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Effect of Phototherapy on Serum Level of Calcium, Magnesium and Vitamin D in Infants With Hyperbilirubinemia

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ABSTRACT

Background and Objective: Phototherapy is one of the therapy methods for jaundice caused by hyperbilirubinemia. Vitamin D and bilirubin have two distinct routes of metabolism yet part of their syntheses is common in the liver and thus they may influence each other's synthesis. One of the consequences of phototherapy not previously studied in detail is hypocalcaemia and hypomagnesaemia. The current study aimed at investigating the effect of phototherapy on serum level of calcium, magnesium, and vitamin D.

Methods: The current semi-experimental investigation was conducted on 50 term infants with jaundice that had phototherapy indication. Bilirubin, calcium, magnesium, and vitamin D were measured in their blood samples at admission and then 48 hours after beginning the phototherapy. Data were analyzed with SPSS version 16 using paired-samples *t* test.

Results and Discussion: The serum calcium was 9.85 mg/dL before phototherapy and significantly decreased after it (9.51 mg/dL) (P <0.001). Also, the mean serum magnesium was 2.21 mg/dL before phototherapy and significantly decreased after it (2.06 mg/dL) (P=0.047). The mean of serum vitamin D significantly increased after phototherapy (before 17.44 mg/dL and after 21.77 mg/dL) (P <0.0001). The current study showed that phototherapy could decrease the level of calcium and magnesium and increase the level of vitamin D.

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Introduction

About 60% of term infants and 80% of preterm infants have hyperbilirubinemia in the first week of birth. Severe hyperbilirubinemia might progress towards acute encephalopathy or kernicterus if not treated (1). Kernicterus is a neural syndrome observed due to indirect deposit of bilirubin in basal ganglia and nucleus of brain stem. As a result, neural symptoms are mostly related to engagement of the mentioned areas. Various factors play a role in kernicterus and some of which are as follows:

Level of indirect bilirubin crossing the brain blood barrier and the vulnerability of neurons are amongst the influential factors (2-4). According to previous studies, kernicterus is rarely observed among healthy term infants in the absence of hemolysis in pink that its total serum level of bilirubin is <25 mg/dL (5).

The aim of therapy is to prevent neurotoxicity as a result of indirect bilirubin and avoidance of unwanted damages. Phototherapy, and in case of failure changing the blood are early therapy methods used to maintain maximum total bilirubin under pathologic levels (6). The side effects of phototherapy include rash, dehydration, nasal obstruction, chills, trauma to the eye, increase in insensible excretion of water, diarrhea, increase in body temperature, fever, tanned child syndrome, ocular injury, bronze baby, DNA damage, and nose block due to covering eyes (7).

Magnesium plays a role in protecting the neural system against hypoxia and neurotoxic effects of bilirubin, through blocking NMDA receptor. Magnesium ion is one of the most important complex antagonist regulators of bilirubin molecule/ionic canal/NMDA receptor in humans. Bilirubin leads to hyperactivity of the NMDA receptor and exerts neurotoxic effects through binding to NMDA, which has a key role in synaptic physiologic functions and memory (8, 9).

The signs of disorder in magnesium and calcium are, to some extent, similar. In the recent years, limited research showed that phototherapy should be considered as a risk factor for hypocalcemia (10, 11) and its mechanism is probably based on the effect of phototherapy on the decrease of melatonin leading to decrease in melatonin, spatter of reduced glucocorticoid, and increase in calcium absorption from bone that causes hypocalcemia (5).

Vitamin D is one of the most important elements in the body with an important role in hemostasis of calcium, structure of skeleton, neuromuscular, and immune system of the body. The two main sources of vitamin D are diet and synthesis through skin in response to ultra violet light. The lack of vitamin D in children is known as rickets and symptoms of its increase (hypervitaminosis D) are similar to those of hypercalcemia such as hypotonia, anorexia, polyuria, and polydipsia. Treatment of hypervitaminosis D is only possible through avoiding vitamin D and decreasing calcium consumption. The active form of vitamin D can increase the absorption of calcium by the intestine. Therefore, the level of vitamin D might change in infants with a disorder in the rate of calcium ion during phototherapy (12). The changes in blood levels of calcium, magnesium, and vitamin D might affect each other, rarely examined by recent studies; thus, the current study aimed at investigating the effect of phototherapy on serum level of calcium, magnesium, and vitamin D.

Materials and method

The current semi-experimental investigation was conducted on 50 term infants (gestational age: >37 weeks) under four weeks of age weighing >2500 g with phototherapy indication hospitalized due to jaundice at Mostafa Khomeini Hospital, Tehran, Iran with their parents' consent. The subjects with cephalohematoma, infancy infection, glucose-6-phosphate dehydrogenize (G6PD) deficiency, or symptoms of hemolysis such as positive Coombs test, hemolytic jaundice as a result of ABO or Rh incompatibility, blood change, and those of mothers with diabetes or under treatment with phenobarbital, and mothers receiving magnesium sulfate or oxytocin before delivery were excluded from the study. All the subjects were matched by coombs result and only infants with negative Coombs result were included.

The data were collected in two phases. First, the information was obtained from the subjects` files, examination, and interview with the mothers; in the second phase, the laboratory data of the subjects were obtained during the treatment. Before phototherapy and 48 hours after phototherapy, blood samples were collected and complete blood count, bilirubin (with photometric method using 2,4-dichloroaniline), calcium (with photometric method using cresolphthalein complexone), magnesium (with photometric method using xylidyl blue), and vitamin D (by the enzyme-linked immunosorbent assay (ELISA) using kit 25-(OH) vitamin D) were tested. To perform phototherapy, the subjects were placed at a distance of 15 to 20 centimeters from the light source (eight blue fluorescent lights) with a wave-length range of 420 to 470 nm above their heads. Also, a fiber optics blanket specific to phototherapy was put under their bodies and eyes and genitals were completely covered. After completing the tests, the required information was collected and recorded. Subjects were excluded from the study if during the treatment process another problem was observed besides jaundice. The obtained data were analyzed with SPSS version 16 and paired-samples *t* test.

The researchers were committed to the ethical guidelines of the Declaration of Helsinki and approval for the study protocol was obtained from the Institutional Review Board at Shahed University, Tehran, Iran.

Results

The current study was conducted on 50 infants of which 27 were male (%54) and 23 female (46%). The mean± standard deviation (SD) of calendar age of the population under the study was 5.52 ± 2.45 days, with the youngest being two days old and the oldest 14 days. The mean gestational age was 38.14 ± 0.83 weeks, with the youngest being 37 weeks and oldest 41 weeks; the mean weight during the hospital stay was 3177.4 ± 373.62 g.

Evaluation of the average level of serum bilirubin in subjects measured at two different times (at hospitalization and discharge) showed a significant decrease in the level of bilirubin; level of bilirubin in those subjects after phototherapy had an average value of 8.53±1.6 µmol/L, which was less than that of hospitalization time 15.19± 2.24 µmol/L (*P* <0.05) (Table 1).

Statistical analysis showed that 48 hours after phototherapy, average serum calcium level in the subjects was 9.51 ± 0.54 mg/dL, which was less than that of the hospitalization time (9.85 ± 0.64 mg/dL). This decrease was statistically significant (*P*<0.001) (Table 2).

Regarding the serum level of magnesium in the subjects, the average was 2.06 ± 0.39 mg/dL after phototherapy, which was less than that of the hospitalization time (2.21 ± 0.57 mg/dL) and the difference was statistically significant (*P*=0.047) (Table 3).

The average serum vitamin D level in the subjects was 21.77 ± 8.58 mg/dL after phototherapy, which was more than that of the hospitalization time (17.44 ± 6.48 mg/dL); this decrease was also statistically significant (*P*=0.000).

Table 1. Average Level of Total and Direct Bilirubin, Before and After Phototherapy

Time of Test	Total Bilirubin (Mean± SD) mg/dL	Maximum / Minimum	Direct Bilirubin (Mean± SD) mg/dL	Maximum / Minimum	*P-value*
Hospitalization time	15.19± 2.29	20.25	0.426± 0.15	0.85	<0.05
		8		0.2	
48 hours after Phototherapy	8.53± 1.6	13.8	0.33 ± 0.07	0.6	
		5.54		0.2	

SD, standard deviation

Table 2. Average Level of Total and Direct Bilirubin, Before and After Phototherapy

Time of Test	Serum Calcium Level (Mean± SD) mg/dL	Maximum / Minimum	*P-value*
Hospitalization time	9.85 ± 0.64	11.2	<0.001
		8.7	
48 hours after phototherapy	9.51 ± 0.54	10.7	
		8.3	

SD, standard deviation

Table 3. Average Level of Serum Magnesium, Before and After Phototherapy

Time of Test	Serum Magnesium Level (Mean± SD) mg/dL	Maximum / Minimum	*P-value*
Hospitalization time	2.21 ± 0.57	4	<0.001
		0.7	
48 hours after phototherapy	2.06 ± 0.39	2.8	
		1.2	

SD, standard deviation

Table 4. Average Level of Serum vitamin D, Before and After Phototherapy

Time of Test	Serum vitamin D Level (Mean± SD) mg/dL	Maximum / Minimum	*P-value*
Hospitalization time	17.44 ± 6.48	37	<0.0001
		7.5	
48 hours after phototherapy	21.77 ± 8.58	49	
		10.8	

SD, standard deviation

Discussion

Hyperbilirubinemia or jaundice is a common problem and it is often considered benign in infants. Jaundice might be observed at the birth or any time during infancy. Therefore, if hyperbilirubinemia, which is non-conjugation, is not treated early, bilirubin crosses the blood-brain barrier and exerts its neurotoxic effects. Its therapy includes medicine therapy, blood change, and phototherapy (13). Phototherapy is a therapeutic method with the following consequences: rashes, dehydration, increase in body temperature, ocular injury, hypocalcemia, hypomagnesemia, etc. (14, 15). One of the elements influenced by phototherapy is vitamin D. Although, vitamin D and bilirubin have two distinct routes of metabolism, yet, since part of their syntheses is common in the liver, they may influence each other’s synthesis. Therefore, it can be concluded that phototherapy might influence the level of blood in both elements (16). Calcium, magnesium, and vitamin D are important elements in the body and phototherapy can lead to the decrease of serum calcium and magnesium in the blood. On the other hand, decrease in calcium and magnesium can cause certain complications such as apnea, muscular tick convulsion, and decrease in absorption of vitamin D, which causes a decrease in the absorption of calcium. Therefore, any changes in the blood level cause irreparable effects, and might also influence the absorption of other elements (1). The current study aimed at investigating the effect of phototherapy on serum level of calcium, magnesium, and vitamin D in infants with jaundice at Mostafa Khomeini Hospital, Tehran, Iran. Results of the current study showed that the level of calcium in term infants undergoing phototherapy with average of 9.51 mg/dL was less than that of the hospitalization time with an average of 9.85 mg/dL and this decrease was statistically significant; similar to the results of the study by Barak et al. that showed calcium level of serum was reduced significantly, 24, 48, and 72 hours after phototherapy. Also, the outcomes of the current study were in accordance with those of the investigations by Setehi et al. that showed 90% of preterm infants and 75% of full-term infants during phototherapy developed hypocalcemia (18). In the study undertaken by Imani et al., serum bilirubin and magnesium levels were measured before and after phototherapy, both of which showed a significant decrease (8). Also, Khosravi et al., reported that phototherapy can decrease the total magnesium (15). The results of these two studies as well as the results of the current study showed that average serum magnesium level decreased after phototherapy. In the study conducted by Sarici et al., there was a positive relationship between the levels of bilirubin and magnesium in ionized plasma. In the group with severe hyperbilirubinemia, magnesium level of ionized serum was significantly higher in comparison with that of the moderate group. Also, in this group, there was a positive and significant relationship between serum level of magnesium and intensity of hyperbilirubinemia (19). In the current study, the serum level of magnesium decreased through relieving hyperbilirubinemia and it maybe that the increase in the plasma level of magnesium was due to synchronization with hyperbilirubinemia; hence, after decrease in bilirubin, the level of magnesium decreased. In the current research, mean vitamin D before and after phototherapy was 17.44 and 21.77 mg/dL, respectively; hence, the results showed that phototherapy can significantly decrease the level of vitamin D. In the study by Gillies et al., on 33 infants, plasma level of vitamin D increased in 17 term and pre-term infants 48 hours after phototherapy, although the increase was not significant. The results of their study showed that phototherapy might cause an increase in vitamin D that was in accordance with the results of the current study (20).

Conclusion

Based on the findings of the current study, phototherapy can significantly decrease in the levels of calcium and magnesium and an increase in the level of vitamin D in jaundice term infants undergoing phototherapy. Therefore, it is suggested that further studies be conducted on the effect of phototherapy on the levels of calcium, magnesium, and vitamin D on premature and pre-term infants.

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Conflict of interest

The authors declared no conflict of interest.

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