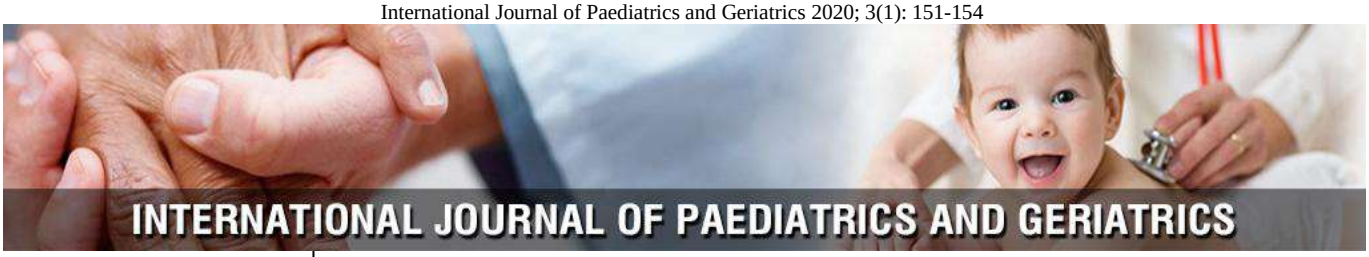

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Association between phototherapy and serum calcium levels in newborns: A institutional cross-sectional study

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Abstract
Introduction: Hyperbilirubinemia is one of the most prevalent problems in neonates. Phototherapy is one of the routine methods for management of hyperbilirubinemia.
AIM: The aim of this study is to evaluate significant change in serum calcium level in term newborns who are undergoing phototherapy and to find out the association between effect of phototherapy on serum calcium levels in newborns.
Methods: 60 newborns with neonatal hyperbilirubinemia admitted in newborn nursery were selected for the study. Serum calcium estimation was done before phototherapy. All newborns were subjected to double surface phototherapy. After 48 hours of phototherapy serum calcium was estimated and compared with earlier value.
Results: Mean serum bilirubin level and mean serum calcium levels before phototherapy were 15.2 ± 1.25 mg/dl and 9.2 ± 1.2 mg/dl respectively. While after phototherapy we observed that mean serum bilirubin level and mean serum calcium levels were 11.2 ± 2.6 mg/dl and 8.11 ± 0.54 mg/dl respectively. The difference of these before and after phototherapy were also found to be statistically significant (p= <0.05). 37 (61.6%) of newborns had a decrease in serum calcium level from the initial value while only 9 (15%) newborns (5% females, 4% males) developed hypocalcemia after 48 hours of phototherapy.
Conclusion: The level of mean serum calcium showed a significant decline after phototherapy. This shows that hypocalcemia is one of the major complications of phototherapy. The frequency of hypocalcemia is increased with increased duration of phototherapy.

Keywords: Hyperbilirubinemia, Jaundice, Hypocalcemia, Phototherapy, newborns

Introduction

Neonatal jaundice / Hyperbilirubinemia is one of the commonest issues affecting newborns. It is observed in up to 60% of term infants and 80% of preterm infants [1]. In most of the babies, there is no underlying disease, and this early jaundice (termed as physiological jaundice) is generally harmless. However, pathological jaundice may coexist with physiological jaundice. When severe jaundice goes untreated for too long, it can lead to kernicterus. With manifestations of convulsions & sonologically seen deposition of bilirubin in basal ganglia leads to athetoid cerebral palsy and hearing loss [2, 3]. Therefore no intervention is required in most cases but 5-10 % of them have significant hyperbilirubinemia and use of phototherapy becomes mandatory.

Phototherapy plays a significant role in the treatment and prevention of hyperbilirubinemia in neonates. This relatively common therapy lowers the serum bilirubin level by transforming bilirubin into water-soluble isomers that can be eliminated without conjugation in the liver [4]. To make the phototherapy more effective, double surface intensive phototherapy must be used in neonatal jaundice care. The American Academy of Pediatrics (AAP) defines intensive phototherapy as a spectral irradiance of at least 30 μW/cm^2/nm over the relevant bandwidth. Besides useful effect, some complications such as diarrhea, skin rash, excessive irritability, hyperthermia, DNA damage, and hypocalcemia are seen with phototherapy treatment [5, 6].

Hypocalcemia is one of the lesser known but potential adverse effect of phototherapy. Neonatal hypocalcemia is defined as total serum calcium concentration of <7 mg/dl or ionised calcium concentration of <4 mg/dl. Ramagnoli *et al* for the first time suggested the association of hypocalcemia with phototherapy in preterm newborns [7].

There are several theories to explain the effect of phototherapy on calcium metabolism. Phototherapy decreases melatonin level and corticosterone secretion. Melatonin stimulates secretion of corticosterone, which decreases calcium absorption by bones. Phototherapy leads to inhibition of pineal gland via transcranial illumination, resulting in a decline in melatonin level and, as a result, hypocalcemia develops [8]. As hypocalcemia is accompanied by a decrease in serum melatonin concentration, this effect can be prevented by shielding the occiput [9].

From previous studies it was shown that there is significant hypocalcemia in babies undergoing phototherapy even though there is some difference in prevalence in different studies. This present study was undertaken to evaluate significant change in serum calcium level in term newborns who are undergoing phototherapy and to find out the association between effects of phototherapy on serum calcium levels in newborns.

Material and Methods

This cross-sectional study was conducted in Dept. of Pediatrics. The study was approved by the institutional research committee and the ethical committee.

This study was conducted on 60 full-term neonates with jaundice, who received phototherapy for treatment of neonatal indirect hyperbilirubinemia (exaggerated physiological jaundice). We excluded any neonates suffering from birth asphyxia, congenital malformation, septicemia, and hypothyroidism, infant of diabetic mother, hemolytic anemia, any newborn needing exchange transfusion, neonatal hypocalcemia, or ABO or Rh incompatibility. The neonates (n=25) in the control group were babies who had physiological neonatal jaundice managed without phototherapy or exchange transfusion.

After getting written consent from one of the parents, all babies fullfilling the inclusion criteria were enrolled in the study. Complete history and appropriate physical examination was done in all selected cases. Laboratory investigations were applied while taking blood for routine investigations, serum calcium estimation was also done before phototherapy.

All newborns were subjected to double surface phototherapy using blue light 420-470 nm (Phoenix medical systems photo therapy unit of 46 w). The babies were monitored for any symptoms of hypocalcemia during phototherapy. After 48 hours of phototherapy along with serum bilirubin, serum calcium was also estimated and compared with earlier value to find out any significant difference in serum calcium value. Serum calcium value of <7mg/dl was considered as hypocalcemia.

Thereafter, all data were tabulated and analyzed statistically to detect hypocalcemia as a complication of phototherapy. Those babies who developed hypocalcemia were supplemented with oral calcium and their serum calcium was rechecked after 24 hrs of discontinuation of phototherapy.

Statistical Analysis

Data were analyzed using computer software, Statistical Package for the Social Sciences. Data were expressed in frequency and percentage as well as mean and standard deviation (SD). To elucidate the associations and comparisons between different parameters, the Chi-square test was used. Paired Student's t-test was used to compare mean values. P <0.05 was considered statistically significant.

Results

In our study, a total of 60 newborns were included out of which 30 were males (50%) and 30 females (50%). The mean gestational age of the study population was 38.12 ± 0.68 weeks and mean postnatal age was 3.82 ± 1.24 days. The mean birth weight of the study population cam to be was 2.41±0.18 kg. 39 newborns were born via normal vaginal delivery and 21 via cesarean section.

The serum bilirubin level among neonates of the study group was 15.2 ± 1.25 mg/dl, whereas the serum bilirubin level among the neonates of the control group was 5.9 ± 0.21 mg/dl. This difference was statistical significant between both studied groups regarding total serum bilirubin level ($P < 0.05$).

The serum calcium level of neonates in study group before phototherapy was 9.2 ± 1.2 mg/dl while that of control group was 9.0 ± 0.8 mg/dl. There was no statistical significant difference between both studied groups regarding total serum calcium level on arrival ($P > 0.05$).

Table 1: comparison between case ad controls in relation to total serum bilirubin levels and serum calcium before phototherapy

Variables	Study group	Control group	P value
Total serum bilirubin	15.2 ± 1.25 mg/dl	5.9 ± 0.21 mg/dl	P<0.05
Serum calcium	9.2 ± 1.2 mg/dl	9.0 ± 0.8 mg/dl	p>0.05

After phototherapy, within study group, the mean serum bilirubin level before phototherapy was 15.2 ± 1.25 mg/dl, whereas the mean serum bilirubin level after phototherapy as recorded was 11.2 ± 2.6 mg/dl. The decrease in mean values of the serum bilirubin levels after phototherapy, as compared with serum bilirubin levels before phototherapy in the study group was found to be statistically significant ($P < 0.05$)

The mean serum calcium level of neonates in study group after phototherapy was 8.11 ± 0.54 mg/dl. There was reduction in serum calcium level after phototherapy and the difference of these before and after phototherapy was found to be statistically significant (p value <0.05)

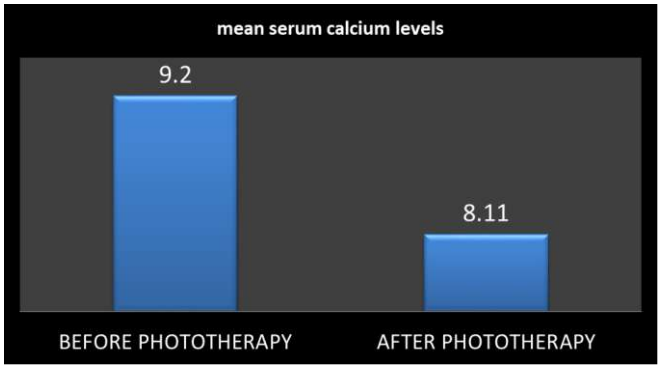

Fig 1: Mean Serum Calcium Level of Neonates Before and After Phototherapy within Study Group

After phototherapy we observed that about 37 (61.6%) of newborns had a decrease in serum calcium level from the initial value. Only 9 (15%) newborns (5% females, 4% males) developed hypocalcemia after 48 hours of phototherapy. The maximum patients had serum calcium level in the range of 7.50–7.82 mg/ dl.

Table 2: Distribution of Cases Based on Severity of Hyocalcemia

Severity of hypocalcemia	Frequency (N=9)	Percentage
Mild Hypocalcemia (8-7.5 mg/dl)	6	66.6%
Severe Hypocalcemia (<7.5 mg/dl)	3	33.3%

No significant association was found between reduction in serum calcium value and other parameters like age of onset of jaundice, birth weight and type of feeding.

Discussion

Neonatal jaundice is one of the leading causes of NICU admission. One of the known side effects of phototherapy is hypocalcaemia since Romagnoli first suggested the association of hypocalcaemia and phototherapy in preterms [7].

In the present study, the study group study group included 60 neonates, 30 boys (50%) and 30 girls (50%) with mean serum bilirubin level and mean serum calcium levels before phototherapy were 15.2 ± 1.25 mg/dl and 9.2 ± 1.2 mg/dl respectively. While after phototherapy we observed that mean serum bilirubin level and mean serum calcium levels were 11.2 ± 2.6 mg/dl and 8.11 ± 0.54 mg/dl respectively. The difference of these before and after phototherapy were also found to be statistically significant (p= <0.05).

After phototherapy we observed that about 37 (61.6%) of newborns had a decrease in serum calcium level from the initial value. Only 9 (15%) newborns (5% females, 4% males) developed hypocalcemia after 48 hours of phototherapy. The maximum patients had serum calcium level in the range of 7.50–7.82 mg/ dl.

Our results are in similarity with an Iranian study done by Thehari *et al* reported that out of 147 term babies about 56% babies had a reduction in serum calcium level after phototherapy and 7% newborns developed hypocalcaemia after 48 hours of phototherapy [10].

In yet another study by Rozario CI *et al.* [11] who also reported that out of 100 newborns studied 67 babies had a decrease in serum calcium level after 48 hrs of phototherapy. And this reduction in calcium level was found to be statistically significant. Only 3 babies developed hypocalcemia. Karamifar *et al.* [8] and Ehsanipour *et al.* [9] also reported the incidence of hypocalcemia after 48 h of phototherapy was 15 and 14.4%, respectively in their studies.

Mostafa *et al.* [12] also found hypocalcemia after exposure to phototherapy, with a higher percentage among the preterm neonates, as compared with full-term neonates.

However in contrast some authors reported higher incidence of hypocalcemia in their studies. These included Arora *et al* who reported that 56% term babies developed hypocalcemia [13]. And Yadav *et al.* reported 66% term babies had hypocalcemia [14]. Similarly, in 2006, Medhat from Cairo University observed 75% of term and 90% of preterm developed hypocalcaemia after phototherapy [15].

The etiology of hypocalcemia in infants treated with phototherapy is believedby different authors as: Hakinson and Hunter hypothesized that phototherapy inhibits pineal secretion of melatonin which blocks the effect of cortisol on bone calcium. So, cortisol increases bone uptake of calcium and induces hypocalcaemia.

In present study, there was no significant association between reduction in serum calcium level and other parameters like, birthweight, postnatal age and type of feeding Similar results were reported by Rozario CI *et al.* and Karamafir *et al.* in their studies [11, 8].

Conclusion

The level of mean serum calcium showed a significant decline after phototherapy. This shows that hypocalcemia is one of the major complications of phototherapy in addition to dyselectrolytemia, body color changes, dehydration, retinal changes, genital abnormalities. The frequency of hypocalcemia is increased with increased duration of phototherapy. Further, studies with a larger sample size are required to validate these findings.

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