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Original Article

Correlation between Prolonged Hyperbilirubinemia and Serum Zinc Level in Term Neonates

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ABSTRACT

Background: Prolonged hyperbilirubinemia is defined as jaundice persisting more than two and three weeks of life in term and preterm neonates, respectively. In total, 15-40% of jaundiced neonates became prolonged. The most common causes of prolonged hyperbilirubinemia are breastfeeding, infection, hypothyroidism, and continued hemolysis. Given the fact that no study was conducted on the association between the serums zinc level and prolonged hyperbilirubinemia, this study aimed to compare the healthy neonates with newborns suffering from prolonged hyperbilirubinemia in terms of serum zinc level.

Methods: This cross-sectional analytical descriptive study with a control group included all neonates who had a history of hospital admission and phototherapy due to hyperbilirubinemia at Amirkola Children's Hospital, Babol, Iran. After discharge, on the 14th day of birth, all neonates followed up at the outpatient clinic. The serum bilirubin was checked and the neonates were assigned into the case (with prolonged hyperbilirubinemia) and control (without prolonged hyperbilirubinemia) groups. Both groups were matched regarding confounding factors. Serum zinc level was measured using the colorimetric method and the two groups were compared in this regard.

Results: In total, 60 neonates in the case (n=30) and control (n=30) groups were investigated in this study. The serum zinc levels in the case and control groups were 83.7±35.35 and 92.73±38.13 µg/dl, respectively. There was no significant difference between the two groups in terms of the serum zinc level (P=0.34).

Conclusion: There is no statistically significant correlation between the serum zinc level and prolonged hyperbilirubinemia in term neonates who had been treated with phototherapy.

Keywords: Hyperbilirubinemia, Jaundice, Neonate, Term birth, Zinc

Introduction

In total, one-third of neonatal admission in Iran is due to the neonatal hyperbilirubinemia (1). Prolonged hyperbilirubinemia is defined as total bilirubin level higher than 10 mg/dl over two and three weeks of life in term and preterm neonates, respectively. It may be due to infections, hypothyroidism, hemolysis, and unknown reasons. Most of the causes of severe jaundice could be considered as the cause of prolonged hyperbilirubinemia; however, the association between the prolonged hyperbilirubinemia and the serum zinc level is not clear. Trace elements are necessary for normal protein functions, and zinc is one of the most abundant trace elements in human (2). Its deficiency in infants and children can cause stunted growth, neurological disorder, and precipitate infections (3). In several studies, zinc has been investigated for its role in decreasing the bilirubin levels by the inhibition of the normal enterohepatic circulation of unconjugated bilirubin (4-8). Moreover, it is an integral component of nearly 300 enzymes in different species of all living beings (9). This study was carried out to determine the relationship between the serum zinc levels and prolonged hyperbilirubinemia in full-term neonates.

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Methods

This cross-sectional analytical descriptive study with a control group included 60 full-term neonates who had a history of admission and phototherapy for neonatal hyperbilirubinemia at Amirkola Children's Hospital (ACH) affiliated to Babol University of Medical Sciences, Babol, Iran. The inclusion criterion was the neonates older than 14 days who were discharged from ACH due to the neonatal hyperbilirubinemia with unknown etiology. They were divided into two groups of the case (n=30) who developed prolonged hyperbilirubinemia after discharge and control groups (n=30) which included neonates with the same characteristics who had not got prolonged hyperbilirubinemia.

On the other hand, the neonates with prematurity, intrauterine growth retardation, hypothyroidism, infection, zinc sulfate intake by the mother and the infants with a history of taking phenobarbital by their mother and other drugs, including cotoneaster, manna, and Sisymbrium irio were excluded from the study.

The study population included the neonates who were admitted to ACH and received conventional phototherapy. They were discharged with serum bilirubin of lower than 10 mg/dl. Subsequently, they were followed up at 14th day of life at the outpatient clinic of ACH. The total serum bilirubin (TSB) and direct bilirubin level were measured at ACH laboratory. The neonates were assigned into two groups regarding the TSB level higher than 10 mg/dl (case) and lower than 10 mg/dl (control).

Both groups were matched regarding the confounding factors, including age; birth weight, gender, and mode of feeding (i.e. breastfeeding). In the case group, the laboratory tests to diagnose the neonatal hyperbilirubinemia included total and direct bilirubin measurement, complete blood count test, thyroid-stimulating hormone, thyroxin, urine analysis, and urine culture.

The TSB was measured using a spectrometric method (Darman Kav Co, Iran) in the ACH laboratory. Additionally, the serum zinc level was measured on 14th day of birth in the case and control groups using a Chlorometric method (Zist Shimi Co, Iran) in the biochemistry laboratory of Babol University of Medical Science. The serum zinc level was expressed as micrograms per deciliter, and the level of lower than 75 µg/dl was considered as zinc deficiency (10). Figure 1 depicts the schematic representation of the protocol of the study.

Ethical considerations

The study protocol was approved by the Ethics Committee of Babol University of Medical Sciences, Babol, Iran (MUBABOL.HRI.REC.1396.13).

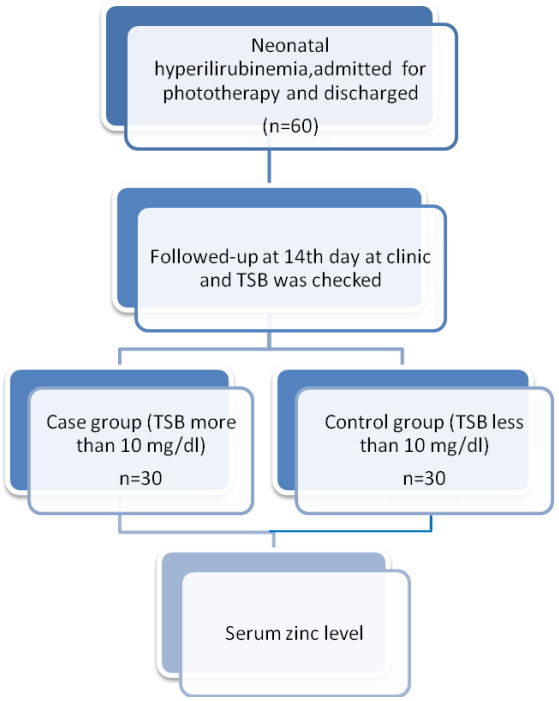

Figure 1. Schematic representation of the protocol of the study
*TSB=Total Serum Bilirubin

Statistical analysis

Data were analyzed in SPSS software (version 22.0) through t-test and Chi-square test to analyze the qualitative and quantitative variables, respectively. A p-value less than 0.05 was considered statistically significant.

Results

Totally, 60 neonates in two groups of the case (n=30) and control (n=30) with and without prolonged hyperbilirubinemia, respectively, were included in this study. Moreover, 16 neonates in the case group and 14 newborns in the control group were females (P=0.72). The mean birth weight scores were obtained at 3391±410.6 and 3373±338.1 grams in the case and control groups, respectively (P=0.86). Regarding the type of delivery in the case group, 18 (60%) and 12 (40%) neonates were born vaginally and by cesarean section, respectively. Furthermore, 16 (53.3%) and 14 (46.7%) neonates in the control group were born vaginally and by cesarean section, respectively (P=0.6).

The mean ages at the initiation of phototherapy were 4.33±1.88 and 3.83±1.46 days in the case and control groups, respectively (P=0.25). The mean scores regarding the duration of hospitalization in the case and control groups were 3.53±0.89 and 3.47±1.17 days, respectively (P=0.8). There was no significant difference between the two groups in terms of the baseline data, such as gender, birth weight, and type of delivery. A comparison of the demographic characteristics of the neonates in the two groups was shown in Table 1.

It can be seen that the mean TSB levels on admission day were 16.41±2.2 and 16.45±1.3 mg/dl in the case and control groups, respectively (P=0.49). Moreover, the mean TSB level at the time of discharge in the case and control groups were 8.94±0.6 and 8.66±0.67 mg/dl, respectively (P=0.12). Regarding the mean TSB level on the 14th day of birth, the case and control groups obtained 13.29±0.3 and 6.31±1.01 mg/dl, respectively (P=0.0001).

Table 2 summarizes the mean TSB levels in the case and control groups at the time of admission and discharge as well as the 14th day of birth.

The serum zinc level was below 75 µg/dl in 15 (50%) and 11 (42.3%) neonates in the case and control groups, respectively (P=0.29). Moreover, the serum zinc level in both groups was not statistically correlated with gender, birth weight, and type of delivery (P>0.05).

Table 1. Comparison of the demographic characteristics of case and control groups

Variables	Case group (N=30)	Control group (N=30)	P-value
Gender n (%)			
Male	14(46.7%)	13(43.3%)	0.72
Female	16(53.3%)	17(56.7%)	
Birth weight (gram) Mean ± SD	3391±410.6	3373±338.1	0.86
Type of delivery n (%)			
Vaginally	18 (60%)	16 (53.3%)	0.6
Cesarean section	12 (40%)	14 (46.7%)	
Age of admission (days) Mean ± SD	4.33 ± 1.8	3.83 ± 1.46	0.25
Duration of hospitalization (days) Mean ± SD	3.53 ± 0.89	3.47 ± 1.17	0.8

Table 2. Comparison of the *TSB level and serum zinc level between the two groups

Variables	Case group (N=30) Mean ± SD	Control group (N=30) Mean ± SD	P-value
TSB level on admission day (mg/dl)	16.41 ± 2.2	16.47 ± 1.3	0.49
TSB level on discharge day (mg/dl)	8.94 ± 0.60	8.66 ± 0.67	0.12
TSB level on 14th day of birth (mg/dl)	13.29 ± 0.3	6.31 ± 1.01	0.0001
Serum zinc level (µg/dl)	83 ± 35.35	92.73 ± 38.13	0.34

*TSB=Total Serum Bilirubin

Discussion

The result of this study showed no statistically significant difference between neonates with prolonged hyperbilirubinemia and those without this condition regarding the serum zinc levels. To the best of our knowledge, no study was performed to compare serum zinc levels in neonates with or without prolonged hyperbilirubinemia.

Some studies were conducted to show the effect of phototherapy on the serum zinc level. Accordingly, the results of a study by El-Mazary et al. on neonates with indirect hyperbilirubinemia showed no changes in serum zinc level before and after phototherapy (11). In another study in Iran, Boskabadi H. et al. (2015) compared the serum

zinc levels in healthy neonates and those with hyperbilirubinemia. Their results revealed the lower levels of serum zinc in neonates with hyperbilirubinemia, compared to that in the control group (12).

Mosayebi et al. performed a study in Iran to determine the effect of phototherapy on the serum zinc level in neonates. They found that phototherapy resulted in a significant increase in the serum zinc level in neonates with severe (total serum bilirubin ≥18 mg/dl) hyperbilirubinemia (13).

According to the findings obtained from this study, the lack of difference between the two groups regarding the serum zinc level might be due to the effect of phototherapy on serum zinc level. In spite of this fact, the condition was the same in both groups.

In the study conducted by Boskabadi et al. (2015), the serum zinc level was not correlated with the type of delivery and gender (11). Similarly, in this study, serum zinc level was not statistically correlated with gender, type of delivery, and birth weight.

In the present study, there was no significant correlation between prolonged hyperbilirubinemia and the serum zinc level. It might be because of no observed difference between the two groups on discharge day in terms of the serum zinc level. On the other hand, it might be attributed to the effect of phototherapy on the serum zinc level; however, due to the presence of the same conditions for phototherapy and discharge, its effect might be negligible.

Limitation of the study

Although this study paved the way on the correlation between prolonged hyperbilirubinemia and serum zinc level in term neonates, it suffers from some limitations, including lack of significant difference between the case and control groups regarding the serum zinc level. This can be attributed to the probable effect of phototherapy on the serum zinc level. If the zinc level can be measured before, during, and after phototherapy, the difference might be significant. Therefore, it is suggested that further studies measure the serum zinc level more frequently than that performed in this study.

Conclusion

This study showed no statistically significant correlation between the serum zinc level and prolonged hyperbilirubinemia; however, further studies are required to be conducted on the measurement of serial serum zinc level before, during, and after phototherapy.

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Conflicts of interests

None to be declared.

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