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Effect of phototherapy on serum calcium levels in neonates receiving double surface LED phototherapy for neonatal jaundice

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Abstract

Background: To study the occurrence of hypocalcaemia in neonates with physiological unconjugated hyperbilirubinemia after 48 hours of phototherapy or at the end of phototherapy, in case duration of phototherapy was less than 48 hours.

Methods: This prospective study was conducted on 100 term neonates (61 males and 39 females) admitted to Neonatal intensive care unit of Shri B M Patil Medical College and Hospital, Vijayapura, Karnataka with unconjugated hyperbilirubinemia and requiring phototherapy. Total Serum bilirubin levels and serum calcium levels were checked before and after phototherapy. Neonates were assessed for clinical features of hypocalcemia i.e. jitteriness, irritability/excitability, lethargy and convulsions.

Results: After phototherapy, there was hypocalcemia in 35.0% neonates. The difference between pre and post phototherapy serum calcium levels were found to be statistically significant ($p < 0.001$). 2.86% of neonates developed jitteriness among those who had hypocalcemia. Hypocalcemia was more in subjects who received phototherapy for longer duration.

Conclusions: Hypocalcaemia is a common complication of phototherapy. Therefore, calcium supplementation should be done in all neonates undergoing phototherapy.

Keywords: hyperbilirubinemia, hypocalcemia, phototherapy, term neonates

Introduction

Neonatal jaundice is a common and benign problem in neonates. Jaundice is observed during first week of life in approximately 60% of term neonates and 80% of preterm neonates [1]. Untreated severe unconjugated hyperbilirubinemia is potentially neurotoxic.

Phototherapy is one of the routine method for management of hyperbilirubinemia. However, it is not a harmless intervention. It can produce adverse effects such as dehydration, temperature instability, skin rashes, loose stools, retinal damage, hypocalcemia, bronze baby syndrome, redistribution of blood flow and genotoxicity. It causes photo oxidation of bilirubin into water soluble or less lipophilic colorless form of bilirubin which is readily excreted in bile, feces and urine. Hypocalcemia is one of the lesser known adverse effects of phototherapy.

It is defined as total serum calcium concentration of $< 7 \text{ mg/dl}$ (1.75 mmol/L) in preterm and serum calcium $< 8 \text{ mg/dl}$ (2 mmol/L) in term neonates. It can cause serious complications like neuromuscular irritability, myoclonic jerks, jitteriness, convulsion, cyanosis, apnea and laryngospasm. 2 Cardiac manifestations like tachycardia, heart failure, prolonged QT interval and decreased contractility are also seen due to hypocalcemia [2].

Aims and objectives was to study the occurrence of hypocalcaemia in neonates with physiological unconjugated hyperbilirubinemia after 48 hours of phototherapy or at the end of phototherapy, in case duration of phototherapy is less than 48 hours.

Methods

This study was conducted in Neonatal Intensive Care Unit (Department of Pediatrics) at Shri B M Patil Medical College and Hospital, Vijayapura, Karnataka.

Study period: 1 year (june 2018 to May 2019)

Ethical approval for the study was obtained from the Institutional Ethical Review Committee.

It was Hospital based prospective study and 100 term neonates were enrolled.

Inclusion criteria

Full term neonates (37 completed weeks to 41 weeks) with unconjugated hyperbilirubinemia requiring phototherapy.

Exclusion criteria

Newborns

- To a diabetic mother
- With onset of jaundice within 24 hrs of age
- With perinatal asphyxia (Apgar <4 at 1 minute of birth)
- Whose mother had history of taking Anti- convulsants
- Fed with cow’s milk
- Who had exchange transfusion
- With jaundice lasting more than 14 days of life
- With sepsis
- With jaundice having hypocalcemia prior to the start of phototherapy
- Babies born with apparent major congenital anomalies
- ABO incompatibility.

Written & informed consent was taken from parents / guardians of all eligible subjects in their preferred language. Complete maternal history was taken and maternal risk factors like hypertension, diabetes mellitus, oligohydramnios, anaemia, epilepsy, fever, any rash, any drug intake during pregnancy other than iron and folic acid supplementation were ruled out. Complete history and physical examination was carried out in all neonates included in the study. Dermographic and clinical variables were recorded. It included birth weight, sex, gestational age, mode of delivery, time of appearance of icterus in hours, maternal blood group and Rh status, baby blood group and Rh status, anthropometric measurements (weight, length and head circumference) of infant at the time of admission and duration of phototherapy.

Total serum bilirubin (TSB), serum calcium, serum albumin, G6PD, Direct Coombs Test (DCT), Reticulocyte count and thyroid profile were sent in all cases. TSB and Serum calcium levels before and at the end of phototherapy were recorded. The first sample was considered as control. Hypocalcemia was considered as total serum calcium of <8mg/dl. Neonates were clinically assessed for features of hypocalcemia.

A conventional phototherapy equipment, containing four blue light fluorescent lamps with wavelengths of 410-470nm, was placed at a distance of 25-35cm from the skin surface of neonates under standard protocol with eyes and genitals completely covered. The irradiance during phototherapy was measured and maintained consistently at 15µW/cm2/nm at the level of infant’s skin.

Statistical analysis

Data were analysed using SPSS version 17 software. Descriptive statistical analysis was done and continuous variables were described as mean and standard deviation and categorical variables in number and percentage. Students paired t test and unpaired t test had been used to assess continuous variables for pair matched samples with 95% confidence limit. p value less than 0.001 was considered statistically significant.

Results

The study group included 100 neonates, 61 boys (61.0%) and 39 girls (39.0%), with mean gestational age of 38.16±0.95 weeks and mean birth weight of 2.66±0.33 kilograms. 57.0% neonates were delivered by normal vaginal delivery and 43.0% by lower segment caesarean section. Mean time of appearance of icterus and duration of phototherapy was 102.60±48.10 hours and 42.48±10.15 respectively (Table 1).

Table 1: Dermographic features of newborns.

Variable	Mean and number (%)
Gestational age (weeks)	38.16±0.95
Birth weight (kilograms)	2.66±0.33
Time of appearance of icterus (hours)	102.60±48.10
Duration of phototherapy (hours)	42.48±10.15
Type of delivery	
Normal vaginal delivery	57 (57.0%)
Lower segment caesarean section	43 (43.0%)

Mean total serum bilirubin levels before and at the end of phototherapy was 19.48±2.78mg/dl and 11.18±3.11mg/dl respectively. Mean serum calcium levels before phototherapy was 9.14±0.78mg/dl and it reduced to 8.53±0.77mg/dl after phototherapy. It was found that there was significant reduction (p<0.001) in mean total serum bilirubin and mean serum calcium levels after phototherapy as compared to pre phototherapy levels (Table2).

Table 2: Comparison between mean total serum bilirubin and serum calcium levels before and after receiving phototherapy.

Test	Admission time	After phototherapy	p-value
Total serum bilirubin (mg/dl)	19.48±2.78	11.18±3.11	0.000
Total serum calcium (mg/dl)	9.14±0.78	8.53±0.77	0.000

Serum calcium levels after phototherapy was >8mg/dl in 65.0% of subjects and hypocalcemia i.e. serum calcium levels <8mg/dl was noted in 35.0% of subjects (Table 3, Figure 1).

Table 3: Descriptive data of serum calcium levels post phototherapy.

Variable	N=100
Hypocalcemia (<8mg/dl)	35/100 (35.0%)
Normal calcium (>8md/dl)	65/100 (65.0%)

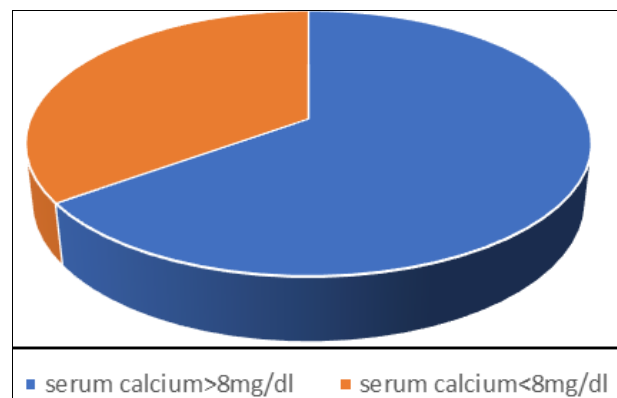


Fig 1: Incidence of hypocalcemia in term neonates after phototherapy.

Table 4: Descriptive data of symptoms among hypocalcemic cases post phototherapy.

Variable	N=35/100
Symptomatic (jitteriness)	1/100 (2.86%)
Asymptomatic	34/100 (97.14%)

Out of 35 subjects who had hypocalcemia, only one subject (2.86%) was symptomatic and developed jitteriness. Rest of the subjects (97.14%) were asymptomatic (Table 4). Also, incidence of hypocalcemia was more in neonates who received phototherapy for 48 hours (77.1%) as compared to neonates who received phototherapy for 24 hours (22.9%) (Table 5, Figure 2).

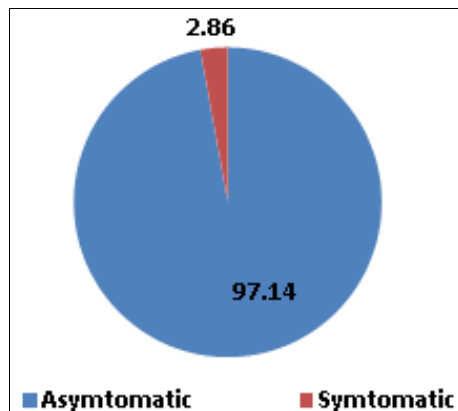


Fig 2: Incidence of symptomatic hypocalcemia.

Table 5: Incidence of hypocalcemia based on the duration of phototherapy.

	Hypocalcemia	Percentage
24 hours	8	22.9%
48 hours	27	77.1%
Total	35	100%

Discussion

Phototherapy is an appropriate and commonly used measure to reduce indirect bilirubin level in newborns. Romagnoli *et al.* was the first to suggest the association of hypocalcemia in newborn following phototherapy [3].

The mechanism of hypocalcemic effect of phototherapy was reported by inhibition of pineal gland via transcranial illumination, resulting in decline of melatonin secretion which blocks the effect of cortisol on bone calcium. Cortisol has a direct hypocalcemic effect and increases bone uptake of calcium and induces hypocalcemia [4].

In this study, there was a significant decrease in serum calcium levels after 48 hours of phototherapy ($p < 0.001$). The mean serum calcium in this study after phototherapy was 8.53 ± 0.77 mg/dl. This was in correlation with studies done by Bahbah *et al.* (8.58 ± 0.76) and Singh *et al.* (8.42 ± 1.19) [5, 6].

In an Iranian study, 7.5% neonates developed hypocalcemia after receiving phototherapy [7]. In our study, hypocalcemia was observed in 35.0% of neonates after phototherapy. Shrivastva *et al.*, also observed hypocalcemic effect of phototherapy in 30.0% of term neonates [8]. Sethi *et al.*, observed hypocalcemia in 75% of term neonates after phototherapy [9].

None of the hypocalcemic neonates were clinically symptomatic in studies by Tehrani *et al.* and Reddy *et al.* [7, 10]. In our study, symptomatic hypocalcemia was observed in

2.86% of neonates which was similar to studies by Yadav *et al.* and Sethi *et al.* who also observed symptomatic hypocalcemia in term neonates [11, 9]. Bahbah *et al.*, observed jitteriness in 14% and convulsions represented 10% of hypocalcemic cases [5].

In a study by Reddy *et al.*, the incidence of hypocalcemia was 18.8% when duration of phototherapy was >48 hours as compared to duration <48 hours (10.9%) [10]. Out of total 35 cases of hypocalcemia in our study, incidence of hypocalcemia was more in neonates who received phototherapy for 48 hours (77.1%) as compared to neonates who received phototherapy for 24 hours (22.9%).

Conclusion

Phototherapy induced hypocalcemia is a significant problem. Careful estimation of calcium status should be done before starting and during phototherapy for neonatal jaundice and close monitoring of neonates for signs of hypocalcemia should be done. Calcium supplementation can be considered as prophylaxis in neonates undergoing phototherapy.

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