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Original

Zinc level alternation after phototherapy in neonates with hyperbilirubinemia

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Abstract

Introduction: One of the old treatment methods for unconjugated hyperbilirubinemia in neonates is blood exchange transfusion, which is expensive, possibly high-risk, and time-consuming. Today phototherapy as a novel method can be a good alternative.

Objectives: This study aimed to evaluate the zinc level alternation after phototherapy in neonates with hyperbilirubinemia.

Patients and Methods: A descriptive-analytical study was conducted on 85 infants with hyperbilirubinemia who underwent phototherapy referred to the pediatric hospital in Bandar- Abbas, Iran from 2017 to 2018. Healthy infants over two days with idiopathic jaundice with a gestational age greater than 34 weeks and only breast-feed were enrolled. Serum zinc levels were measured before and after phototherapy, and their changes were evaluated.

Results: Out of 85 neonates, 42 (49.4%) were male and 43 (50.6%) were female with a mean gestational age of 37.83 ± 0.58 weeks and admission age of 4.15 ± 1.70 days. Zinc level before phototherapy was 84.98 ± 52.06 (µg/dL) and after phototherapy was 234.41 ± 280.98. The difference between serum zinc levels before and after the phototherapy was significant therefore, the zinc level significantly increased after the phototherapy

Conclusion: Results showed that phototherapy increases serum zinc levels, which can cause zinc toxicity. It is wise to measure serum zinc levels before and during phototherapy and seek the appropriate medical care.

Keywords: Hyperbilirubinemia, Neonatal jaundice, Zinc Level, Phototherapy.

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Introduction

Jaundice has been known as a clinical sign in infants and the most prevalent reason for hospitalization after discharge from the maternity ward (1). The indirect bilirubin deposition in the neuron membrane results in persistent neuronal damage. Detection and treatment of neonatal hyperbilirubinemia are the principal aims of inhibiting bilirubin encephalopathy and its chronic sequels (2). There have been several treatments for unconjugated hyperbilirubinemia in neonates, including blood exchange transfusion and phototherapy, which are expensive, possibly high-risk, and time-consuming (3). Novel therapeutic approaches are essential for decreasing raised serum bilirubin. The unconjugated bilirubin level could be reduced by preventing enterohepatic circulation and could be adopted as a potential treatment for inhibiting bilirubin neurotoxicity (1). Zinc salts can inhibit the enterohepatic circulation of bilirubin apparently via the precipitation of unconjugated bilirubin in the intestine (4).

Intracellular zinc has two roles: protein synthesis and cell membrane called structural zinc, and the role of catalyst and signal transmitter, called free zinc. The intracellular concentration of free zinc is less than its extracellular concentration; therefore transferring zinc from inside the cell to the outside requires energy. The changes associated with a decrease in ATP levels are associated with an increase in intracellular zinc concentration. In its normal state, the cell tries to regulate the intracellular surface. The dual effects of zinc on the nerves (neurotoxic and neuroprotective) are known; however the exact mechanism of these two actions have not yet been determined. Zinc has a significant impact on the activity of all cells, such as neurons that are very sensitive to hypoxia. Similar effects of zinc activity are seen in cells outside the central nervous system (CNS), and it is worth mentioning that their low-sensitivity to hypoxia significantly increases the cytotoxic impact of zinc ions (5).

Consequently, many clinical experiments have focused on evaluating the impacts of zinc supplementation on hyperbilirubinemic neonates using phototherapy (6). Some metal ions, including zinc, could be chelated due

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Implication for health policy/practice/research/ medical education

In a descriptive-analytical study conducted on 85 infants with hyperbilirubinemia who underwent phototherapy, we found that phototherapy significantly increased serum zinc levels.

to the chemical composition of bilirubin. Therefore, the decrease of bilirubin due to phototherapy can lead to a rise in serum zinc amount, and resulting in zinc toxicity by extra zinc supplementation (7).

Objectives

This study aimed to investigate the serum zinc level alterations before and after phototherapy in hospitalized hyperbilirubinemia infants undergoing phototherapy.

Patients and Methods

Study design and participants

This descriptive-analytical study was conducted on 85 neonates with hyperbilirubinemia who underwent phototherapy in the pediatric hospital in Bandar-Abbas, Iran from 2017 to 2018. Full-term, healthy appropriate for gestational age and particularly breast-fed infants at the age of 2 to 28 days admitted for evaluation of non-hemolytic jaundice and Jaundice were enrolled in the study. The individuals who had undergone exchange transfusion or any congenital malformation were excluded. The infants who had been formula-fed, inborn errors of metabolism, confirmed infection or sepsis, and had jaundice in the first 24 hours of life were also excluded from the study.

Data collection and measurements

In this study, a two-part checklist was conducted, the first part containing demographic information of infants (gender, gestational age, birth weight, age of admission, type of delivery, and type of phototherapy), and the second part included laboratory information (bilirubin level, serum zinc level, and hemoglobin at hospitalization and also zinc after phototherapy). Hyperbilirubinemia management was carried out mainly by the American Academy of Pediatrics (AAP) guidelines (8,9). Serum bilirubin and neonatal zinc levels were measured before and after the phototherapy by spectrometry with a Selectra-2 analyzer. It should be noted that the tests of all newborns were checked in a laboratory. Data were collected and the difference between serum zinc levels before and after phototherapy was evaluated.

Statistical analysis

Data were analyzed by Statistical Package for the Social Sciences (SPSS) version 26. Quantitative variables were conducted to describe the data center means, and standard deviations were used to describe the data distribution. The Kolmogorov-Smirnov test was employed to evaluate the da, normality. Descriptive tests such as mean, variance, and standard deviation, and analytical tests such as chi-square and paired t-tests were used to explore the difference between serum zinc levels before and after the phototherapy. A p-value less than 0.05 were considered significant.

Results

Results showed that the mean gestational age was 37.83 ± 0.58 weeks, neonatal age was 4.15 ± 1.70 days, birth weight was 3164.29 ± 388.10 g, admission bilirubin level was 16.32 ± 1.58 mg/dL, zinc level before phototherapy was 84.98 ± 52.06 µg/dL, and zinc level after phototherapy was 234.41 ± 280.98 µg/dL. Out of the 85 neonates, 42 (49.4%) were male, and 43 (50.6%) were female. The type of delivery in 35 (41.2%) neonates was Cesarean section (C/S) and 50 (58.8) were vaginal (Table 1).

According to the paired t-test, a significant difference was found between serum zinc levels before and after the phototherapy, so that the zinc level significantly increased after the phototherapy (Table 2).

Results showed that before phototherapy, 58.8% of infants had normal zinc levels and 41.2% had abnormal zinc levels. After phototherapy, 27.1% of infants had normal zinc levels and 72.9% had abnormal zinc levels. Chi-square showed that the frequency of infants with normal or abnormal levels of zinc before and after

Table 1. Demographic characteristics of infants who participated in the study

Variables		Frequency	Percent
Gender	Male	42	49.4
	Female	43	50.6
Type of delivery	Vaginally	50	58.8
	Cesarean section	35	41.2
Type of phototherapy	Single	18	21.2
	Double	15	17.6
	Intensive	52	61.2
		Mean	**Standard deviation**
Gestational age (wk)		37.83	0.58
Age of admission (days)		4.15	1.70
Birth weight (g)		3164.26	388.1
Total serum bilirubin level on admission day (mg/dL)		16.32	1.58

Table 2. Comparison of the serum zinc level before and after the phototherapy

Variables	Mean	Standard deviation	Mean difference	*P* value
Before the phototherapy (µg/dL)	84.98	52.06	149.43	<0.001*
After the phototherapy (µg/dL)	234.41	280.98		

* Paired t-test.

Table 3. Comparison of the frequency of infants with normal and abnormal serum zinc levels before and after the phototherapy

Variable		Before phototherapy		After phototherapy		*P* value
		Frequency	Percent	Frequency	Percent	
Serum zinc level	Normal	58.8	80	27.1	23	<0.001*
	Abnormal	41.2	35	72.9	62	
Variables			**Frequency**		**Percent**	
Zinc levels alternation		Decreased	14		16.5	
		Increased	66		77.6	
		Unchanged	5		5.9	

*Chi-square

phototherapy changed significantly, and the majority of people changed from normal to abnormal (Table 3). According to the variations in serum zinc levels before and after phototherapy, neonates fall into three groups, as shown in Table 3, serum zinc levels in 14 (16.5%) infants decreased, in 66 (77.6%) increased, and in the 5 (5.9%) infants were unchanged.

Discussion

In this study, serum zinc levels increased significantly after phototherapy (approximately 150 mg/dL). During phototherapy, 77.6% of neonates revealed a rise in serum zinc levels to the extent that 41.2% had elevated serum zinc levels up to abnormal. This result is consistent with the other investigations (10-13). The mechanism between zinc level and phototherapy has been investigated in previous studies (4,14,15). In normal pH, the molecular composition of bilirubin can bind with metal ions such as zinc; therefore, zinc salts can precipitate unconjugated bilirubin. In addition, zinc salt can inhibit the enterohepatic circulation of unconjugated bilirubin. Our results showed that patients with severe hyperbilirubinemia associated with increased serum zinc levels after phototherapy compared to patients with mild to moderate hyperbilirubinemia; however, the results were borderline statistically significant. Previously, El-Mazary et al (16) assessed the variations in serum levels of some trace elements (copper, zinc, and magnesium) after intensive phototherapy in full-term neonates with indirect hyperbilirubinemia. The results did not affect serum zinc level and did not change it significantly. Baiomi et al (17) stated that serum zinc levels increased significantly after phototherapy to reach 75.45 ± 14.94 µg/dL. Phototherapy was related to a considerable rise in serum zinc levels in neonates. Samra et al (18) stated on a highly statistically meaningful increase in the level of zinc after phototherapy than before phototherapy. In the present investigation, no significant relationship between changes in serum zinc levels with age, gender, preterm delivery, number of pregnancies, type of delivery, and birth weight were seen. The relationship between bilirubin levels at admission and changes in serum zinc levels seems to be direct (10,19). In addition, a statistically significant relationship between the types of phototherapy with variations in serum zinc levels was detected, which can be concluded that the more intense in the phototherapy causes increase rate of serum zinc levels also increases. Therefore, the association of higher bilirubin levels with a further increase in serum zinc levels can be attributed to the fact that higher bilirubin will be associated with an increase in the intensity of phototherapy.

Conclusion

According to the findings of the present survey, it can be said that phototherapy is associated with a rise in serum zinc levels. Therefore, we conclude that before phototherapy zinc level should be measured, and the necessary treatment should be managed based on it.

Limitations of the study

We did not ethically allow to provide a control group with the same bilirubin level who were not treated with phototherapy. Alteration in bilirubin levels before and after phototherapy was not measured.

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Authors' contribution

Conceptualization: RG and HS.
Methodology: FJ.
Validation: BD.
Formal analysis: RG.
Investigation: FJ.
Resources: HS and BD.
Data curation: RG and FJ.
Writing—original draft preparation: BD.

Writing—review and editing: RG.
Visualization: HS.
Supervision: RG.
Project administration: BD.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical issues

The research was conducted in accordance with the tenets of the Declaration of Helsinki. This study resulted from a research project with Ethical code (IR.HUMS.REC.1397.225), approved by the ethics committee of Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Informed consent was also obtained from the children's parents. Ethical considerations in this study were approved by obtaining the ethics code from the ethics committee of Hormozgan University of Medical Sciences. Besides, ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

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