

Effect of Phototherapy Treatment on Urinary Calcium Excretion in Neonates with Jaundice in Zahedan, Iran

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ABSTRACT

Background: One of the recognized symptoms of phototherapy in neonates is hypocalcemia and hypercalciuria, and its etiology has not been identified yet. The present study investigated the recurrence of hypercalciuria among neonates with jaundice treated with phototherapy.

Methods: This cross-sectional diagnostic examination was conducted on 100 newborns with jaundice treated with phototherapy in Ali-ibn-Abi-Talib hospital in Zahedan, Iran, during 2013 and 2014. In the present study, the subjects were collected in an accessible way after agreement and considering exclusion criteria. Calcium and creatinine (Ca/Cr) proportion in urinary tests of the neonates was estimated at the baseline and 24 h after the onset of phototherapy. The information was analyzed utilizing paired t-test.

Results: The mean of gestational age was 38.5 ± 2.5 weeks. Out of 100 cases, 53 newborns (53%) were male and 47 (47%) were female. The mean scores of birth weight was 2.52 ± 0.59 kg and neonatal serum bilirubin level was 16.5 ± 0.92 mg/dl. Ca/Cr ratios in neonates with jaundice were 0.28 ± 0.21 and 0.40 ± 0.34 before and after the phototherapy, respectively. Regarding that, the increase in Ca/Cr ratio was statistically significant ($P < 0.001$). Hypercalciuria was not observed in the neonates before the phototherapy; however, it was noticed in 13 neonates after the phototherapy. Ca/Cr ratios in neonates with hypercalciuria and other newborns were 1.16 ± 0.19 and 0.29 ± 0.18 , respectively. Furthermore, the difference between the two groups was statistically significant ($P < 0.001$).

Conclusion: Based on the results of this study, it was suggested that the neonates undergoing the phototherapy were at risk of hypercalciuria and the increased amount of urinary calcium excretion by means of phototherapy.

Keywords: Hypercalciuria, Jaundice, Phototherapy

Introduction

Jaundice in newborns occurs when the level of bilirubin rises to more than 5-6 mg/dl (80 - 103 mM/lit) (1). Jaundice is observed in 60% of term neonates and 80% of preterm newborns during the first seven days post-delivery (2). Expanded centralization of unconjugated bilirubin results in encephalopathy or neuropathy (1, 3).

All neonates demonstrate a few degrees of bilirubin level in their blood (i.e. more than 2 mg/dl); nonetheless, noticeable jaundice can be detected in only 50% of the term newborns, which is observed over 5 mg/dl. Jaundice prevalence in preterm neonates is reported as 80% that is much

higher compared to that in term infants (4).

Two essential remedial techniques, including blood transfusion and phototherapy, can be specified to prevent from unconjugated bilirubin encephalopathy. Due to different reactions of blood transfusion, the phototherapy technique is favored and considered the first-line treatment in term and preterm newborns with hemolytic or non-hemolytic jaundice. In spite of the symptoms, such as diarrhea, maculopapular rash, hyperthermia, lack of hydration, porphyria rash related with transient porphyria, and bronze baby syndrome, phototherapy is one of the most common types

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of therapy. Furthermore, it prevents neonatal unconjugated hyperbilirubinemia. Follow-up contemplates demonstrated any unfavorable outcomes in neonates undergoing phototherapy during the earliest stages of their lives (1).

Furthermore, phototherapy is effective on oxidation - anti oxidation system, and exposes newborns to oxidative stress (5, 6). A few investigations revealed that hypocalcemia occurs in term and preterm newborns in response to phototherapy. The presence of hypocalcemia in approximately 14% of the neonates undergoing phototherapy was reported in the examinations performed by Eghbalian and Karimifar (7, 8).

In another investigation, 90% of the preterm newborns and 75% of term neonates experienced hypocalcemia after phototherapy. Furthermore, a highlighted decrease in ionized calcium occurred in the two groups of patients (term and pre-term) compared with the control group (9). In a study conducted by Jain, predominance of hypocalcemia in preterm newborns was higher than that in term neonates. Moreover, common presence of hypocalcemia was straightforwardly linked with an increase in the level of bilirubin in the treatment standard (10).

A recent constrained study has demonstrated that phototherapy ought to be considered as a risk factor for hypocalcemia. In another study, it was discovered that phototherapy might prompt the reduction of melatonin. Therefore, glucocorticoid discharge decreased extensive calcium consumption from the bone and hypocalcemia (11, 12). Other investigations demonstrated that with the exposure of juvenile rats to white fluorescent, the centralization of calcium in their blood serum diminished (13).

Accordingly, the mentioned study was conducted on open-eyed rats, while the eyes of neonates were constantly closed during phototherapy. Consequently, it is difficult to increase the level of melatonin in these newborns. Calcidiol in no way reduce the hypocalcemia caused by phototherapy in preterm neonates. Subsequently, most likely Vitamin D did not play an important role in this type of Hypocalcemia (14).

Hypocalcemia is one of the regular neonatal metabolic disorders, which is linked to the aggregate with calcium below 2 mM/lit, 1.87 mM/lit, or 1.75 mM/lit. Nevertheless, a better definition for Hypocalcemia is presented below 1.1 mM/lit (4.4 mg/dl). Symptomatic or asymptomatic hypocalcaemia in newborns, similar to neonates of diabetic mothers, preterm newborns, or neonatal

asphyxia are often considered possible due to obscure reasons. From a clinical perspective, as the centralization of ionized calcium is remained inside a typical range, the potential danger of a physiological brokenness increases with the reduction in ionized calcium centralization (3).

In a study performed by Alizadeh-Taheri et al., 147 newborns with jaundice undergoing phototherapy, calcium serum level was diminished in 83 neonates (56%) (15). It is plausible that the incidence of hypocalcemia resulting from phototherapy is originated due to hypercalciuria. Hypercalciuria is characterized as the proportion of urinary calcium to creatinine level higher than 0.85 mg/dL (15).

Currently phototherapy is the best therapy for jaundice. In this regard, restricted examinations raised hypocalcemia as one of the phototherapy outcomes. Given the prevalence of hypocalcemia and hypomagnesemia in neonates, and the opposing consequences of a number of studies, the researchers of the present study investigated the incidence of hypercalciuria in newborns with jaundice experiencing phototherapy and neonates with jaundice not undergoing phototherapy.

Methods

This cross-sectional study was conducted on 100 healthy breastfed newborns with jaundice that were admitted to Ali-ibn-Abi-Talib hospital during 2014 and 2015.

Criteria

All healthy breastfed neonates with jaundice, including full-term neonates, weighed more than 2500 grams. The subjected newborns were fed by formula and completely examined at the time of admission. In addition, the exclusion criteria were the prescription of antibiotics, sepsis, neonatal asphyxia, respiratory distress, diabetic mothers, need for blood transfusion, observation of any pathological jaundice, effective phototherapy, serum therapy, and urinary tract infection.

Measurements

Serum bilirubin test was routinely performed on the study population. If indirect serum bilirubin levels of the neonates were higher than 16 to 18 mg/dl the newborns were admitted for continuous phototherapy in the Neonatal Ward of Ali-ibn-Abi-Talib Hospital. The gestational age was calculated based on the modified Ballard scoring. Weight measurements for the neonates were carried out by means of Mika weights scale (Japan) with the difference of 100 gr. The random

urinary calcium and creatinine samples of these neonates were measured at the baseline and 24 h after the onset of phototherapy. Urinary calcium was calculated by means of the spectrophotometric method and the creatinine was measured using Jaffe reaction method. The ratio of urinary calcium to creatinine was estimated. If the ratio was higher than 0.85 it was considered as hypercalciuria.

Data Analysis

The SPSS software (version 20.0) was utilized for all the statistical analyses. The results were calculated as mean±standard deviation and compared based on the paired t-test. The Chi-square test was applied for the qualitative measurements. P-value less than 0.05 was considered statistically significant.

Results

In this study, 100 newborns with jaundice were admitted to neonatal ward during 2014 to 2015, and then they were examined in terms of hypercalciuria. The mean gestational age of the neonates was 38.5±2.5 weeks. Out of all the case, 53 (53%) subjects were male and 47 (47%) were female (Table 1). In this study, the mean birth

weight and the neonatal serum bilirubin level were considered 2.52±0.59 kg and 16.5±0.92 mg/dl, respectively. Based on the findings it was indicated that the urinary calcium in newborns with jaundice treated by phototherapy was 2.9±3.5 mg/dl before phototherapy, which significantly increased to 5.1±5.9 after phototherapy (P<0.001).

Urinary creatine was 18.1±18.0 before phototherapy, which significantly increased to 25.8±23.7 after phototherapy. Calcium and creatinine (Ca/Cr) ratios in neonates with jaundice were 0.28±0.21 and 0.40±0.34 before and after phototherapy. In this regard, Ca/Cr ratio was increased as statistically significant (P<0.001) (Table 2). Urinary Ca/Cr ratio in all newborns was less than 0.85 before phototherapy, and it was considered to be in normal range. However, this ratio was higher than normal range after phototherapy in 13 newborns (Table 3).

Table 1. Demographic characteristics of research samples at baseline

Parameter	Mean±SD
Gestational age (week)	38.5±2.5
Weight (kg)	2.52±0.59
Serum bilirubin (mg/dl)	16.5±0.92
Gender (male/female)	53/47

Table 2. Comparison of calcium and creatinine ratio and urinary calcium and creatinine ratio in newborns before and after phototherapy

Variables	Before phototherapy	After phototherapy	P-value for test
	Mean±SD	Mean±SD	
Calcium	2.9±3.5	5.9±5.1	P<0.001
Creatinine	18.0±18.1	23.7±25.8	P<0.001
Calcium and creatinine	0.28±0.21	0.4±0.34	P<0.001

Table 3. Frequency distribution of the newborns after phototherapy in terms of calcium and creatinine

Calcium and Creatinine	Frequency	Percentage
Less than 0.85 (Normal Range)	87	87%
Equal to or higher than 0.85 (Hypercalciuria)	13	13%

Discussion

Hyperbilirubinemia is a typical neonatal issue and phototherapy is a viable and non-invasive technique for the reduction of neonatal bilirubin level. Normal results of phototherapy incorporate fecal incontinence, skin rash, hyperthermia, dehydration, DNA damage, shuddering attacks, optic damage, nasal congestion, and bronze baby syndrome. Hypocalcemia is one of the less regular consequences of phototherapy.

Some explorations have indicated a part of phototherapy, in which hypocalcemia is developed. Based on a comparative investigation carried out by Hooman et al., it was demonstrated

that the urinary calcium level in neonates with jaundice treated by phototherapy was considered higher than that before phototherapy (16). The mean of urinary creatinine was 18.1±18.0 preceding phototherapy, which increased to 25.8±23.7 after phototherapy.

Ehsanipoor and Karimifar reported the observation of hypocalcemia in newborns undergoing phototherapy as 15% and 7.8%, respectively (17, 8). Jain BK et al. indicated the presence of hypocalcemia in 30% of the term neonates 48 h after phototherapy (10). In a study carried out by Yadavs, 66.6% of hypocalcemia rate

was observed among term newborns (18). Additionally, Medhat revealed that hypocalcemia was noticed in 75% of the term neonates (19). In an investigation performed by Bahbah et al. 50 newborns with jaundice experienced phototherapy (20). Contrastively, 25 physiologic cases were reported with no need for phototherapy. Hypocalcemia was detected in 26% of the neonates 48 h after phototherapy.

Sethi demonstrated that more than 90% of preterm newborns and 75% of term neonates suffered from hypocalcemia following phototherapy (9). In another investigation, term newborns undergoing phototherapy were reported with bilirubin level higher than 15 mg/dL and they were compared with healthy newborns. Hypocalcemia was observed in 66.6% of the cases (21).

In the present investigation, the urinary Ca/Cr value in newborns with jaundice undergoing phototherapy was 0.4 ± 0.34 , which indicated a significant increase after phototherapy. Hypercalciuria was not observed in the neonates before phototherapy; however, it was noticed in some cases after phototherapy. In an investigation carried out by Hooman et al., 27 preterm newborns were compared with 23 term newborns. 6 percent before phototherapy, 52 % after onset of phototherapy, and 32.7 percent after end of phototherapy showed Hypercalciuria. The means of urinary Ca/Cr proportion before phototherapy, after the onset of phototherapy, and after phototherapy were 0.03, 0.85, and 0.60, respectively.

Hypercalciuria was mainly observed in preterm neonates. No significant relationship was noticed among hypercalciuria and age, sexual orientation, weight, bilirubin level, serum calcium, and urine osmolality. In the mentioned investigation, hypercalciuria was detected 48 h after phototherapy mostly in preterm newborns. Furthermore, 52% of the neonates demonstrated urinary Ca/Cr proportion higher than 0.85, which is in line with the findings of the present study (16).

Study limitation

The only limitation of this study was the lack of a suitable place for the subjects' parents to follow the interventions during phototherapy procedure. Accordingly, they were removed from the investigation.

Conclusion

It appears that the significance of periodical

increment in urinary calcium excretion in neonates undergoing phototherapy was related with the hydration of newborns during phototherapy, kidney ultrasound regarding kidney stones (particularly instances of phototherapy withdrawal or reused phototherapy), and consideration of bone thickness (particularly in preterm newborns). Based on the results, it is recommended to perform further studies on a larger population estimating PTH and vitamin D levels in newborns 24 h before and during phototherapy and kidney ultrasound.

Ethical consideration

The current article was adapted from a medical thesis (Code: 1433) at Medical School in University of Medical Sciences of Zahedan, Iran.

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Conflicts of interests

The authors declare that there is no conflict of interest.

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