

Original Research Article

Phototherapy induced hypocalcemia in neonatal hyperbilirubinemia and correlation of hypocalcemia with the duration of phototherapy

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ABSTRACT

Background: Neonatal hyperbilirubinemia is common morbidity in the 1st week of life. Approximately 5-10% of them requires intervention like phototherapy and even exchange transfusion. Phototherapy has various adverse effects and hypocalcemia is one of them. Thus, assessment of serum calcium levels after phototherapy should be done in neonates with jaundice. Objectives were to study prevalence of hypocalcemia in neonates with unconjugated hyperbilirubinemia receiving phototherapy and to observe association of hypocalcemia with duration of phototherapy.

Methods: This was a prospective observational study conducted over a period of 18 months among 75 neonates (both term and preterm) in the neonatal intensive care unit of Manipal teaching hospital, Pokhara. Total serum calcium level was measured at 0 hours (control), 12 hours, and after 48 hours and data were analyzed using statistical package for social sciences version 21.

Results: Hypocalcemia was found only in term neonates (n=8; 14%). Of those who had hypocalcemia, the majority experienced hypocalcemia after 48 hours of starting phototherapy. The mean difference of total serum calcium level before and after phototherapy in preterm and term neonates was found to be statistically significant. Hypocalcemia was not found to be associated with the duration of phototherapy.

Conclusions: The present study concludes that though there is a reduction in the serum calcium with increased duration of phototherapy, however, it does not fall to the level where treatment is required. Hence it is not recommended to monitor serum calcium levels in neonates receiving phototherapy.

Keywords: Hypocalcemia, Jaundice, Neonates, Phototherapy

INTRODUCTION

Jaundice is the yellowish coloration of the skin, sclera, and mucus membrane resulting from the accumulation of bilirubin.¹ It is a common morbidity observed in the neonate during the first week of life in approximately 60% of term and 80% of preterm neonates.² In most of the neonates no intervention is required however, 5-10% of the cases have clinically significant jaundice, which requires treatment.^{2,3} High level of unconjugated bilirubin may cause permanent neurological damage.^{4,5} There are various modalities of treatment for neonatal

hyperbilirubinemia and, phototherapy is one of them. Besides the useful effects of phototherapy, some complications like hypocalcemia can be seen during the treatment with phototherapy.⁶

Hypocalcemia refers to total serum calcium level less than 8 mg/dl in term neonates and less than 7 mg/dl in preterm neonates.⁷ Hypocalcemia may cause cardiac and neurological dysfunctions. It may be symptomatic in the form of jitteriness, apnea, lethargy, stridor, irritability, and seizures.⁸

This study was undertaken to see occurrence of hypocalcemia in preterm and term neonates with hyperbilirubinemia receiving phototherapy, as phototherapy-induced hypocalcemia can be a significant problem.

Objectives

Objectives of the study were to study the prevalence of hypocalcemia in term and preterm neonates receiving phototherapy and to see the association of hypocalcemia with the duration of phototherapy.

METHODS

This was a prospective observational study conducted over a period of 18 months from January 2018 to June 2019 among 75 neonates (both term and preterm) in the neonatal division of Manipal teaching hospital, Pokhara, a tertiary care referral centre of western Nepal. All preterm (34 to less than 37 weeks) and term (37 to 40 weeks) neonates with jaundice and receiving phototherapy were included in the study. However, neonates with jaundice requiring exchange transfusion, birth asphyxia, sepsis, respiratory distress, ABO and Rh incompatibility, neonatal seizure, IUGR (Intrauterine growth retardation) babies, infants of diabetic mother and neonates with conjugated hyperbilirubinemia and prolonged jaundice were excluded from the study.

Ethical clearance was taken from the institutional ethical review committee, Manipal college of medical sciences, and teaching hospital and informed written consent from the parents in their preferred language was obtained. The socio-demographic and clinical details of the neonates were recorded and entered in pre-designed proforma. In the enrolled neonates, serum total bilirubin and serum calcium levels at 0 hours, 12 hour and after 48 hours were

sent in all cases. The serum calcium level estimated just before starting of phototherapy was considered as control and serum calcium level less than 7 mg/dl in preterm neonates and less than 8 mg/dl in term neonates is considered as hypocalcemia.

Data were analyzed using statistical package for social sciences version 21 (SPSS). Continuous variables were described as mean and standard deviation and categorical variables in number and percentage. Hypocalcemia in term and preterm was compared using Fischer exact test. Pearson correlation was applied to see an association between hypocalcemia and the duration of phototherapy. Paired sample t-test was used to compare the means of calcium level before (0 hours) and after (12 hours, 48 hours) phototherapy; with a 95% confidence limit and $p < 0.05$ was considered statistically significant.

RESULTS

The baseline socio-demographic and clinical parameters of the enrolled neonates are shown in Table 1.

Three (5.3%) term neonates experienced hypocalcemia at 12 hours after starting of phototherapy. Similarly, eight (14%) term neonates had hypocalcemia 48 hours after starting of phototherapy. None of the preterm neonates enrolled in the study experienced hypocalcemia after starting of phototherapy. It was observed that occurrence of hypocalcemia was not significantly associated with the duration of phototherapy as shown in Table 2.

On comparing the 0 hours calcium level with subsequent hours, the mean difference in total serum calcium levels in both term, and preterm babies were found to be statistically significant (Table 4), and the difference was seen to be more significant in term babies.

Table 1: Demographic profile of neonates admitted for neonatal hyperbilirubinemia.

Variables	Preterm	Term
Age in hours (Mean $\pm$ SD)	114.11 $\pm$ 45.99	122.28 $\pm$ 44.15
Sex		
Male	9 (25.7%)	26 (74.3%)
Female	9 (22.5%)	31 (77.5%)
Gestational age in weeks (Mean $\pm$ SD)	36.11 $\pm$ 0.75	38.96 $\pm$ 0.86
Birth weight in grams (Mean $\pm$ SD)	2511.11 $\pm$ 249.44	3172.81 $\pm$ 375.96
TSB in mg/dl at 0 hours (Mean $\pm$ SD)	18.5 $\pm$ 2.31	18.05 $\pm$ 1.96
Serum calcium in mg/dl at 0 hours (Mean $\pm$ SD)	9.48 $\pm$ 0.94	9.62 $\pm$ 0.84
Duration of phototherapy in hours (Mean $\pm$ SD)	62 $\pm$ 9.48	63.59 $\pm$ 9.75

Table 2: Serum calcium level at 12 hours and, after 48 hours.

Duration of phototherapy	Serum calcium level	Preterm, n (%)	Term, n (%)	P value
At 12 hours	Hypocalcemia present	0	3 (5.3)	1*
	Hypocalcemia absent	18 (100)	54 (94.7)	
	Total	18	57	
After 48 hours	Hypocalcemia present	0	8 (14)	0.18*
	Hypocalcemia absent	18 (100)	49 (86)	
	Total	18	57	

*Fischer exact test

Table 4: Comparison of serum calcium at 0 hour with subsequent hours (at 12 hours and after 48 hours) in term and preterm neonates receiving phototherapy.

Gestational age (Weeks)	Comparison of serum calcium (Hours)	Mean paired difference (mg/dl) $\pm$ SD	P value
Preterm (34-37)	0 and at 12	0.527 $\pm$ 0.600	0.002
	0 and after 48	0.705 $\pm$ 0.861	0.003
Term (38-41)	0 and at 12	0.522 $\pm$ 0.719	<0.001
	0 and after 48	0.915 $\pm$ 0.779	<0.001

Table 5: Correlation of hypocalcemia in term neonates with duration of phototherapy.

Correlation	R	CI for r	P value
Negative	-0.043	-0.737 to 0.771	0.92

r: Coefficient of correlation, CI: Confidence interval.

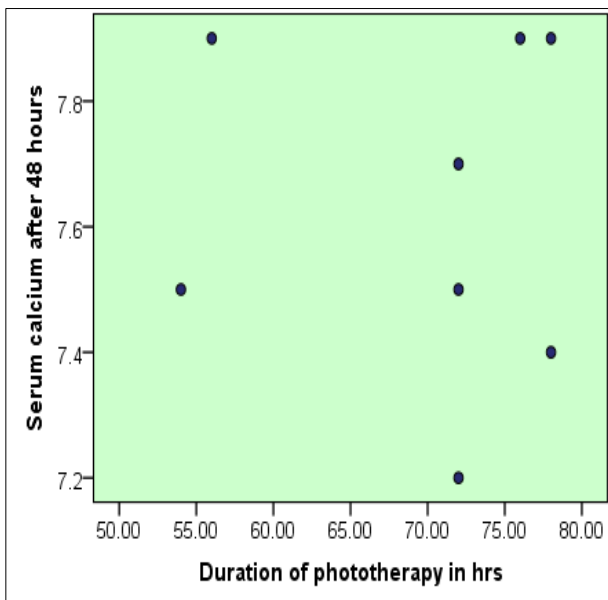


Figure 1: Scatter plot diagram of correlation of hypocalcemia and duration of phototherapy in term neonates.

Correlation analysis of a duration of phototherapy with hypocalcemia showed a negative but insignificant correlation with a coefficient (r of -0.043 and a $p=0.92$ (Table 5 and Figure 1). The diagram shows most of the hypocalcemia in term neonates were seen after 70 hours of phototherapy.

DISCUSSION

Phototherapy is a relatively safe and widely accepted method for the treatment of NNJ. Most clinical experiences suggest that the long-term side effects of phototherapy are minimal, absent, or unrecognized.⁹

The mean gestational age of our study group for preterm and term neonates were 36.11 ± 0.75 weeks and

38.96 ± 0.86 weeks respectively which was similar to studies of Jain et al (34.3 ± 1.16 weeks and 37.55 ± 0.69 weeks) and Reddy et al (34.94 ± 1.24 weeks and 39.26 ± 0.68 weeks).^{10,11}

In the various other studies, gestational ages of preterm and term neonates were appropriate for age which is similar to this study.^{8,10,12,13}

Mean birth weight of preterm and term in this study were 2511.11 ± 249.44 grams and 3172.81 ± 375.96 grams respectively which were relatively higher to study conducted by Reddy AT et al in which mean birth weight in preterm and term were 2240 ± 340 grams and 2980 ± 410 grams respectively.¹¹ Similarly in a study by Karamifar et al the mean birth weight was 2077 ± 316 grams and 2889 ± 474 grams respectively.¹⁴ In a study done by Taheri et al mean birth weight in term neonates was 3182 ± 430 grams which were agreed with the term neonates of our study.¹⁵

After subjecting 75 neonates with jaundice for phototherapy, hypocalcemia was seen in none of the preterm neonates after 12 hours and 48 hours. However, in term neonates, 5.3% developed hypocalcemia at 12 hour and, 14% after 48 hours of phototherapy. In the study by Chandrashekhar prevalence of hypocalcemia was seen in 11%, 27%, and 68.5% at 24 hours, 36 hours, and 48 hours of phototherapy in preterm neonates and 6%, 14%, and 16% at 24 hours, 36 hours and 48 hours of phototherapy in term neonates respectively however, in this study serum calcium level of less than 7 mg/dl was considered as hypocalcemia in both term and preterm which is in contrast to this study.¹⁶ Similarly in the study by Arora et al hypocalcemia was detected in 4 (9%) and 20 (44%) preterm babies at 24 hours and 48 hours of phototherapy respectively and hypocalcemia was detected in 23 (42%) and 30 (56%) of term babies at the end of 24 hours and 48 hours of phototherapy respectively.⁸

Several studies have shown the prevalence of hypocalcemia ranging from 12.63% to 14% in term neonates after 48 hours of phototherapy, which is similar to the prevalence of 14% in this study.^{6,8,17} Similarly in other studies the prevalence of hypocalcemia range from 3% to 9% in term neonates after 48 hours of phototherapy, which was lower than this study.^{5,11,14,19,21} Similarly several other studies have shown the prevalence of hypocalcemia ranges from 30% to 70% after 48 hours of phototherapy in full-term neonates, which was higher than this study.^{13,22-5}

Various studies have shown hypocalcemia after 48 hours of phototherapy in preterm neonates with the prevalence ranging from 22.6% to 90%.^{4,5,10,13,22} None of the preterm in this study developed hypocalcemia after phototherapy which makes our study different from other studies; this could be because the number of preterm babies enrolled in this study was small in number.

In the present study, the mean difference of total serum calcium level between 0 and 48 hours was 0.705 ± 0.861 mg/dl and 0.915 ± 0.779 mg/dl in preterm and term neonates respectively and this finding was shown to be statistically significant. Similarly in a study on term neonates, Bhat JA et al. showed a significant difference in mean total serum calcium between 0 and 48 hours of phototherapy of 0.879 ± 0.795 mg/dl.⁶ However, no studies have shown this difference in preterm neonates. Also, the mean differences of total serum calcium level in term neonates between 0 and 12 hours were 0.522 ± 0.719 mg/dl and this finding was statistically significant. However, no other study has shown similar results at the same duration of phototherapy.

The present study shows a negative but insignificant correlation between the duration of phototherapy and hypocalcemia in term neonates during correlation analysis, with a coefficient (r) of -0.043 and p=0.92 which is similar to the study by Bhat et al.⁶ This indicates that the duration of phototherapy causes little or no significant hypocalcemia in term neonates before the discharge. However, no similar studies have been published to date which could indicate or determine the correlation between the duration of phototherapy and hypocalcemia before discharge i.e., after 48 hours.

CONCLUSIONS

The present study concludes that though there is a reduction in the serum level of calcium with increasing duration of phototherapy, it does not fall to the level where treatment is required. Hence it is not recommended to monitor serum calcium levels in neonates receiving phototherapy.

This study did not find any association between hypocalcemia with the duration of phototherapy.

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