegetarian diet, over supplementation of Iron during pregnancy may also adversely affect absorption of zinc(43,44). Depending on the zinc bioavailability in the habitual diet of the pregnant woman, about 2 to 4 mg of additional dietary zinc is required daily to meet these additional needs (45,46). This translates into 18%–36% more zinc per day in the diets of pregnant compared to non-pregnant women. However, irrespective of their usual zinc intake, most women do not report increased intakes of zinc in their diet during pregnancy (47). This suggests that homeostatic adjustments are the primary mechanisms for meeting the increased zinc requirements of pregnancy (45) . A study in Turkey in 2000 measured the Serum concentrations of zinc, magnesium, manganese and copper in neonates with jaundice and healthy neonates together with their mothers. They found that Serum zinc

concentrations in neonate with jaundice and their mothers were significantly lower than those of the control group and their mothers, and they attribute the
maternal serum zinc deficiency to the nutritional state in their country (48). Another study in India measured the serum concentration of zinc,
iron ,and copper in pregnant women and their newborns, and healthy non pregnant women of a comparable age. They found that serum concentration of zinc in pregnant women and their babies were significantly lower than that of control , however, the serum zinc level of
newborn was significantly higher than their mothers. Zinc is passively transferred from mother to fetus through the placenta and there is also reduced zinc binding capacity of maternal blood during pregnancy which facilitates efficient transfer of zinc from the mother to her fetus resulting in an increase level of zinc in cord blood (49).

In conclusion: serum concentration of zinc in neonates with jaundice was significantly lower than that in healthy control.

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