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# The Effect of Phototherapy on Serum Levels of 25-Hydroxyvitamin D in Neonatal Hyperbilirubinemia

**Research Article**

**Yadollah Zahed Pasha[1], Mousa Ahmadpour Kacho[2], Nima Ravan[3*], Mahmoud Haji Ahmadi[4]**

1, 2. Professor of Neonatal-Perinatal Medicine, School of Medicine, Non-Communicable Pediatric Disease Research Center, Amirkola Hospital, Babol University of Medical Sciences, Babol, Iran
3. Student Research Committee, Babol University of Medical Sciences, Babol, Iran
4. Assistant Professor of Biostatistics, School of Medicine, Non-Communicable Pediatric Disease Research Center, Babol University of Medical Sciences, Babol, Iran

## Abstract

Background: Hyperbilirubinemia is one of the common problems in neonates; the most effective and commonly used treatment method is phototherapy. The aim of this study was to investigate the effect of phototherapy on the calcium to urine creatinine ratio and serum level of 25-hydroxyvitamin D in icteric neonates hospitalized in term neonates treated with phototherapy at Amirkola Hospital in Babol in year 2018. Method: This study was performed on 60 term neonates (36 boys and 24 girls) with mean age of 1.24±4.88 who underwent phototherapy. The ratio of calcium to urine creatinine and serum levels of 25-hydroxyvitamin D was determined before and 72 hours after phototherapy. Findings: The results of this study showed that the mean serum level of 25-hydroxyvitamin D in icteric neonates before phototherapy was 28.12 ng/dl and after 72 hours of phototherapy was 26.17 ng/dl, which was significantly decreased (P=0.03). Also, the calcium to urinary creatinine ratio in the icteric neonates before phototherapy was 0.16 and after 72 hours phototherapy was 0.17 which significantly increased (P=0.03). Conclusion: Phototherapy reduces serum levels of 25-hydroxyvitamin D and increases urinary excretion of calcium in term neonates.

**Keywords:** *Hyperbilirubinemia, Phototherapy, 25-Hydroxyvitamin D* .

## Introduction

Bilirubin is one of the ultimate catabolism products that precipitate in the skin and mucous membranes of babies and causes jaundice. Jaundice or hyperbilirubinemia is one of the common problems of neonates during the first week of life and one of the main causes of concern for parents [1]. Jaundice affects 60% of term neonates and 80% of preterm neonates in their first week of birth [2]. Although the pathophysiology of jaundice is similar in term and preterm neonates, preterm neonates are at higher risk for jaundice [3]. Jaundice usually occurs 2-4 days after birth, and lasts about one to three weeks [4]. Although there are different causes for neonatal jaundice, neonatal jaundice is usually benign and requires no therapeutic intervention [5]. Different ways to treat jaundice have been proposed, which is currently the most appropriate treatment for phototherapy.

Phototherapy means lightning on the skin of neonates who have been overexpressed by excessive bilirubin. The use of this therapeutic approach has begun 50 years ago with the goal of preventing indirect neuropathic complications of indirect hyperglycemia [6]. Phototherapy uses light energy to make changes in the shape and structure of the bilirubin molecules that are deposited in the skin and subcutaneous tissues and by converting bilirubin into water-soluble isomers that can be excreted in the urine and feces without need for conjugation in the liver, it can reduce serum bilirubin levels [7]. The effectiveness of phototherapy depends on the type of light source used (ie, dose, spectral radius curve and penetration depth), the distance between light and the baby, the jaundice etiology, and total serum bilirubin level at the onset of phototherapy [8].

Vitamin D is a unique and essential micronutrient whose main function is to maintain calcium homeostasis and bone health. Physiologically, there are two active forms of vitamin D, both called calciferol, known as vitamins D2 and D3. Vitamin D deficiency can interfere with calcium metabolism and reduce serum calcium levels (hypocalcaemia) [9]. To detect the deficiency of this vitamin, 25-hydroxyvitamin D is a benchmark. 25OHD level is a good way to estimate the presence of vitamin D [10]. Reducing serum calcium that occurs as a result of vitamin D reductions is one of the harmful effects of phototherapy on children, although the exact mechanism is still unclear. The wavelength of vitamin D photo biosynthesis is between 280 and 320 nm. In this wavelength, 25-hydroxyvitamin D is converted to active

*Corresponding Author:
**Nima Ravan,**
Student Research Committee,
Babol University of Medical Sciences,
Babol, IRAN.
E-mail: nimaravan65@gmail.com

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form of vitamin D (D3). Adult studies have shown that higher wavelengths (110-300 nm) also trigger D3 production [11]. Conventional phototherapy devices used to treat neonatal jaundice may emit radiation above the visible spectrum (400-710 nm) [12] and although the Plexiglas protector in these devices is effective in controlling the amount of ultraviolet radiation (that is, less than 400 nm), there is evidence that the amount of ultraviolet radiation emitted by these devices cannot be ignored [13]. However, few studies have been done on the effects of phototherapy on serum levels of 25-hydroxyvitamin D in neonates [14].

Therefore, this study was designed to investigate the effect of phototherapy on serum level of 25-hydroxyvitamin D and calcium excretion (colosire) in icteric neonates hospitalized at Amirkola Hospital in Babol in year 2018.

**Research hypothesis**

Phototherapy can change the serum levels of 25-hydroxyvitamin D and calcium in the icteric neonates.

**Research background**

Barak et al. (2014) examined the effect of phototherapy on serum levels of total calcium and 25-hydroxyvitamin D in neonates with jaundice. This study was performed on 100 neonates (57 boys and 43 girls) with exacerbated physiologic jaundice. The level of vitamin D in neonates at 0, 24, 48 and 72 hours were 9.34, 9.52, 10.22 and 10.5 ng/dl, respectively, which was an insignificant increase. This study showed that phototherapy cannot significantly reduce vitamin D in neonates [15].

Mutlu et al. (2013) studied the relationship between vitamin D and Hyperbilirubinemia in neonatal blood. The results showed that reduction of serum vitamin D could result in a significant increase in bilirubin in the blood and in the production of jaundice. In this experiment, the effect of phototherapy on the amount of vitamin D was not reported [16].

Mashal Khan and colleagues evaluated the incidence of hypocalcemia in 2016 in neonates exposed to jaundice under phototherapy in Karachi. This study was performed on 123 neonates with an average age of 8 days, and it was determined that 22.76% of neonates under phototherapy had hypocalcemia after phototherapy, indicating a significant effect of phototherapy on calcium in the body of neonates [17].

Bahbah et al. (2015) measured the effect of phototherapy on serum calcium levels in neonates with jaundice. 50 neonates (25 girls and 25 boys) under phototherapy were enrolled. After examining the levels of calcium before and after phototherapy, it was concluded that phototherapy has a significant effect on the reduction of calcium levels in the icter neonates, and hypocalcemia is one of the complications of phototherapy [18].

**Research method**

This study was interventional and quasi-experimental. The newly born neonates of the term hospitalized to the Amirkola hospital of Babol after the first 72 hours of birth in 2018; who were selected for phototherapy in the neonatal department due to jaundice.

**Admission criteria**

Neonates born hospitalized due to neonatal icter after the third day of birth with total bilirubin more than 15 mg/dl, weight over 2500 grams, infant feeding only with breast milk and not receiving probiotic or vitamin A + D on day 5 on routine.

**Exit criteria**

ABO incompatibility, G6PD deficiency, sepsis, congenital malformation, neonate replacement, use of phenobarbital in mother and baby, mother with hypercalcemia or hypoxemia or hypo or hyperparathyroidism, symptomatic racism in mother, use of any drug containing calcium and vitamin D by the mother, bone marrow in the mother, bilirubin directly above 1 mg/dl, and heart-liver disease were excluded.

A total of 60 neonates with jaundice were enrolled. The neonates were healthy and physically free of hats or other hides. Neonatal characteristics including age, weight, gender and neonatal bilirubin levels were recorded in information forms. From these neonatal, 2 cc blood sample was taken before phototherapy, and then phototherapy was started on the basis of the internal protocol by a conventional phototherapy device (8 lamps manufactured by David Company, China 40 Watts, with light blue wavelengths of 410-470 nm) that were placed 20 cm from of the neonate's body, and blood samples were taken again 72 hours after the start of phototherapy. Sampling time was about two hours after breastfeeding. Then, 25-hydroxyvitamin D levels were measured at two sections before and after the intervention with a special 25-hydroxyvitamin D kit manufactured in Iran, by Ideal Company. The ratio of calcium to urine creatinine was measured before and after phototherapy in the laboratory of Amirkola Hospital.

**Table 1: Total bilirubin serum (mg/dl)**

| Gestational age | Phototherapy | Exchange of blood | | Interrupting phototherapy |
|---|---|---|---|---|
| | | *Without factor risk | With Factor Risk | |
| Term | 15 | 25 | 20 | 10 |

**Note:** Risk factors include sepsis, incompatibility of blood groups, G6PD deficiency, asphyxia, hemolysis, and hypopalbuminemia. These criteria are valid for after 72 hours.

Data were collected by a demographic questionnaire and serum levels of 25-hydroxyvitamin D and calcium and creatinine administration levels. Data was analyzed using SPSS V.24 software and Paired sample t tests were used. P value less than 0.05 was considered significant.

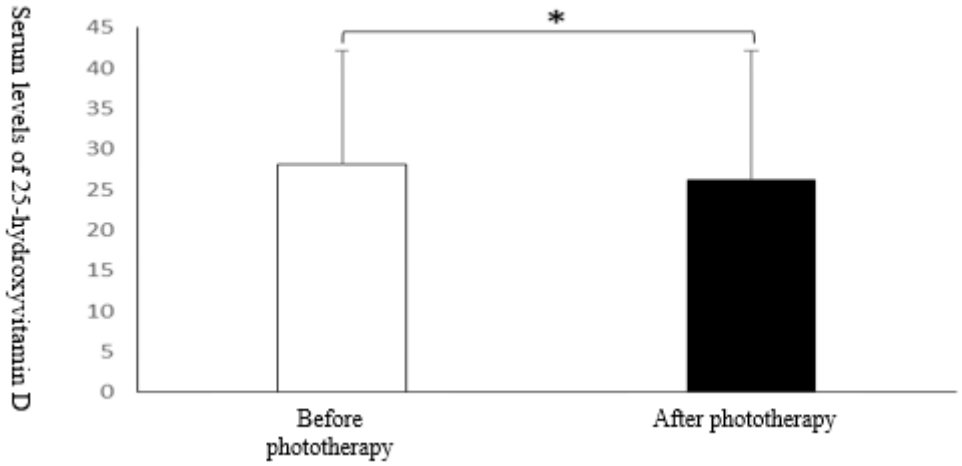
**Findings**

In this study, 60 neonates, 24 girls (40%) and 36 boys (60%) were treated with phototherapy with a mean ± SD of 1.24±4.88 days.

**Table 2: The serum levels of 25-hydroxyvitamin D and calcium to urine random creatinine ratios in icteric neonates (n = 60)**

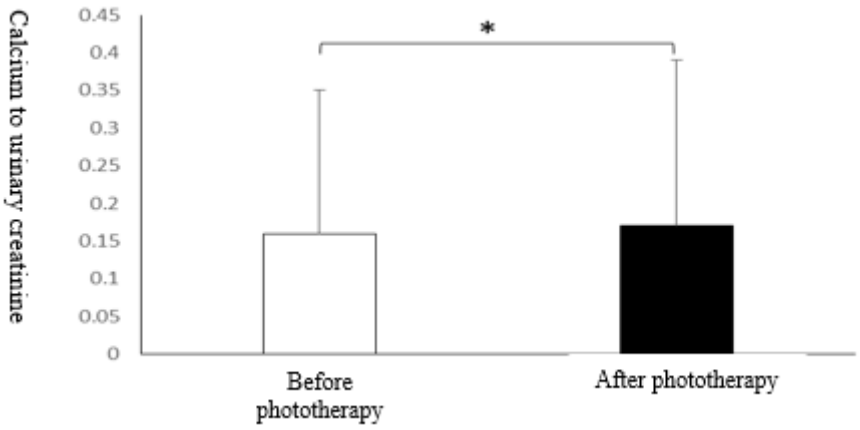
| Variable | Before phototherapy | After phototherapy | P value |
|---|---|---|---|
| Serum levels of 25-hydroxyvitamin D (ng/dl) | 14.07±28.12 | 15.98±26.17 | 0.03 |
| The ratio of calcium to urine creatinine | 0.17±0.16 | 0.22±0.17 | 0.03 |

The mean serum levels of 25-hydroxyvitamin D in neonates before and after phototherapy were 28.12 ng/dl and after phototherapy were 26.17 ng/dl, as well as the ratio of calcium to urinary creatinine in icteric neonates before phototherapy was 0.16 and after phototherapy was 0.17.




**Graph 1: Serum level of 25-hydroxyvitamin D in icteric neonates before and after phototherapy**

The results of this study showed that serum levels of 25-hydroxyvitamin D in the icteric neonates decreased significantly after phototherapy than before (P=0.03, t=2.17)




**Graph 2: The ratio of calcium to urine random creatinine in the icteric neonates before and after phototherapy**

The results of this study showed that the ratio of calcium to urine random creatinine in the icteric neonates after phototherapy was significantly higher than before (P=0.03, t=-2.26). In the study of calcium to urinary creatinine ratios with a 0.8-value as hypercalciuria, this ratio was more than 0.8 in one of the neonates after phototherapy treatment.

**Discussion**

The results of this study showed that phototherapy in hyperbilirubinemia in neonates caused a significant decrease in serum levels of 25-hydroxyvitamin D and a significant increase in calcium urinary excretion after phototherapy than before phototherapy. Hypocalcemia is one of the unusual consequences of phototherapy. The exact mechanism for the creation of hypocalcemia following phototherapy has not yet been determined [19].

The results of this study showed a significant reduction in serum levels of 25-hydroxyvitamin D in the icteric neonates after phototherapy than before phototherapy. Unlike the current study, Arikan et al. in 2017 did not see any significant changes in vitamin D levels in neonates receiving phototherapy [20]. Gillies et al. (1984) measured serum levels of 25-hydroxyvitamin D before and 48 hours after phototherapy in 33 neonates, and did not report any significant increase in 25-hydroxyvitamin D levels within 48 hours of phototherapy [21]. No significant change in the level of vitamin D reported in these two studies may be due to the small sample size of neonatal phototherapy (30 and 33 neonates, respectively) compared to the current study (60 neonates).

The results of this study showed that the ratio of calcium to urine random creatinine in the icteric neonates after phototherapy was significantly higher than before. Of course, considering the 0.8% for calcium to urinary creatinine ratio as hypercalciuria, only one of the neonates (1.66% of neonates) had hypercalciuria after phototherapy. Imani et al. In a study of 100 neonates with jaundice in Zahedan in this study, in this study, 53% of boys and 47% of girls reported a significant increase in urinary calcium to creatinine ratio 24 hours after phototherapy compared to before. None of the neonates studied before hypercholesterolemia phototherapy [22]. The results of this study were in line with the results of Gupta et al. (2018), which reported a significant increase in the ratio of calcium to creatinine after phototherapy in term neonates [23], but it contradicts the study of Hooman et al. (2009), which reported a ratio of calcium to urine creatinine greater than 0.8 in 52% of neonates in 48 hours after phototherapy [24].

Because the wavelength phototherapy device transmits beyond the visible spectrum and the optimal wavelength of vitamin D synthesis, it may produce a temporary effect in reducing the synthesis or even damage to vitamin D. Since calcium excretion in neonates is directly related to sodium urinary rejection, phototherapy may increase the urinary excretion of sodium, which has been done in some previous studies, which also causes hypercalciuria.

**Conclusion**

The results of this study showed that termed neonates undergoing phototherapy are at increased risk of elevated calcium excretion and decreased serum levels of 25-hydroxyvitamin D. It is suggested that further studies in this field be conducted with a control group that does not need phototherapy and also to measure serum levels of vitamin D and urinary calcium after phototherapy is discontinued.

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