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Original Research Article

A Study to Evaluate Phototherapy Induced Hypocalcemia and Its Correlation Of With the Duration of Phototherapy in Neonatal Hyperbilirubinemia

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Abstract

Aim: The aim of the present study wads to assess the prevalence of hypocalcemia in neonates with unconjugated hyperbilirubinemia receiving phototherapy.

Material & Methods: A prospective observational study conducted over a period of 24 months among 200 neonates (both term and preterm) in the Department of Paediatrics.

Results: The average age of preterm and term newborns was 118.12±42.78 and 122.28±41.19, respectively. Males outnumbered females in preterm and term neonates. In this study, the mean birth weight for preterm and term was 2723.17±246.44 and 3132.78±370.90 grams, respectively 10 term neonates developed hypocalcemia 12 hours after phototherapy. After 48 hours of phototherapy, 20 term neonates developed hypocalcemia. No preterm neonates in the study developed hypocalcemia after phototherapy. Hypocalcemia was not connected with phototherapy duration. The mean difference in total serum calcium levels in term and preterm neonates was statistically significant, with term babies having a greater difference. The connection between phototherapy duration and hypocalcemia was negative but negligible (r = -0.045, p=0.95).

Conclusion: Serum calcium decreases with phototherapy time, but not to the point of treatment. Thus, infants getting phototherapy should not have blood calcium levels monitored.

Keywords: Hypocalcemia, Jaundice, Neonates Phototherapy

Introduction

Hyperbilirubinemia is a frequent and, in most instances, benign clinical syndrome in newborns. Phototherapy is utilized for treating of newborn hyperbilirubinemia. [1] Phototherapy May Cause To Problems Including Skin Rash, Diarrhea, Heat, Chills, Dehydration, DNA Damage To Lymphocytes, Retinal Degeneration, Bronze Baby Syndrome Notably In Cholestatic Jaundice And PDA Opening In Lbws And Hypocalcemia. [2] Romagnoli [3] Was The First To Suggest The Link Between Hypocalcaemia And Phototherapy In Preterms. Hakinson [4] And Hunter [5] Proposed That Phototherapy Decreases Pineal Release Of Melatonin Which Prevents The Impact Of Cortisol On Bone Calcium. So, Cortisol Increases Bone Absorption Of Calcium And Promotes Hypocalcaemia. Kim [6] hypothesized reduced production of parathormone as the etiology of hypocalcemia. In Hooman's study the urine calcium excretion was considerably greater in phototherapy group. [7]

Complications of phototherapy are dehydration, diarrhea, skin rash, hyperthermia, retinal degeneration, DNA damage to lymphocytes, patent ductus arteriosus (PDA), bronze baby syndrome, and hypocalcemia. [2] Melatonin concentration is lowered in babies with phototherapy which in turn leads to hypocalcemia. [8] First of all the relationship between phototherapy and hypocalcemia was observed by Shafiq MB et al. in premature newborns. Phototherapy may cause to problems including skin rash, diarrhea, heat, chills, dehydration, DNA damage to lymphocytes, retinal degeneration, bronze baby syndrome notably in cholestatic jaundice and PDA opening in LBWs and Hypocalcemia. [9,10] Besides the positive effects of phototherapy, several problems like hypocalcemia might be detected during the treatment with phototherapy. [10] It leads to suppression of pineal gland by transcranial light, resulting in a drop in melatonin level and as a result, hypocalcemia occurs. [11] Hypocalcemia refers to total blood calcium level less than 8 mg/dl

in term infants and less than 7 mg/dl in preterm neonates. [12] Cardiovascular and neurological problems can result from hypocalcemia. It can cause jitteriness, apnea, lethargy, stridor, irritability, and seizures. [13]

Hence, this study was done to evaluate incidence of hypocalcemia in preterm and term infants with hyperbilirubinemia undergoing phototherapy, as phototherapy generated hypocalcemia might be a serious concern.

Material & Methods

A prospective observational study conducted over a period of 24 months among 200 neonates (both term and preterm) in the Department of Pediatrics, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India.

Inclusion Criteria: 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.

Exclusion Criteria: 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.

Methodology

Ethical clearance was taken from the institutional ethical review committee 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.

Statistical Analysis: 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

Table 1: Demographic profile of neonates admitted for neonatal hyperbilirubinemia

Variables		Preterm	Term
Age in hours (Mean ± SD)		118.12±42.78	122.28±41.19
Sex	Male	30	66
	Female	30	74
Gestational age in weeks (Mean ± SD)		36.24±0.76	37.83±0.84
Birth weight in grams (Mean ± SD)		2723.17±246.44	3132.78±370.90
TSB in mg/dl at 0 hours (Mean ± SD)		17.3±2.38	19.03±1.94
Serum calcium in mg/dl at 0 hours (Mean ± SD)		9.43±0.91	9.63±0.81
Duration of phototherapy in hours (Mean ± SD)		66±8.52	65.55±8.72

The mean age of preterm and term neonates was 118.12±42.78 and 122.28±41.19. There were more males as compared to females in preterm and term neonates. Mean birth weight of preterm and term in this study were 2723.17±246.44 grams and 3132.78±370.90 grams respectively.

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	10	
	Hypocalcemia absent	60	130	1
	Total	60	140	
After 48 hours	Hypocalcemia present	0	20	
	Hypocalcemia absent	60	120	0.17
	Total	60	140	

10 term neonates experienced hypocalcemia at 12 hours after starting of phototherapy. Similarly, 20 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.

Table 3: Comparison of serum calcium at 0 hour with subsequent hours (at 12 hours and after 48 hours) in term and preterm neonates receiving phototherapy

Gestationalage (Weeks)	Comparison of serum calcium(Hours)	Mean paireddifference (mg/dl) ± SD	P value
Preterm(34-37)	0 and at 12	0.518±0.602	0.006
	0 and after 48	0.713±0.858	0.007
Term (38-41)	0 and at 12	0.528±0.712	<0.001
	0 and after 48	0.915±0.775	<0.001

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 and the difference was seen to be more significant in term babies.

Table 4: Correlation of hypocalcemia in term neonates with duration of phototherapy

Correlation	R	CI for r	P value
Negative	-0.045	-0.740 to 0.773	0.95

Correlation analysis of a duration of phototherapy with hypocalcemia showed a negative but insignificant correlation with a coefficient (r of −0.045 and a p=0.95).

Discussion

Bilirubin buildup causes yellow skin, sclera, and mucous membranes. [14] About 60% of term and 80% of preterm infants have it in the first week of life. [2] Most newborns do not need treatment for jaundice, but 5-10% need. [15,16] High unconjugated bilirubin levels can harm the brain permanently. [17,18] One treatment for newborn hyperbilirubinemia is phototherapy. Phototherapy has benefits but sometimes causes issues like hypocalcemia. [19] Phototherapy causes 8.7% of full-term infants to have hypocalcemia. [20] After more than 48 hours of phototherapy, 39% of term and 53% of preterms had hypocalcemia. [21] Unless recognized and treated early, newborns with hypocalcemia, a significant phototherapy consequence, have a higher death risk than those with normocalcemia. [21,22]

The mean age of preterm and term neonates was 118.12±42.78 and 122.28±41.19. There were more males as compared to females in preterm and term neonates. Mean birth weight of preterm and term in this study were 2723.17±246.44 grams and 3132.78±370.90 grams respectively. 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. [23] Hypocalcemia refers to total serum calcium level less than 8 mg/dl in term neonates and less than 7 mg/dl in preterm neonates. [24] Hypocalcemia may cause cardiac and neurological dysfunctions. It may be symptomatic in the form of jitteriness, apnea, lethargy, stridor, irritability, and seizures. [25]

10 term neonates experienced hypocalcemia at 12 hours after starting of phototherapy. Similarly, 20 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. In the study by Chandrashekhar [26] 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. Phototherapy is the most effective therapy for management of neonatal hyperbilirubinemia which lowers serum bilirubin level by converting bilirubin into non-toxic excretable form. [27] Phototherapy converts unconjugated bilirubin to more polar stereoisomer by a process called photo isomerization. The substance formed cannot cross the blood brain barrier and is not neurotoxic and later on excreted out of the body via urine and bile. [28]

The mean difference in total blood calcium levels in term and preterm neonates was statistically significant, with term babies having a greater difference. The connection between phototherapy duration and hypocalcemia was negative but negligible (r = -0.045, p=0.95). This suggests that term neonates' hypocalcemia before discharge is minimal due to phototherapy. However, no analogous studies have been published to investigate the link between phototherapy duration and hypocalcemia before discharge (after 48 hours).

Conclusion

The present investigation found that phototherapy reduces serum calcium, but not to the point of treatment. Thus, infants getting phototherapy should not have blood calcium levels monitored.

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