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Research Article

EFFECT OF PHOTOTHERAPY ON SERUM CALCIUM AND MAGNESIUM LEVELS IN NEWBORNS WITH HYPERBILIRUBINEMIA ADMITTED TO NEONATAL INTENSIVE CARE AT A TERTIARY CARE TEACHING HOSPITAL IN THE KOLHAN REGION OF JHARKHAND

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ABSTRACT

Objectives: Neonatal jaundice is a medical condition causing yellowish skin discoloration, leading to hospital readmissions in the first 2 weeks of life. It affects 60% of full-term babies and 80% of premature infants. Severe jaundice can cause kernicterus and neurological damage. Treatment options include phototherapy, exchange transfusions, or pharmacological therapy. Phototherapy is the safest and most effective treatment, but it can lead to hypocalcemia and hypomagnesemia due to its effect on the pineal gland. The present study shows the effect of phototherapy on serum calcium and magnesium levels in hyperbilirubinemia.

Methods: A prospective observational study was conducted on 221 neonates with hyperbilirubinemia who were treated with phototherapy. We measured bilirubin, calcium, and magnesium levels in their blood samples at admission and 48 h after initiation of phototherapy. The data were analyzed using Epi-Info software.

Results: Before phototherapy, the mean serum calcium was 8.79±1.44, but it decreased significantly to 8.13±1.67 (p<0.05). Before phototherapy, the mean serum magnesium level was 3.22±0.72 and reduced considerably to 2.56±0.50 (p<0.05). After phototherapy, total serum bilirubin levels reduced dramatically (from 13.07±3.41 to 8.63±3.10) (p<0.05).

Conclusion: The present study shown that phototherapy has a significant effect on the levels of serum calcium, magnesium, and total serum bilirubin by reducing the level.

Keywords: Phototherapy, Hyperbilirubinemia, Calcium, Magnesium.

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INTRODUCTION

Neonatal jaundice is a clinical indication of increased total serum bilirubin, also known as neonatal hyperbilirubinemia, which results from bilirubin accumulation in an infant's skin. The defining traits of neonatal jaundice encompass yellowish pigmentation of the skin, sclerae, and mucous membranes. Neonatal hyperbilirubinemia is a common condition and in most cases, it is benign problem. It affects 60% of full-term babies and 80% of premature infants [1]. Severe hyperbilirubinemia can cause bilirubin encephalopathy (Kernicterus) leading to neurological problems [1]. Free bilirubin can cross the blood-brain barrier and get deposited in the membranes of neurons and glia, hurting mitochondria, stopping oxidative phosphorylation, and encouraging cell death. Bilirubin accumulation is mostly seen in the brain stem nucleus and basal ganglia. It affects axonal and dendritic growth in the central nervous system and can be caused by neonatal decreased conjugation ability of bilirubin [2-4]. Kernicterus is rare in healthy infants with a serum bilirubin level below 25 mg/dL [5]. Phototherapy is the safest and effective commonly used treatment option for neonatal jaundice.

Although the majority of cases do not require phototherapy, only nearly in 5–10% of cases phototherapy is needed. Phototherapy leads to some complications but potential complications are hypocalcemia and hypomagnesemia. It increases the risk of hypocalcemia due to its effect on the pineal gland by transcranial illumination. Magnesium plays a role in neuroprotection through an inhibitor of the N-methyl-D-aspartate receptor and it is one of the most important complex antagonist regulators of bilirubin molecule. Most of the changes are due to the displacement of magnesium between cells, leading to increased plasma levels of magnesium due to cellular degradation or defense mechanisms [6-8].

Hypocalcemia can cause a lot of problems, including irritability in the muscles, myoclonic jerks, jitteriness, seizures, cyanosis, apnea, laryngospasm, and heart problems such as tachycardia, heart failure, a longer QT interval, and less contractility. Recent research indicates that phototherapy may be a risk factor for hypocalcemia, despite the similar signs of disorders in magnesium and calcium [9].

Recent research in this area has mostly ignored the potential interplay between changes in calcium and magnesium blood levels, so the present study set out to fill that gap by studying how phototherapy affects serum calcium and magnesium levels with hyperbilirubinemia.

METHODS

This hospital-based prospective observational study was conducted from January 2022 to September 2023 (18 months) at the Neonatal Intensive Care Unit (NICU), Department of Pediatrics, Mahatma Gandhi Memorial Medical College Hospital in Jamshedpur, Jharkhand. The Institutional Ethics Committee of MGM Medical College, Jamshedpur, Jharkhand, approved this study with an ethical clearance number of IEC/05/21 (Reg.no: ECR/1621/Inst/JH/2021). We performed this before and after phototherapy study on 221 neonates suffering from hyperbilirubinemia.

After getting written informed consent from parents/caretakers, all babies fulfilling the inclusion criteria were enrolled in the study. A complete history and an appropriate physical examination were done in all selected cases. Birth weight and age in hours at the time of diagnosis of hyperbilirubinemia were noted.

We included all neonates with unconjugated hyperbilirubinemia who were admitted to the NICU and needed phototherapy as per American Academy of Pediatrics guidelines.

The study did not include newborns that had birth asphyxia, congenital abnormalities, women with diabetes and hypothyroidism, hemolytic anemia, newborns who needed exchange transfusions, ABO or Rhesus incompatibility, neonatal hypocalcemia, or newborns whose parents did not give consent.

We obtained the data in two distinct stages. Initially, we acquired the essential data through the bedhead ticket, examination, and interviews with the parents. We collected the individuals' laboratory data during the second phase, both before and 48 h after initiation of phototherapy treatment. We obtained blood samples before and after phototherapy to measure bilirubin, calcium, and magnesium levels using the photometric method.

To carry out phototherapy, the participants were positioned at a distance of 15–20 cm from the light source, which consisted of eight blue fluorescent bulbs emitting wavelengths ranging from 420 to 470 nm, positioned above their head and we ensured complete coverage of their eyes and genitals.

Blood samples were collected and serum total and direct bilirubin, serum calcium, and serum magnesium were tested with the fully automated biochemistry analyzer EM200 by Transasia Bio-Medicals Ltd. The Multi-Disciplinary Research Unit, MGM Medical College, Jamshedpur, performed all tests.

The normal range of serum calcium levels is 7.6–10.4 mg/dL, magnesium levels are 1.5–2.2 mg/dL, serum total bilirubin levels are 4–12 mg/dL, and serum direct bilirubin levels are 0–0.4 mg/dL. The normal range of tests was used as per the respective kit literature. All kits were used in ERBA Mannheim XL system packs.

The Epi-Info program was utilized for statistical data analysis, allowing for the reporting of descriptive data in terms of mean and frequencies and paired sample t-tests to examine serum calcium, magnesium, and bilirubin levels. A $p<0.05$ was considered statistically significant.

RESULTS

Sociodemographic characteristics of study participants

The study involved 221 newborns, with 110 males and 111 females. About 76.5% of the population was from rural areas, with 109 Hindus, 11.3% Muslims, and 35% from other religious communities. About 62.4% were non-tribal (Table 1).

Neonatal characteristics of study participants

The study found that 60% of babies were more than 37 weeks of gestational age with 61.5% having a birth weight below 2.5, and 57% were born through normal vaginal delivery. The neonates had a mean birth weight of 2.29±1.15 kg, a length of 48.92±3.46 cm, and a head circumference of 33.09±2.36 cm (Table 2).

Maternal characteristics of study participants

The majority of the mothers had received the tetanus vaccination. About 45% of mothers were within the age range of 18–22, 33% fell within the age range of 23–27, and 17% fell within the age range of 28–32 (Table 3).

Post-natal history of the study participants

In 129 (58.4%) cases, jaundice typically began between 48 and 72 h, and in 65 (29.4%) cases, it began between 24 and 48 h (Table 4).

Effects of phototherapy on serum bilirubin, calcium, and magnesium levels

Tables 5 and 6 display the mean values for both total and direct serum bilirubin. The total serum bilirubin level falls. The data presented in Tables 7 and 8 indicate a decline in serum calcium and magnesium levels following phototherapy. The study revealed significant differences ($p<0.05$) in mean values for total and direct bilirubin, calcium, and magnesium levels before and after the study.

Table 1: Sociodemographic characteristics (n=221)

Variables	n (%)
Gender	
Male	110 (49.8)
Female	111 (50.2)
Place of residence	
Urban	52 (23.5)
Rural	169 (76.5)
Religion	
Hindu	109 (49.3)
Muslim	25 (11.3)
Christian	8 (3.6)
Other	79 (35.7)
Community	
Tribal	83 (37.6)
Non-tribal	138 (62.4)
Age of neonates (in hours)	
24–48	81 (36.7)
49–72	67 (30.3)
73–96	40 (18.1)
97–120	22 (10.0)
121–144	11 (5.0)
Mean±SD	69.83±31.069

Table 2: Neonatal characteristics

Variables	n (%)
Gestational age	
>37 weeks	134 (60.6)
<37 weeks	87 (39.4)
Mode of delivery	
NVD	128 (57.9)
LSCS	93 (42.1)
Birth weight	
<2.5	136 (61.5)
>2.5	85 (38.5)
Weight (kg) (Mean±SD)	2.29±1.15
Length (cm) (Mean±SD)	48.92±3.46
Head circumference (Mean±SD)	33.09±2.36

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section

Table 3: Maternal characteristics

Variable	n (%)
Immunization with TT	
Yes	210 (95.0)
No	11 (5.0)
Mother age group	
18–22	101 (45.7)
23–27	73 (33.0)
28–32	39 (17.6)
>32	8 (3.6)

Table 4: Post-natal history

Variable	n (%)
Appearance of jaundice	
Within 24 h	2 (0.9)
After 24 h	25 (11.3)
24–48 h	65 (29.4)
48–72 h	129 (58.4)

Table 5: Total serum bilirubin levels before and after phototherapy

Before phototherapy (Mean±SD)	After phototherapy (Mean±SD)	Correlation	p-value
13.07±3.41524	8.63±3.10	0.625	0.000

p-considered significance at <0.05

Table 6: Bilirubin direct levels before and after phototherapy

Before phototherapy (Mean±SD)	After phototherapy (Mean±SD)	Correlation	p-value
0.34±0.10	0.21±0.08	0.451	0.000

p-considered significance at <0.05

Table 7: Calcium levels before and after phototherapy

Before phototherapy (Mean±SD)	After phototherapy (Mean±SD)	Correlation	p-value
8.79±1.44	8.13±1.67	0.578	0.000

p-considered significance at <0.05

Table 8: Magnesium levels before and after phototherapy

Before phototherapy (Mean±SD)	After phototherapy (Mean±SD)	Correlation	p-value
3.22±0.72	2.56±0.50	0.606	0.000

p-considered significance at <0.05

DISCUSSION

Phototherapy plays a significant role and is an effective method in the treatment and prevention of neonatal hyperbilirubinemia. The current study found that the mean age and birth weight of 221 neonates were 69.83±31.06 h and 2.29169±1.15 kg, respectively. The female-to-male ratio was 1:1. Most of the participants were resident of rural regions and 37.6% belonged to tribal communities.

About 111 (50.2%) were female and 110 (49.8%) were male. Kale *et al*. [10] and Rozario *et al*. [11] observed a similar gender ratio, while Goyal *et al*. [12] reported 61.0% male and 39.0% female.

Term neonates were 134 (60.6%) and preterm 87 (39.4%). Yeasmin *et al*. [13] and Kale *et al*. [10] observed the closest results reporting that 81.0% were term neonates and 19.0% were preterm neonates. Singh *et al*. [14] noted that 33% of the cases were preterm neonates while 67% were term neonates.

In this study, a significant percentage of newborns (136 or 61.5%) were in the low birth weight group, followed by 85 or 38.5%, who had a normal birth weight. 42.1% of newborns underwent a cesarean section, while 57.9% underwent a normal vaginal delivery. Goyal *et al*. [12] and Gupta *et al*. [15] reported similar findings, reporting 57.0% of neonates delivered by normal vaginal delivery and 43.0% by cesarean section.

Romagnoli *et al*. [16] suggested an association between hypocalcemia and phototherapy in premature newborns. Hakanson *et al*. [17] and Alizadeh-Taheri *et al*. [18] proposed that phototherapy suppresses the release of melatonin from the pineal gland, hence preventing cortisol from affecting calcium levels in the bones. Cortisol improves bone calcium absorption and causes a decrease in blood calcium levels, resulting in hypocalcemia.

The study found that total serum bilirubin levels in newborns dropped significantly before and after phototherapy. Specifically, mean bilirubin direct levels dropped significantly (p<0.05), which is similar to what Yeasmin *et al*. [13] found.

In this work, we found low level of calcium before and after phototherapy in neonatal hyperbilirubinemia. The mean calcium levels were 8.799±1.44 mg/dL pre-phototherapy and 8.133±1.67 mg/dL after phototherapy. There was a statistically significant difference ($p<0.05$). The study was conducted by Panneerselvam K. *et al.* [19], Rozario CI *et al.* [11], and Kale AV *et al.* [10]. Goyal S *et al.* [12] also reported a significant reduction in mean serum calcium levels in neonates both before and after phototherapy.

Following phototherapy, the calcium level dropped. Phototherapy duration is shorter in normal calcium patients than in hypocalcaemia. To prevent hypocalcaemia, oral calcium supplementation and head coverings are recommended to prevent light exposure and melatonin reduction [20, 21].

Serum magnesium levels decreased significantly following phototherapy, according to our findings. Phototherapy reduces serum magnesium levels due to increased plasma magnesium levels associated with hyperbilirubinemia. Since only 1% of the body's magnesium is extracellular, we attribute this decrease to bilirubin reduction. Increased bilirubin leads to higher plasma magnesium levels due to cellular degradation or defense mechanisms. Similar to our findings, the Eghbalian *et al*. [8] and Shahriarpanah *et al*. [22] studies found that phototherapy significantly lowered the total serum magnesium levels. A study by Sapkota [23] discovered a link between serum bilirubin levels and magnesium levels. This means that a rise in magnesium levels during hyperbilirubinemia may counteract the harmful effects of bilirubin.

CONCLUSION

The outcomes of the study showed that following phototherapy, serum levels of magnesium and calcium significantly decreased. By supplying magnesium supplements, this study may aid in preventing the hypoxic and neurotoxic effects of bilirubin.

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CONFLICT OF INTEREST

The authors assert that they do not possess any conflicts of interest.

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