ORIGINAL ARTICLE

Assessment serum calcium levels in neonates undergoing phototherapy for hyperbilirubinemia

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Received: 10-10-2023
Accepted: 15-12-2023

How to cite this article:
Manhas K, Rai PL, Sharma SK. Assessment Serum Calcium Levels in Neonates Undergoing Phototherapy for Hyperbilirubinemia. Int J Adv Integ Med Sci 2023;8(3)16-20.

Source of Support: Nil,
Conflicts of Interest: None declared.

Background: Neonatal hyperbilirubinemia is a common condition requiring phototherapy, which can affect serum electrolyte levels, particularly calcium. **Objective:** The study was to investigate changes in serum calcium levels in term babies undergoing phototherapy for neonatal hyperbilirubinemia and assess the risk of hypocalcaemia. **Materials and Methods:** Prospective interventional study conducted on 61 neonates with hyperbilirubinemia requiring phototherapy. Serum calcium levels were measured before and after phototherapy. **Results:** Hypocalcemia occurred in 57.38% of neonates, with a significant decrease in calcium levels after phototherapy. Pre-term neonates were more vulnerable to hypocalcemia. **Conclusion:** Phototherapy affects serum calcium levels, and hypocalcaemia is a common adverse effect. Monitoring calcium levels during phototherapy is crucial to prevent long-term complications.

KEY WORDS: hypocalcemia, neonatal hyperbilirubinemia, phototherapy, serum electrolyte levels, term babies

INTRODUCTION

Neonatal Jaundice (NJ), defined as an abnormally high concentration of bilirubin more than 85.mmol/l (5 mg/dL) in the circulating blood.[1] It affects about 60% of term and 80% of preterm infants,[2] usually occurs during 1st days of life. Newborn hyperbilirubinemia is the most common abnormal physical finding in the 1st week of life, affecting 60% of term and 80% of pre-term infants. It is characterized by yellowish discoloration of mucous membranes due to accumulated indirect bilirubin. While unconjugated hyperbilirubinemia is a normal physiological occurrence in most infants, severe jaundice develops in over two-thirds of newborns, making it a significant concern in the neonatal period.[3]

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Neonatal hyperbilirubinemia can have serious consequences if left untreated, including neurotoxicity, brain development complications, and increased risk of readmission to the hospital.[4] Premature infants are particularly at risk and require prompt medical intervention.[5] Phototherapy is a widely used approach to manage hyperbilirubinemia, converting bilirubin into water-soluble isomers for excretion without liver conjugation.[6] Its effectiveness depends on factors such as light source, distance, and initial bilirubin levels.[7] While phototherapy can reduce the need for exchange transfusion, it may also have adverse effects like hyperthermia, hypocalcemia, and skin rashes.[8] Despite these risks, the benefits of phototherapy outweigh its drawbacks, making it a crucial treatment option for neonatal hyperbilirubinemia.[9]

Numerous studies have investigated that the safety of phototherapy in managing neonatal hyperbilirubinemia, many have concentrated on its impact on serum electrolytes. Hypocalcemia is an anonymous adverse effect of phototherapy. Studies indicate that around 90% of preterm and 75 % of full-term neonates witness hypocalcemia after undergoing phototherapy.

This study examines changes in serum electrolyte levels in term babies undergoing phototherapy for jaundice, focusing on the potential risk of hypocalcemia. Phototherapy can affect calcium absorption, leading to increased release from bones and potentially causing complications. The study aims to inform interventions to prevent long-term complications in newborns.

MATERIALS AND METHODS

The present prospective interventional study was conducted at the Department of Paediatrics, Rohilkhand Medical College and Hospital in Bareilly, UP, over a period of 1 year, after obtaining clearance from the Board of Studies and Ethical Committee (NICU). The study aimed to investigate serum calcium levels in neonates undergoing phototherapy for neonatal hyperbilirubinemia. A total of 61 patients were selected using simple random sampling, and the study subjects were chosen based on specific inclusion and exclusion criteria. The inclusion criteria consisted of neonates diagnosed with neonatal hyperbilirubinemia requiring phototherapy and parents who consented to participate in the study. Exclusion criteria comprised of neonates who are sick with other diagnosis, neonates with congenital malformation and neonates with conjugated hyperbilirubinemia.

After approval from the Institutional Ethical Committee, all patients were selected as per inclusion and exclusion criteria. A detailed history, complete physical examination and routine and appropriate investigations were done for all newborns receiving phototherapy in the department of pediatrics. As soon as patient is clinically diagnosed with neonatal hyperbilirubinemia and admitted in NICU, sample for serum bilirubin along with serum calcium was sent before starting phototherapy Serum calcium levels was repeated after 24 h and 48 h of starting phototherapy Sample sent was then analysed for levels of total serum calcium by biochemistry department (automatic analyzer machine). If any time during the study hypocalcemia occurred in newborn then it was treated as per unit protocol Hypocalcemia is defined as total serum calcium of less than 7 mg/dL in preterm neonates and less than 8 mg/dl in term neonates.

The statistical analysis was conducted using the statistical software SPSS version 25.0, after the loading of the data into the Microsoft Excel spreadsheet. The numerical data were represented using the mean and standard deviation, while the categorical data were presented using the frequency and percentage of each group. The Chi-square test was used to analyze the frequency differences between the two groups. A $P = 0.05$ was considered statistically significant.

RESULTS

The majority of neonates treated for hyperbilirubinemia were aged 7–8 days (32.79%), with a slight female predominance (55.74%) observed in the cohort. Nearly half of the neonates (47.54%) were preterm, highlighting their vulnerability to hyperbilirubinemia. Most neonates had reassuring APGAR scores (50.82%), indicating favorable initial post-birth conditions. Additionally, a higher incidence of cesarean sections (55.74%) was noted, possibly reflecting medical intervention trends or underlying maternal/neonatal conditions. These findings provide valuable insights into the characteristics of neonates requiring phototherapy for hyperbilirubinemia (Table 1). Anthropometric measurements revealed consistent growth metrics, with a mean weight of 2.54 kg and mean length of 48.18 cm (Table 2). Among 61 neonates, 29 neonates were pre-term and 32 neonates were term, and mean serum calcium was 8.62 and 7.36 mg/dL, respectively (Table 3).

Table 4 outlines the incidence of hypocalcemia in a cohort of 61 neonates receiving phototherapy for hyperbilirubinemia, revealing that hypocalcemia is presented in 57.38% (35 neonates) of the cases. This majority indicates that more than half of the neonates developed low calcium levels during the course of phototherapy. In contrast, 42.62% (26 neonates) did not

Table 1: Describing the study groups as per variables

Variables	*N*	%
Age (in days)		
4–5 days	14	22.95
6–7 days	18	29.51
7–8 days	20	32.79
9–10 days	9	14.75
Gender		
Male	27	44.26
Female	34	55.74
Gestational age		
Preterm	29	47.54
Term	22	36.07
Postterm	10	16.39
Apgar score		
0–3 (low)	4	6.56
4–6 (moderately abnormal)	26	42.62
7–10 (reassuring)	31	50.82
Mode of delivery		
Lower segment cesarean section	34	55.74
Normal vaginal delivery	27	44.26
Total	61	100.0

Table 2: Describing the study groups as per anthropometric measurements

Anthropometric measurements	Mean	SD
Weight	2.54	0.399
Length	48.18	1.024

Table 3: Data distribution according to pre-term and term o

Newborns	No of newborn	Mean serum calcium
Pre-term	29	8.62
Term	32	7.36

experience hypocalcemia, indicating that the condition was absent or the calcium levels remained within normal limits for these individuals.

Significant reduction in bilirubin levels post-phototherapy, with mean levels decreasing from 14.23 mg/dL before treatment to 9.13 mg/dL at 48 h, affirming the effectiveness of phototherapy in managing hyperbilirubinemia. Initial mean bilirubin level of 14.23 mg/dL reduced to 9.13 mg/dL after 48 h of phototherapy (Table 5). A statistically significant decrease in calcium levels following phototherapy, with mean levels dropping from 9.43 mg/dL initially to 8.13 mg/dL at 48 h, suggesting an impact of phototherapy on serum calcium levels. Initial mean calcium level of 9.43 mg/dL decreased to 8.13 mg/dL after 48 h (Table 5). Serum calcium levels were affected in 13 neonates who received phototherapy for 24 h and in 48 neonates who received phototherapy for 48 h. The impact of duration of phototherapy on serum calcium levels was found to be significant ($P < 0.05$) (Table 6).

Around 50% of pre-term had decrease in serum calcium level and 2/3rd of term babies in the study showed decline in serum calcium level after phototherapy (Table 7).

DISCUSSION

Neonatal hyperbilirubinemia is the most common physical abnormality observed during the 1st week of life.[10] There is apprehension about releasing healthy full-term newborns early because of reports of brain damage caused by bilirubin, leading to long-term effects such as kernicterus (Maisals, 2006).[11] Early identification of hyperbilirubinemia in babies who are discharged from the hospital early is crucial. Hence, the present study aimed to investigate the effects of phototherapy on serum electrolyte levels, particularly calcium, in term babies with jaundice, and to identify the incidence of hypocalcemia, in order to inform preventive measures and interventions to minimize potential long-term complications.

Table 4: Describing the study groups as per hypocalcemia

Hypocalcemia	Frequency	Percentage
Present	35	57.38
Absent	26	42.62
Total	61	100

Table 5: Describing the study groups as per pattern of bilirubin level before and after phototherapy

	Mean	SD	*P*-value
Bilirubin level			
Before phototherapy	14.23	0.78	0.001
24 h after phototherapy	12.78	1.28	
48 h after phototherapy	9.13	1.18	
Calcium level			
Before phototherapy	9.43	0.83	0.014
24 h after phototherapy	9.16	1.04	
48 h after phototherapy	8.13	0.50	

Table 6: Duration of phototherapy

Duration of phototherapy (h)	No. of Neonates	Mean serum calcium level	*P*-value
24 h	13	8.64	0.002
48 h	48	7.23	0.014

The present study found that a majority of neonates (32.79%) were aged 7–8 days, with a slight female predominance (55.74%); consistent anthropometric measurements (mean weight 2.54 kg, mean length 48.18 cm); nearly half (47.54%) were pre-term; most had reassuring APGAR scores (50.82%); and a higher incidence of cesarean sections (55.74%). Phototherapy significantly reduced bilirubin levels (from 14.23 mg/dL to 9.13 mg/dL) but also decreased calcium levels (from 9.43 mg/dL to 8.13 mg/dL), with over half (57.38%) of neonates developing hypocalcemia post-phototherapy.

Most of the subjects fell within the age range of 1 week, and phototherapy was most frequently given during this period. About 46% of the study patients were in the age category of 7–8 days, which had the largest proportion. Karamifar *et al*.[12] discovered an approximate result indicating that the mean chronological age was5.69 (±2.6) days. However, Taheri *et al*.[13] identified a higher mean with a standard deviation of 6 (±3) days for chronological age.

This study of 61 neonates with hyperbilirubinemia revealed a slight female predominance, with 55.74% being female, contrasting with Rozario *et al.*'s[14] findings of a male majority. Anthropometric measurements were similar to those in Usharani M's (86) study. Notably, 47.54% of neonates were pre-term, 36.07% full-term, and 16.39% post-term. Apgar scores showed 6.56% required emergency attention, 42.62% were moderately abnormal, and 50.82% were reassuring, with no correlation observed as in Chandrashekar[15] study. Unlike Rozario *et al.*'s[14] findings, most neonates in this study were born via LSCS. Gestational age and delivery mode varied, with some similarities to Durga and Ravi Kumar[16] study, which found a mean gestational age of 37.96 weeks and a male-to-female ratio of 1.17:1. Overall, these findings highlight the importance of monitoring neonates with hyperbilirubinemia for potential complications.

The results of our study indicate a notable decrease in bilirubin concentrations in newborns following phototherapy, both at 24 and 48 h. The average bilirubin concentration was 14.23 mg/dL before phototherapy, decreased to 12.78 mg/dL after 24 h, and further decreased to 9.13 mg/dL by 48 h, demonstrating a consistent positive reaction to the phototherapy treatment. Bahbah *et al*.[17] discovered similar findings, with a mean total serum bilirubin level of 15.48 (±2.10) mg/dL before phototherapy, which reduced to 12.41 (±1.12) mg/dL after phototherapy.

Table 7: Effect of phototherapy on s. calcium

Effect of phototherapy on serum calcium	Frequency		Percentage
	Preterm	Term	
Decrease	16	22	62.2
Increase	13	10	37.8
Total	29	32	100

In our study, 61 newborns undergoing phototherapy for hyperbilirubinemia, 57.38% exhibited hypocalcemia, with more than half displaying reduced calcium levels, while 42.62% did not show hypocalcemia, indicating normal calcium levels.

In their groundbreaking study, Romagnoli *et al*. (1979)[18] were the first to propose a link between hypocalcemia and phototherapy in premature babies. Similarly, Hakanson and Bergstrom[19] recorded this observation in neonatal rats. There is a limited amount of research on the hypocalcemic effect of phototherapy, with studies conducted by Tan,[20] Sethi *et al*.,[21] and Hakanson and Bergstrom.[20] The table displays the fluctuations in calcium levels observed in newborns receiving phototherapy for hyperbilirubinemia. Prior to the administration of medication, the average value was 9.43 mg/dL, exhibiting a moderate level of variability. Following a period of 24 h, there was a modest drop to 9.16 mg/dL, accompanied by an increase in variability. After 48 h, the fall in levels was more pronounced, reaching 8.13 mg/dL, suggesting a more consistent reaction to phototherapy.

Sethi *et al*. (1990)[21] conducted a study on the impact of phototherapy on 20 full-term and 20 preterm infants with hyperbilirubinemia. Researchers noted that 75% of full-term and 90% of preterm newborns experienced hypocalcemia following phototherapy. In a similar manner, Medhat[22] found that 75% of full-term infants and 90% of preterm infants had hypocalcemia following phototherapy. The findings of the current investigation align with the aforementioned studies. Jain *et al*.[23] also found that phototherapy caused a decrease in calcium levels in 30% of full-term neonates and 55% of preterm neonates, which is a smaller percentage compared to the research stated above. In 2004, Hunter[24] proposed the hypothesis that phototherapy suppresses the release of melatonin from the pineal gland, hence preventing cortisol from affecting calcium levels in the bones. Unregulated cortisol has a direct impact on lowering calcium levels and enhances the absorption of calcium by bones.

In a study conducted by Ehsanipour *et al*. (2009),[25] the researchers examined the impact of phototherapy on icteric infants by evaluating the frequency of decreased serum calcium concentration. The results showed a significant reduction in serum calcium levels within 48 h after phototherapy compared to before treatment (P = 0.001). Furthermore, 82% of the infants experienced hypocalcemia 48 h after phototherapy. Eghbalian and Monsef[26] conducted a study in Hamedan on 63 full-term infants weighing above 2500 g. The study revealed that phototherapy might cause hypocalcemia, and it was seen that one of the children experienced sleep apnea as a result of hypocalcemia. Therefore, the administration of calcium prophylaxis was indicated for such situations.

In our study around 50% of preterm was found to have low calcium levels in serum and 2/3rd of term babies in study showed decrease in calcium levels in serum after phototherapy. Sethi *et al*. conducted a study to examine the effect of phototherapy on 20 full-term and 20 preterm infants with hyperbilirubinemia. Hypocalcaemia was detected in 75% of full-term infants and 90% of preterm neonates following phototherapy. In 2006, Medhat[22] found that 75% of full-term babies and 90% of preterm babies developed hypocalcemia after undergoing phototherapy. According to a study conducted by Jain,[27] there was a greater occurrence of low calcium levels in newborns with elevated levels of blood bilirubin. Furthermore, it is possible that this study focused on measuring total serum calcium rather than ionised calcium. Ionised calcium is the dynamic element that is regulated by the several physiological mechanism that is involved in maintaining calcium balance. The distribution of total calcium levels in serum, whether bound or free and ionized calcium, can be influenced by albumin and pH.

CONCLUSION

The findings illuminate several critical aspects of neonatal care, notably, the age of highest prevalence for phototherapy was within the 1st week of life, with a slight female predominance in hyperbilirubinemia cases. The gestational age distribution underscored the vulnerability of pre-term neonates to hyperbilirubinemia, constituting nearly half of the cohort. In addition, the study highlighted a significant reduction in bilirubin levels following phototherapy, validating the efficacy of this treatment modality in managing NJ. However, a noteworthy finding was the decrease in calcium levels post-phototherapy, leading to hypocalcemia in over half of the treated neonates, a complication necessitating awareness and monitoring. The mode of delivery, particularly the high rate of cesarean sections, further adds a layer of complexity to the neonatal hyperbilirubinemia management paradigm. These insights not only affirm the critical role of phototherapy in NJ treatment but also underscore the importance of vigilant post-therapeutic monitoring for potential complications such as hypocalcemia, guiding future therapeutic protocols and neonatal care strategies.

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