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Original Research Article

The effect of phototherapy on serum calcium level in neonates with hyperbilirubinemia: a cross sectional study

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ABSTRACT

Background: Neonatal Hyperbilirubinemia is one of the leading causes for admission in NICU in the first week of life. This condition if left untreated may lead to irreversible neurological damage hence increasing mortality and morbidity in newborns. Neonatal Hyperbilirubinemia is treated with phototherapy which employs blue wavelengths of light to change unconjugated bilirubin in the skin. The bilirubin is then converted to less toxic water-soluble photo-isomers that are excreted in the bile and urine. There are several toxic effects to the use of this treatment, one of them being hypocalcemia.
Methods: This study has been done at Mahatma Gandhi Institute of Medical Sciences in 2016-2018 on 100 new-borns to prove the effect of phototherapy on serum calcium levels in neonates with hyperbilirubinemia. New-born who were admitted in NICU for Hyperbilirubinemia were screened according to inclusion and exclusion criteria, their sample for serum calcium and serum bilirubin levels were taken as pre and post phototherapy samples.
Results: It was observed that the mean Serum calcium level before phototherapy in neonates was 9.31 mg/dl with standard deviation of 0.69 mg/dl. Whereas after phototherapy mean serum calcium level in neonates was 8.88 mg/dl with standard deviation of 0.73 mg/dl. There was statistically significant mean difference in serum calcium level at before and after phototherapy in neonates ($p<0.0001$).
Conclusions: This study proves the hypothesis that phototherapy can cause hypocalcemia in neonates with hyperbilirubinemia.

Keywords: Hypocalcemia, Neonatal hyperbilirubinemia, Phototherapy

INTRODUCTION

Neonatal hyperbilirubinemia (NNH) is the most common abnormal physical finding during the first week of life. Over two third of newborn babies have been known to develop clinical jaundice. It has also been studied that in most of the neonates, unconjugated hyperbilirubinemia reflects a normal or exaggerated physiological phenomenon.[1] Neonatal hyperbilirubinemia nearly affects 60% of term and 80% of preterm neonates during the first week of life.[2]

Approximately 6-11% of them are proven to have clinically significant jaundice in whom the use of phototherapy becomes necessary.[3] But if left untreated, this condition may lead to neurological manifestations along with other systemic involvement.

Neonatal hyperbilirubinemia is a condition due to the liver's immature excretory pathway for bilirubin and is the most common cause for admission of neonates in the first week of life in current time after postnatal discharge from hospital.[4]

Elevated levels of unconjugated bilirubin is known to cause bilirubin encephalopathy and then kernicterus, with devastating, permanent neurodevelopment handicaps. Hyperbilirubinemia can be treated by phototherapy or

exchange transfusion. Phototherapy employs blue wavelengths of light to change unconjugated bilirubin in the skin. The bilirubin is then converted to less toxic water-soluble photo-isomers that are excreted in the bile and urine without conjugation. As every treatment has its side effects, phototherapy also has known to cause its adverse effects like hyperthermia, feed intolerance, loose stools, skin rashes, bronze baby syndrome, retinal changes, dehydration, hypocalcemia, redistribution of blood flow and genotoxicity.[5]

Phototherapy has a negative impact on numerous parts of the oxidant and antioxidant defense system in newborns with hyperbilirubinemia and exposes them to fatal oxidative stress.[6] Some theories also postulate that melatonin stimulates secretion of corticosterone which leads to decrease in calcium absorption by the bones.

Neonates who are being treated by phototherapy for hyperbilirubinemia are at a greater risk of developing hypocalcemia. Therefore, it is suggested that in such newborns, administration of calcium is to be considered.

Important aspects of phototherapy

Phototherapy has been developed as the most widely used form of treatment in hyperbilirubinemia and its efficiency has now been well established. Nils Rybergs Finsen (1860-1904) was the founder of modern phototherapy. Phototherapy is a simple and easily available therapeutic intervention for effective management of hyperbilirubinemia. With timely intervention in both term and preterm, severest complications of hyperbilirubinemia like kernicterus could be prevented. It is an equipment which consists of 4 blue light fluorescent lamps having the wavelengths of 412-472 nm and placed at a distance of 25-45 cm from the skin surface of neonates according to AAP protocol. Genitalia and eyes are to be covered during phototherapy exposure. Phototherapy has a mechanism where blue wavelengths of light change the unconjugated bilirubin at molecular level in the skin. Further this bilirubin is then converted to a compound which is less in toxicity is a water-soluble photo-isomer that are removed in the bile and urine without further conjugation. As we know every mode of treatment comes with its side effects, phototherapy also has its adverse effects like hyperthermia, recurrent vomiting, loose stools, skin rashes, which could again aggravate in the form of bronze baby syndrome, some ocular manifestations like retinopathies, dehydration, hypocalcemia, and genotoxicity.[7]

Hypocalcemia

Hypocalcemia is one of the many adverse effects of phototherapy which is lesser known in neonatology. It is defined as the serum calcium concentration of <7 mg/dl and <8mg/dl in preterm and term neonates respectively. It can cause several complications like neuromuscular irritability, convulsions, apnea, cyanosis, myoclonic jerks, laryngospasm along with cardiac disturbances like tachycardia, heart failure, decreased contractibility, prolonged QT interval.[8]

Aim and objective of this study was to evaluate the effect of phototherapy on serum calcium levels in neonates with hyperbilirubinemia.

METHODS

This study was conducted at MGM Medical College and Hospital, Aurangabad between November 2016-November 2018 after getting proper approval from the ethical committee members of the institute.

Neonates having hyperbilirubinemia requiring therapy as per AAP guidelines are included in the study while newborns with decreased serum calcium levels, sepsis, apgar score of less than 7 at 5 minutes of birth, or requiring exchange transfusion were excluded. Pretest and pos-ttest counseling was given to the parents. After written consent from the parents those neonates who fulfilled the inclusion criteria fulfilling were performed blood test like serum calcium levels, and serum bilirubin levels at admission and at 48 hours of phototherapy.

Taking all aseptic precaution, peripheral vein was punctured and 2-3 ml of blood collected in a sample bottle out of which 1ml of blood was taken immediately for serum Bilirubin. In addition to CBC and blood group, serum bilirubin was estimated by Jendrassik and Groffs method.

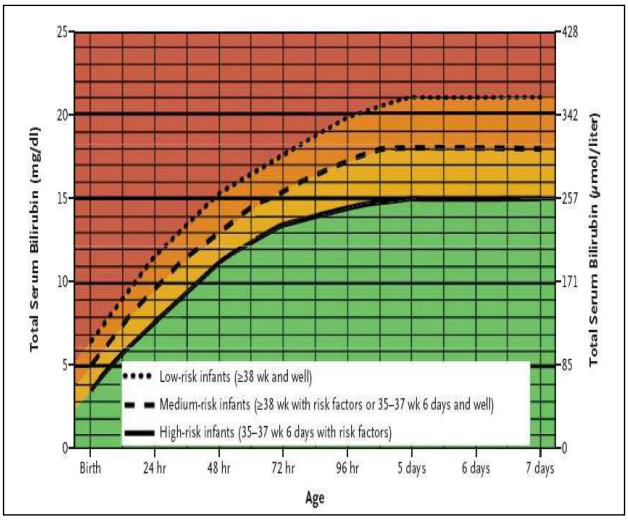
Phototherapy of the brand Bird Medi-tech with 4 blue and 2 white lights with a wavelength of 420-480 nm and irradiance of 6-12 $\mu w/cm^2/nm$ were used and placed at a distance of 30-35cm from skin surface under standard protocol with eyes and genitalia completely covered. Serum calcium along with serum bilirubin was measured at the onset and then at 24 and 48 hours of phototherapy by OCPC method.

Data was compiled and studied. Cases were given single or double surface phototherapy depending upon their serum bilirubin values. Phototherapy was given according to the criteria of American Academy of Pediatrics (Table 1 and Figure 1).

Statistical analysis

The data was compiled in master chart i.e. in MS-EXCEL Sheet and for analysis of this data; SPSS (Statistical package for social sciences) Version 20th was used.

Percentages and frequencies were calculated to show the distribution of various factors like gestational age, mode of delivery, gender. t-test and probability values was calculated to show mean difference between pre and post, Also the significance level of this test was checked at 0.05.



Risk factors = G6PD deficiency, isoimmune hemolytic disease, asphyxia, altered sensorium, hypothermia, sepsis, acidosis, or albumin <3 mg/dl.

Figure 1: Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation.

Table 1: Phototherapy in preterm neonates as per weight and serum bilirubin level.

Weight	Phototherapy (serum bilirubin level)
<1000 gm	Started with in 24 hrs
1000-1500 gm	7-9 mg/dl
1500-2000 gm	10-12 mg/dl
2000-2500 gm	13-15 mg/dl

RESULTS

Out of 100 neonates, 53 (53.0%) were male and 47 (47.0%) were female (Figure 2) from which 81 (81.0%) were term neonates and 19 (19.0%) were pre-term neonates. Out of 100 neonates maximum 44 (44.0%) neonates were having 4-6 days age at the onset of hyperbilirubinemia, 32 (32.0%) were having ≥6 days age at the onset of hyperbilirubinemia and 24 (24.0%) were having age at onset less than equal to 3 days.

The mean age at the onset of hyperbilirubinemia was 4.73 days with standard deviation of 1.56 days. Majority 62 (62.0%) of neonates were having birth weight between 2500-3500 gm whereas only 01 (1.0%) of neonate was having birth weight more than 3500 gm. The mean birth weight of neonates was 2584.04 with standard deviation of 410.7 gm.

Out of 100, 35.0% of neonates had normal vaginal delivery and 65.0% delivered by cesarean section. (Table 2).

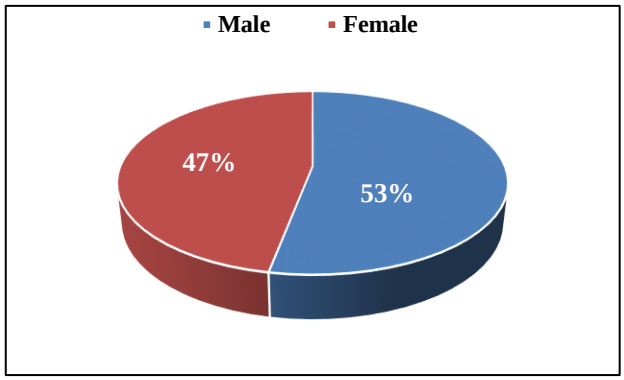


Figure 2: Gender of neonates.

Table 2: Distribution of neonates according to type of delivery.

Type of delivery	No. of neonates	Percentage
Normal vaginal delivery	65	65.0%
Cesarean section	35	35.0%
Total	100	100%

The mean Serum calcium level before phototherapy in neonates was 9.31 mg/dl with standard deviation of 0.69 mg/dl. Whereas after phototherapy mean Serum calcium level in neonates was 8.88 mg/dl with standard deviation of 0.73 mg/dl. There was statistically significant mean difference in Serum calcium level at before and after phototherapy in neonates (p<0.0001) (Table 3).

Table 3: Comparison of mean Serum calcium level before and after of phototherapy in neonates.

Serum calcium level mg/dl	N	Mean±SD	Mean difference	t-value	p-value
Before phototherapy	100	9.31±0.69	0.44	8.02	p<0.0001 S
After phototherapy	100	8.88±0.73			

S: Significant, NS: Not significant

DISCUSSION

Neonatal jaundice or neonatal hyperbilirubinemia is the commonest cause of NICU admission. Phototherapy is widely accepted as a relatively safe and effective method for treatment of neonatal hyperbilirubinemia as described by Cremer et al in 1953 but there are very less number of studies showing the adverse effects of phototherapy.[8]

In present study the mean Serum calcium level before phototherapy in neonates was 9.31 mg/dl with standard deviation of 0.69 mg/dl. Whereas after phototherapy mean Serum calcium level in neonates was 8.88 mg/dl with standard deviation of 0.73 mg/dl. There was statistically significant mean difference in Serum calcium level at before and after phototherapy in neonates ($p<0.0001$).

In a study by Goyal S et al, the mean serum calcium levels before phototherapy was 9.14±0.78 mg/dl and it was decreased to (8.53±0.77 mg/dl) after phototherapy treatment.[9] The difference between pre and post phototherapy serum calcium levels were found to be statistically significant ($p<0.001$). This study was in corresponding to our study.

In a study by Yadav RK et al, there was significant decrease in calcium levels after phototherapy but the difference between our and their study was that they had measured the ionized calcium levels rather than serum calcium levels as in ours.[9]

In a study by Roario CI et al, they concluded that the mean serum calcium level before phototherapy was 9.27±0.73 and after was 8.88±0.70 with a $p<0.001$ which was similar to this study.[10]

In effect of phototherapy on serum calcium level in neonatal Jaundice by Hamed M et al, it was concluded that there is significant difference between serum calcium level post phototherapy in neonatal hyperbilirubinemia. This study was a prospective case control study.[11]

In a study by Arora et al, it was reported that 56% term babies developed hypocalcemia post phototherapy and Jain B K et al, also concluded hypocalcemic effects of phototherapy in 30% term babies and 55% preterm neonates.[12,13] The difference between this and our study was that Jain B K et al, considered serum calcium level <8 mg/dl as hypocalcemia so they have got a higher prevalence of hypocalcemia.

In this study it was found that the comparison of mean serum calcium levels before and after phototherapy between preterm and term neonates wasn't significant $p=0.374$. In a study by Yadav RK et al the comparison between mean serum calcium levels post phototherapy was significant between preterm n term neonates $p<0.0001$.[14]

Out of 100 neonates, 53 (53.0%) were male and 47 (47.0%) were female. Similar gender ratio i.e. 59 babies males and 41 female babies was observed by Rozario IC et al, Whereas Goyal S et al, reported 61.0% boys and 39.0% of girls.[15]

Maximum 81.0% were term and 19.0% were pre-term neonates reported in the present study. Whereas Pankaj Singh K et al observed Preterm neonates were 33% and 67% cases were term neonates. Al-ali MA et al, found that 50.0% were pre-term and term neonates.[16,17]

Out of 100, 35.0% of neonates had normal vaginal delivery and 65.0% delivered by cesarean section. Similar findings were reported by Goyal S et al, 57.0% neonates were delivered by normal vaginal delivery and 43.0% by lower segment caesarean section.[15] In a study by Gupta A et al, it was concluded that there is increased incidence of hyperbilirubinemia in neonates born with caesarian section than in normal vaginal delivery which also was in correlation with our study.[18]

CONCLUSION

There is significant reduction in Serum bilirubin level and serum calcium level after phototherapy, no significant association was found between reduction in Serum bilirubin level and serum calcium level in Preterm and Term neonates but the range of hypocalcemia was variable in the form of very low levels to decrease just beyond borderline levels. This may have clinical impacts and add to the morbidity in neonates. We need further more studies which exactly will prove their correlation post phototherapy also comparison on the various factors like gestational age, gender, mode of delivery. So, authors could say that though phototherapy is widely accepted as a relatively safe and effective method for treatment of neonatal hyperbilirubinemia but we recommend monitoring serum calcium concentrations during and after phototherapy in babies receiving phototherapy.

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