



## INCIDENCE OF PHOTOTHERAPY INDUCED HYPOCALCEMIA IN FULL TERM NORMAL NEWBORN

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### ABSTRACT

**Background:** Neonatal hyperbilirubinemia is one of the most prevalent clinical problem occurring in the neonatal period. Phototherapy is the most commonly used treatment modality with its inherent complications. However, this treatment modality itself may result in hypocalcaemia and create serious complications including convulsion and related conditions.

**Objective:** To determine the effect of phototherapy on serum calcium level in full-term hyper bilirubinemic neonates.

**Materials and Methods:** This study was performed on 198 full-term jaundiced neonates (113 females and 85 males) receiving phototherapy. These neonates had complete normal physical examination other than hyper bilirubinemia. Plasma bilirubin and calcium levels were determined before and after 48 hours of phototherapy.

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

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## INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common clinical problem observed 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 undesired side effects including 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). Nonetheless, no change in blood ions/metabolites has been reported except for calcium concentration; a drop in serum calcium has been noticed in patients undergoing phototherapy (3). 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 in turn is regulated by the pineal gland. Pineal gland in normal human however, is shown to be influenced by the diurnal light-dark cycle (4). There are some reports on hypocalcaemic effect of phototherapy especially in preterm neonates. There are still few studies on hypocalcaemic effect of phototherapy on the term newborns. Then, the aim of this study was to assess the prevalence of phototherapy induced hypocalcaemia among term neonates.

## METHODS AND SUBJECTS

This study was a cross-sectional study performed on 198 healthy term babies of over 2500 gram of weight. These neonates were admitted to the neonatal ward of Rajah Muthiah Medical College, hospital, Chidambaram from January to December 2016 because of indirect hyperbilirubinemia who were managed with phototherapy. 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

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bilirubin levels were measured on arrival and 48 hours after receiving phototherapy. Serum calcium level was measured in or hospital laboratory using the same method for all cases. Hypocalcaemia was considered as total serum calcium of  $< 8$  mg/dL. The study was approved by Ethics Committee of Annamalai University of Medical Sciences.

### Statistical analysis

Data were analyzed and assessed for normality using SPSS version 18. 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 were considered significant.

## RESULTS

The study populations were 198 term neonates (113 females, 85 males), with the mean chronological age and weight of  $6.14 \pm 2.81$  days and  $3126 \pm 477$  grams, respectively. 22.2% of neonates had normal vaginal delivery and 77.8% delivered by cesarean section. Mean  $\pm$  SD of serum bilirubin level was  $16.59 \pm 2.24$  mg/dl at admission and  $14.76 \pm 2.51$  after receiving 48-hour phototherapy ( $p < 0.001$ ). Mean  $\pm$  SD of serum calcium level significantly decreased from baseline values of  $9.56 \pm 0.8$  mg/dl to  $9.22 \pm 0.83$  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 hypocalcaemic neonates were clinically symptomatic.

**Table 1** Demographic features of the newborns

variable	Mean & Number (percentage)
N=198	
Sex (female/male)(%)	113/85 (57.1%/42.9%)
Age at sampling (day)	6.14 $\pm$ 2.81
Age at the onset of hyperbilirubinemia (day)	3.67 $\pm$ 1.81
Weight at sampling (gram)	3126 $\pm$ 477
Type of delivery NVD (%) C/S (%)	44 (22.2%) 154 (77.8%)

**Table 2** Laboratory changes before and after receiving phototherapy

Test	Admission time	After 48 hours	p-value
Total bilirubin level (mg/dl)	16.59 $\pm$ 2.24	14.76 $\pm$ 2.51	0.001
Total calcium level (mg/dl)	9.56 $\pm$ 0.8	9.22 $\pm$ 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 Ca 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 (5). Phototherapy is an appropriate and safe measure to reduce indirect bilirubin level in newborns. Roming *et al* was the first to suggest the association of hypocalcaemia in newborn following phototherapy (6). 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 hypocalcaemia (4). In our term neonatal study population 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, between 7% - 15% of term newborn receiving phototherapy developed hypocalcaemia. In an study done by Alizade only 7% newborns (4.2% females, 10.4% males) developing hypocalcaemia after 48 hours of phototherapy (7). Karamifar *et al* (8) and Ehsanipoor *et al* (9) reported 8.7% and 15% hypocalcaemia respectively in newborns receiving phototherapy. However the reported prevalence of hypocalcaemia in other countries was more than Iranian newborn reports. Jain *et al* (10) reported 66% and Yadav (11) also observed hypocalcaemic effect of phototherapy in 30% term and 55% preterm neonates. Sethi *et al* has 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 (12). Similarly, in 2006, Medhat from Cairo University observed 90% of preterm and 75% of term developed hypocalcaemia after phototherapy (13). Observation of the present study and an 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, the type of fluorescent tube, bilirubin levels and also the patient's skin color may play a role. Muta *et al* reported a significant difference in the serum 25(OH) vitamin D levels between newborns suffering from hyperbilirubinemia and control groups (14). In a study done by Jain, the prevalence of hypocalcaemia was higher in newborns with higher concentration of serum bilirubin (15). 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. pH and albumin may influence the distribution of total serum calcium level, either bound or free and ionized calcium. Then, it can be considered one of the limitations of our study. These findings justify further prospective studies in infants that would include concurrent measurements of ionized calcium and serum 25 (OH) vitamin D. Some reports recommend prescription of calcium to prevent early onset hypocalcaemia in premature newborns. Other similar advices are observed in sick infants of diabetic mothers and those with severe asphyxia (16). In conclusion, although phototherapy induces hypocalcaemia in term infants, but the incidence of phototherapy associated hypocalcaemia is not too high. So, routine measurement of serum calcium level is not recommended in newborn infants. It is done when normal full term newborns on phototherapy showed symptoms of hypocalcaemia.

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