



EFFECT OF PHOTOTHERAPY ON SERUM CALCIUM LEVELS IN NEONATAL JAUNDICE

Pediatrics

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ABSTRACT

Background : To study the effect of phototherapy on serum calcium levels in neonates with unconjugated hyperbilirubinemia.

Methods : This hospital based longitudinal interventional study was conducted on 100 neonates with neonatal hyperbilirubinemia admitted to Neonatal Intensive Care Unit at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. Total serum bilirubin and serum calcium levels of each participants were checked before and at the end of phototherapy. Neonates were also checked for the clinical signs of hypocalcemia i.e. jitteriness, irritability, lethargy, and convulsions.

Results : A total of 100 neonates with neonatal jaundice were included with 55% boys and 45 % girls whose mean age was 3.0 ± 0.95 days. Mean S.Bilirubin level before phototherapy was 13.92 ± 2.32 mg/dl which was reduced to 8.87 ± 2.18 mg/dl. S.Calcium levels pre-phototherapy were 8.66 ± 0.65 mg/dl which were reduced to 7.94 ± 1.05 mg/dl. It was found that 32% of the participants in total exhibited symptoms related to hypocalcemia. More term neonates (56.3%) experienced symptoms related to hypocalcemia compared to pre-terms (43.8%).

Conclusion : It can be deduced that phototherapy induced hypocalcemia is a significant concern and hence, neonates requiring phototherapy may be considered for calcium supplementation.

KEYWORDS

INTRODUCTION :

Neonates are defined as infants born between birth and first 28 days of life. Preterm neonates are those born before a gestational age of 37 completed weeks and term are the ones born at a gestational age of 37 to <42 completed weeks¹. Neonatal jaundice is the most common problem occurring in the first week of neonatal life. It is mostly benign and does not require any treatment². It occurs due to increased hemolysis of RBCs containing fetal hemoglobin and inability of the neonates liver to convert unconjugated bilirubin into conjugated bilirubin. It affects 60% of term neonates and 80% of preterm neonates. It appears as yellowish discoloration of the skin. It can be either physiological or pathological³. Mostly it is physiologic and is self-limiting, but sometimes it may require intervention like phototherapy. If not treated, it may lead to acute or chronic bilirubin encephalopathy (kernicterus)⁴. Pathological hyperbilirubinemia usually does not resolve spontaneously, and is due to hemolytic diseases of newborn such as ABO and Rh incompatibility, other minor blood group incompatibility or Glucose-6-phosphate dehydrogenase deficiency⁵. In most of these cases the bilirubin level can reach to toxicity levels, if not treated promptly and can cause brain damage.

Hyperbilirubinemia is the most common cause of re-admission in neonates. Therefore, it is of utmost importance to manage neonatal hyperbilirubinemia.

Phototherapy plays an important role in the management of Hyperbilirubinemia. It transforms unconjugated bilirubin to water soluble isomers which can be excreted with urine or feces without the need for conjugation in the liver⁶. Like any other treatment modality, phototherapy also has side effects like dehydration, temperature instability, skin rashes, loose stools, retinal damage, riboflavin deficiency, increased red cell osmotic fragility, DNA damage and hypocalcemia⁷.

Hypocalcemia is the lesser known side effect of phototherapy. It is defined as serum calcium levels <8mg/dl in term neonates and <7mg/dl in preterm neonates. The overall prevalence of hypocalcemia in neonates receiving phototherapy was suggested to be 8.7% in full term neonates⁷.

AIMS & OBJECTIVES :

To study the effect of phototherapy on serum calcium levels in neonates with unconjugated hyperbilirubinemia.

METHODS :

The study was conducted in Neonatal Intensive Care Unit (Dept. of Pediatrics) at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala.

This was a hospital based longitudinal interventional study which included 100 neonates with neonatal hyperbilirubinemia conducted between January, 2019 till June, 2020.

INCLUSION CRITERIA

1. Neonates with unconjugated hyperbilirubinemia requiring phototherapy

EXCLUSION CRITERIA

1. Neonates with hyperbilirubinemia requiring exchange transfusion
2. Birth asphyxia
3. Sepsis
4. Infants of diabetic mothers
5. Neonates with serum calcium levels less than 7mg/dl before phototherapy in preterm neonates and less than 8mg/dl in term neonates
6. Respiratory distress
7. Congenital malformation
8. Mothers taking anticonvulsant drugs

A prior approval of The Institutional Ethics committee was obtained. The study didn't impose any financial burden on the parents or guardians of the study group and an informed written consent was taken from the parents/guardians of the participants before conducting the study. All participants were ensured confidentiality. The study was not funded by any agency.

Serum Bilirubin and Serum Calcium levels were assessed for each participant enrolled in this study at the starting and post-phototherapy. The total Serum Bilirubin was assessed using TBI method which is

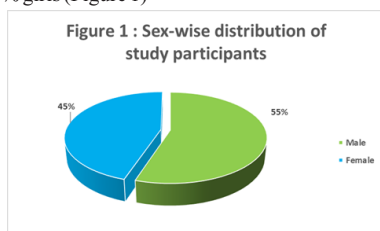
applied in the Siemens Dimension Clinical Chemistry System. In this method, total bilirubin level is measured quantitatively in-vitro from both human plasma and serum. Each participant was further categorized based on their Serum calcium level into hypocalcemic or within normal range.

STATISTICAL ANALYSIS :

Data was entered in excel sheet and then analyzed using statistical software SPSS 20.0. Qualitative variables have been expressed as percentages and quantitative variables have been expressed as mean and standard deviation. Association among qualitative variables has been established by applying χ^2 test. Normality of quantitative data was assessed and further t-test was applied to establish co-relation among quantitative variables. $p \leq 0.05$ has been taken as significant at 95% confidence level.

RESULTS :

A total of 100 neonates with neonatal jaundice were included with 55% boys and 45 % girls (Figure 1)



whose mean age was 3.0 ± 0.95 days. Their mean gestational age was 37.3 ± 2.4 weeks. 33 % of the study participants were pre-term while 67% were term neonates. 47% neonates were delivered by normal vaginal delivery while 53% by lower segment cesarian section. (Table 1)

Table 1 : Demographic profile of the study participants

Variable	Mean
Mean Gestational Age	37.3 ± 2.4 weeks
Mean Age	3.0 ± 0.95 days
Mode of Delivery	No of Participants (%)
Normal Vaginal Delivery (NVD)	47 (47)
Lower Segment Cesarian Section (LSCS)	53 (53)

(Figures in brackets indicate percentages)

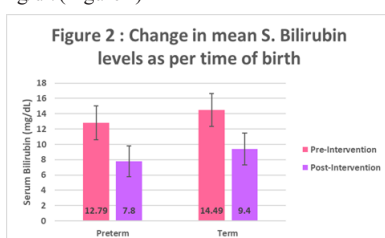
Mean S.Bilirubin level before phototherapy was 13.92 ± 2.32 mg/dl which was reduced to 8.87 ± 2.18 mg/dl. S.Calcium levels pre-phototherapy were 8.66 ± 0.65 mg/dl which were reduced to 7.94 ± 1.05 mg/dl.(Table 2)

Table 2 : Overall Change in mean S. Bilirubin and S. Calcium levels

	Pre - Intervention	Post - Intervention	Paired Sample t-test
S. Bilirubin*	13.92 ± 2.32	8.87 ± 2.18	$t = 23.320$ $df = 99$ $Sig < 0.001$
S. Calcium*	8.66 ± 0.65	7.94 ± 1.05	$t = 7.969$ $df = 99$ $Sig < 0.001$

*Unit : milligram/deciliter (mg/dL)

When categorized as per the time of birth, it was found that for preterm neonates the S.Bilirubin levels pre-phototherapy were 12.79 ± 2.24 mg/dl which reduced to 7.80 ± 2.01 mg/dl. For the term neonates, the S.Bilirubin levels decreased from a baseline of 14.49 ± 2.16 mg/dl to 9.40 ± 2.07 mg/dl. (Figure 2)



Similarly, the S.Calcium levels of preterm neonates reduced from 8.31 ± 0.71 mg/dl to 7.18 ± 0.87 mg/dl. For the term neonates, these levels decreased from 8.82 ± 0.55 mg/dl to 8.32 ± 0.93 mg/dl. (Figure 3)

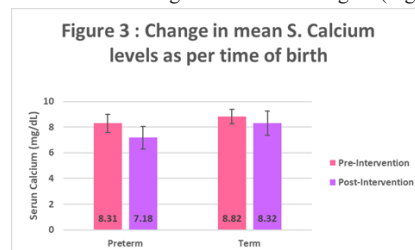


Table 3 : Prevalence of hypocalcemia as per time of birth after phototherapy

	Hypocalcemia		Total	Chi-square
	Yes	No		
Preterm	20 (60.6)	13 (39.4)	33 (100)	$\chi^2 = 1.819$ $df = 1$ $p = 0.177$
Term	31 (46.3)	36 (53.7)	67 (100)	
Total	51 (51)	49 (49)	100 (100)	

(Figures in brackets indicate percentages)

Post-phototherapy, it was found that 51% out of the 100 study participant's were hypocalcemic while the rest 49% were not.(Table 3) It was found that 32% of the participants in total exhibited symptoms related to hypocalcemia. More term neonates (56.3%) experienced symptoms related to hypocalcemia compared to pre-terms (43.8%).(Table 4)

Table 4 : Distribution of symptoms related to hypocalcemia

Symptom	Preterm	Term	Total
Jittery	11 (44)	14 (56)	25 (100)
Irritable	3 (42.9)	4 (57.1)	7 (100)
Lethargy	0 (0)	0 (0)	0 (0)
Convulsion	0 (0)	0 (0)	0 (0)
Total	14 (43.8)	18 (56.3)	32 (100)

(Figures in brackets indicate percentages)

DISCUSSION :

Hyperbilirubinemia is the most common concern in the first week of neonatal life and appears as yellowish discoloration of skin. It is mostly physiologic and self-limiting, but sometimes requires intervention like phototherapy. Phototherapy is the mainstay management of hyperbilirubinemia. Like any other treatment modality, phototherapy also has adverse effects like dehydration, temperature instability, skin rashes, bronze baby syndrome, retinal damage and hypocalcemia. Hypocalcemia is however a lesser known complication of phototherapy. Hence, the present study has been done to see the effects of phototherapy on serum calcium levels.

In the present study, the overall change in mean serum bilirubin levels was from a baseline of 13.92 ± 2.32 mg/dl to 8.87 ± 2.18 mg/dl. This change in the mean value was found to be statistically significant ($t = 23.320$, $df = 99$, $Sig < 0.001$).

Shahriarpanah S et al. (2018) while studying 50 neonates for the effects of phototherapy reported the change in serum bilirubin levels from 15.19 ± 2.29 mg/dl to 8.53 ± 1.6 mg/dl and this change in serum bilirubin levels, pre and post phototherapy was found to be statistically significant.⁸

Usharani M et al. (2017) while studying 30 full term hyperbilirubinemic neonates reported a similar change in the serum bilirubin levels post phototherapy. The change was from 14.04 ± 0.71 mg/dl to 8.13 ± 0.40 mg/dl. Their change in the serum bilirubin levels was also found to be statistically significant.⁶

In the index study the mean serum calcium level changed from 8.66 ± 0.65 mg/dl to 7.94 ± 1.05 mg/dl. This change in the serum calcium level was found to be statistically significant ($t = 7.969$, $df = 99$, $Sig < 0.001$). Mahadev K et al. (2019) reported a change in serum calcium level from a baseline of 9.25 ± 0.56 mg/dl to 8.39 ± 1.99 mg/dl post phototherapy. These results were similar to our study and was statistically significant.⁹ Goyal S et al. (2018) in their study reported that the change in serum bilirubin levels pre and post intervention

was from 9.14 0.78 mg/dl to 8.53 0.77 mg/dl. This change was found to be statistically significant.⁷

In the present study, after phototherapy, out of a total of 55 male participants 61.8% were hypocalcemic, while 38.2% were not hypocalcemic and amongst the 45 female participants majority of the females (62.2%) were not hypocalcemic and 37.8% were hypocalcemic. The association between these two parameters was found to be statistically significant ($\chi^2 = 5.724$, $df = 1$, $p = 0.017$). **Khan M et al. (2016)** while studying 123 term neonates found a similar distribution of hypocalcemia among his female participants with 30.4% being hypocalcemia and the rest 69.6% females being non hypocalcemic. However, only 18.2 % male participants developed hypocalcemia, which was not in concordance with our study.³ In our study, out of a total 51 neonates who were hypocalcemic, higher percentage of term neonates (60.78%) were hypocalcemic compared to 39.21% preterm hypocalcemics. It can be noted that 60.6 %, out of the 33 preterm neonates enrolled in the study, developed hypocalcemia after receiving phototherapy for hyperbilirubinemia. Amongst the 67 term neonates, only 46.3% i.e. a lower percentage, developed hypocalcemia post phototherapy. However, the association between the gestation and hypocalcemia amongst our participants was found to be statistically insignificant ($\chi^2 = 1.819$, $df = 1$, $p = 0.177$). **Gupta R et al. (2018)** from their study reported that out of a total of 29 term participants, 47 % developed hypocalcemia.¹⁰ **Khan M et al. (2016)** reported that only 22.76 % of their term neonates developed phototherapy induced hypocalcemia.³

In the present study, a total of 32 % participants developed symptoms related to hypocalcemia. Amongst these 32 %, majority i.e. 56.3 % were term neonates and rest 43.8 % were preterm neonates. Out of the 32 neonates who developed hypocalcemic symptoms, 78.13 % had jitteriness, those who exhibited jitteriness can be distributed into 56 % term neonates and 44 % preterm. Amongst the rest 21.9 % neonates who developed irritability, 42.9 % were preterm and 57.1 % were term neonates. In the present study out of all the 20 preterm neonates who developed hypocalcemia, 55 % showed jitteriness. Out of the 31 term neonates who developed hypocalcemia, 45.16 % developed jitteriness. **Rastogi D et al. (2016)** reported of a similar distribution where 50 % of their preterm neonates and 38 % of term neonates developed jitteriness.¹¹ **Jain SK et al. (2015)** reported similar distribution where 33.33 % preterm neonates exhibited jitteriness.¹² **Arora S et al. (2014)** reported a similar distribution where 76.9 % of the total hypocalcemic babies developed jitteriness. The prevalence of symptomatic hypocalcemia was more in preterms (69.2 %) than terms (30.8 %) out of a total of 13 symptomatic hypocalcemic babies.¹³

CONCLUSION :

These results suggest that neonates requiring phototherapy, especially preterm and low birth weight babies are at risk of developing phototherapy induced hypocalcemia.

In the light of the above results of the present study, it can be deduced that phototherapy induced hypocalcemia is a significant concern and hence, neonates requiring phototherapy may be considered for calcium supplementation.

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Conflicts of interest : There are no conflicts of interest

Limitations : In our study, the participants were relatively small in number. Thus, the result of this thesis cannot be generalized for a larger population. Therefore, complementary studies with larger sample size and with diverse socio demographic profile should be done.

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