

Incidence of Hypocalcemia in term Hyperbilirubinemic Neonates Receiving Phototherapy

Prabakar S.¹, Arockia John I.², Somasekar R.³

¹Associate Professor, Department of Paediatrics, Madha Medical College and Research Institute, Chennai

²Assistant Professor, Department of Paediatrics, Nandha Medical College and Hospital, Erode

³Professor and HOD, Department of Paediatrics, Madha Medical College and Research Institute, Chennai

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Corresponding Author: Dr. Prabakar. S

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Abstract:

Background: Jaundice in newborns is one of the most prevalent clinical problems occurring in the neonatal period which requires medical attention. Phototherapy is the most commonly used treatment modality with its own complications. However, this treatment itself may result in hypocalcaemia which can create serious complications including convulsion and related conditions.

Objective: To determine the incidence of hypocalcemia in term hyper bilirubinemic neonates receiving phototherapy.

Materials and Methods: This study was performed on 198 term jaundiced neonates (113 females and 85 males) receiving phototherapy. These neonates had complete normal physical examination other than hyper bilirubinemia.

Results: Mean $\pm$ SD of serum calcium level significantly decreased from baseline values of 9.56 ± 0.8 mg/dl to 9.22 ± 0.83 mg/dl after 48-hour phototherapy. Overall, 15 neonates (7.5%) developed hypocalcaemia (calcium concentration less than 8mg/dl).

Conclusion: Although phototherapy lowers serum calcium level in term neonates, the incidence of phototherapy-associated hypocalcaemia is not too much.

Keywords: Hyperbilirubinemia, Neonates, Phototherapy, Hypocalcemia.

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Introduction

Neonatal jaundice is one of the most common clinical problems encountered during the first week of life affecting approximately 80% of preterm and 60% of term infants [1]. Pathophysiological basis of the jaundice is the same in preterm and term neonates, but premature babies are at a higher risk of developing hyperbilirubinemia. High bilirubin level may cause neurological damage even in term babies. Approximately 5-10% of them have clinically significant hyperbilirubinemia. Phototherapy plays a significant role in the treatment and prevention of hyperbilirubinemia in neonates. Phototherapy may also lead to undesirable side effects such as skin rash, diarrhea, hyperthermia, chills, trauma to the eye, nasal obstruction and DNA damage. Bronze baby syndrome is common in babies with conjugated hyperbilirubinemia undergoing phototherapy [2]. In most of the neonates no intervention is required however, 5-10% of the cases have clinically significant jaundice, which requires treatment [3,4] High level of unconjugated bilirubin may cause permanent neurological damage [5,6]. No

change in blood ions/metabolites has been reported in neonates receiving phototherapy except for calcium concentration. A drop in serum calcium has been noticed in patients undergoing phototherapy [7]. Blood coagulation, cell membrane integrity and function, cellular enzymatic activity and neuromuscular excitability are the important functions of ionized calcium. The underlying mechanism for phototherapy induced hypocalcaemia although not yet well understood, but it seems that hypocalcaemia is accompanied by a decrease in serum melatonin concentration which in turn is regulated by the pineal gland. Pineal gland in normal humans however, is shown to be influenced by the diurnal light-dark cycle [8]. There are some reports on the hypocalcaemic effect of phototherapy especially in preterm neonates. There are still few studies of newborns. The aim of this study was to assess the incidence of phototherapy induced hypocalcaemia among term neonates.

Materials and Methods

This study was performed on 198 healthy term babies of over 2500 grams of weight. These neonates were admitted in Madha Medical College and Research Institute, Chennai during January 2023 to June 2024. Neonates who were at risk of hypocalcaemia such as neonatal asphyxia, respiratory distress, sepsis, infant of diabetic mother and maternal consumption of anticonvulsant were excluded. Excluded were also premature newborns, those who had exchange transfusion or parenteral nutritional therapy. Serum calcium and bilirubin levels were measured on arrival and 48 hours after receiving phototherapy. Serum calcium level was measured in our hospital laboratory using the same method for all cases. Hypocalcaemia was considered as total serum calcium of < 8 mg/dL.

Statistical Analysis: Data were analyzed and assessed for normality using SPSS version 24. Descriptive data are presented as mean $\pm$ SD or percentage. We used student's *t* – test to compare

means. A value less than 0.05 was considered significant.

Results

The study population were 198 term neonates (113 females, 85 males), with the mean chronological age and weight of 6.14 ± 2.81 days and 3126 ± 477 grams, respectively. 63.1% of neonates had normal vaginal delivery and 36.9% delivered by cesarean section. Mean $\pm$ SD of serum bilirubin level was 16.59 ± 2.24 mg/dl at admission and 14.76 ± 2.51 after receiving 48-hour phototherapy ($p < 0.001$). Mean $\pm$ SD of serum calcium level significantly decreased from baseline values of 9.56 ± 0.8 mg/dl to 9.22 ± 0.83 mg/dl after 48-hour phototherapy. Overall, 15 neonates (7.5%) developed hypocalcaemia (calcium concentration less than 8mg/dl). There was a significant difference between serum calcium level before and after phototherapy ($p < 0.03$). Fortunately, none of the hypocalcemic neonates were clinically symptomatic.

Table 1: Demographic features of the newborns

Variable(N=198)	Mean & Number (percentage)
Sex (female/male) (%)	113/85 (57.1%/42.9%)
Age at sampling (days)	6.14 ± 2.81
Age at the onset of hyperbilirubinemia (days)	3.67 ± 1.81
Weight at sampling (grams)	3126 ± 477
Type of delivery NVD (%), C/S (%)	125 (63.1%) ,73 (36.9%)

Table 2: Laboratory changes before and after receiving phototherapy

Test	Admission time	After 48 hours	p-value
Total bilirubin level (mg/dl)	16.59 ± 2.24	14.76 ± 2.51	0.001
Total calcium level (mg/dl)	9.56 ± 0.8	9.22 ± 0.83	0.03

Discussion

The regulation of calcium homeostasis in the newborn period has been of considerable interest. At birth, cord blood plasma calcium level exceeds that in maternal blood. The plasma calcium level decreases progressively during the early days of life in normal infants, so by the second or third day of life, the level is lower than that found in older infants and children. In almost all normal full-term infants it returns to normal by 10 days of life [9]. Phototherapy is an appropriate and safe measure to reduce indirect bilirubin level in newborns. Romagnoli et al was the first to suggest the association of hypocalcaemia in newborn following phototherapy [10]. The mechanism of hypocalcaemic effect of phototherapy was reported. It is by inhibiting pineal gland (via transcranial illumination) resulting in decline of melatonin secretion; which in turn blocks the effect of cortisol on bone calcium. Cortisol has a direct hypocalcemic effect and increases bone uptake of calcium and induces hypocalcemia [8]. In our term neonatal study population, after receiving 48 hours of

phototherapy a significant decrease in serum calcium was observed ($p < 0.03$). However, only 15 neonates (7.5%) developed hypocalcaemia below the acceptable threshold after 48 hours of phototherapy. Nevertheless, none of our newborns had symptomatic hypocalcaemia. In an Iranian study done by Alizade only 7% newborns (4.2% females, 10.4% males) developed hypocalcaemia after 48 hours of phototherapy [11]. Ehsanipoor et al [12] and Karamifar et al [13] reported 15% and 8.7% hypocalcaemia respectively in newborns receiving phototherapy. However, the reported prevalence of hypocalcaemia in other countries was more than Iranian newborn reports. Jain et al [14] reported 66% and Yadav [15] also observed hypocalcaemic effect of phototherapy in 30% term and 55% preterm neonates. Sethi et al have studied the effect of phototherapy in 20 term and 20 preterm jaundiced neonates. They observed hypocalcaemia in 90% of preterm and 75% of term neonates after phototherapy [16]. Similarly, in 2006, Medhat from Cairo University observed 90% of preterm and 75% of term developed hypocalcaemia after phototherapy [17]. Observation of the present study

and Iranian study is much lower than the above-mentioned studies from other countries. The reason for this difference is not clearly understood. However, serum vitamin D, bilirubin levels and also the patient's skin color may play a role. In a study done by Jain, the prevalence of hypocalcaemia was higher in newborns with higher concentration of serum bilirubin [18]. In addition, it might also be due to the fact that this study examined total serum calcium and not ionized calcium. Ionized calcium is the active component which is kept under control by the various physiological mechanisms involved in calcium homeostasis. Some reports recommend prescription of calcium to prevent early onset hypocalcaemia in premature newborns. Other similar advices are also observed in studies with sick infants of diabetic mothers and those with severe asphyxia [19]. In conclusion, although phototherapy induces hypocalcaemia in term infants, the incidence of phototherapy associated hypocalcaemia is not too high. So, routine measurement of serum calcium level is not recommended in newborn infants.

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