Original Research Article

Effect of phototherapy on serum calcium level in term newborns

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ABSTRACT

Background: Hyperbilirubinemia is one of the most prevalent problems in neonates. Jaundice is observed during first week of life in approximately 60% of term neonates and 80 % of preterm neonates. Phototherapy is one of the routine methods for management of hyperbilirubinemia. The aim of this study is to assess the effect of phototherapy on serum calcium level in term newborns with neonatal hyperbilirubinemia who undergo phototherapy and to find out the association between effect of phototherapy on serum calcium level and birth weight, postnatal age, type of feeding and blood group incompatibility.

Methods: 100 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: 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 (p value <0.001). Only 3 babies developed hypocalcemia (serum calcium <7 mg/dl). None of them were symptomatic. There was no significant association between reduction in serum calcium level and birth weight, postnatal age, type of feeding and blood group incompatibility.

Conclusions: There is significant reduction in serum calcium level after phototherapy but risk of hypocalcemia is low in healthy full-term neonates. No significant association was found between reduction in serum calcium level and birth weight, postnatal age, type of feed, and blood group incompatibility.

Keywords: Hyperbilirubinemia, Hypocalcemia, Newborns, Phototherapy

INTRODUCTION

Hyperbilirubinemia is one of the most prevalent problems in neonates. Jaundice is observed during first week of life in approximately 60% of term neonates and 80% of preterm neonates.

No intervention is required in most cases but 5-10 % of them have significant hyperbilirubinemia and use of phototherapy becomes mandatory. Jaundice is due to physiological immaturity of the neonates to handle increased bilirubin production. Untreated severe

unconjugated hyperbilirubinemia is potentially neurotoxic.¹

Phototherapy is one of the routine methods for management of hyperbilirubinemia. It plays a significant role in prevention and treatment of hyperbilirubinemia. It is very fortunate that a non-invasive and easily available modality, phototherapy, is effective in degrading unconjugated bilirubin.² Phototherapy with blue light is widely used in clinical practice.³ However, it is not a harmless intervention. Commonly known adverse effects of phototherapy are dehydration, hyperthermia, chills, skin rashes, loose stools, retinal damage, bronze baby

syndrome, redistribution of blood flow, genotoxicity, opening of PDA in LBW and hypocalcemia.^{4,5}

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 ionized calcium concentration of <4mg/dl (<1mol/L). Ionized calcium is crucial for many biochemical processes, including blood coagulation, neuromuscular excitability, cell membrane integrity and function, and cellular enzymatic and secretory activity. Hypocalcemia increases cellular permeability to sodium ions and increases cell membrane excitability.⁶ It can cause serious complications like, convulsions, apnoea stridor irritability, and jitteriness.⁷

Ramagnoli et al for the first time suggested the association of hypocalcemia with phototherapy in preterm newborns.⁸ Hakinson and Hunter hypothesised that phototherapy inhibits secretion of melatonin from pineal gland which blocks the effect of cortisol on bone calcium. So, cortisol increases bone uptake of serum calcium and induces hypocalcemia.^{9,10} Kim suggested that decreased secretion of parathyroid hormone is the cause of hypocalcemia in phototherapy.¹¹

In 2012, Yadav et al study showed that hypocalcemia occurred in 80% of pre-term neonates and in 66.6% of full-term neonates given phototherapy. The occurrences were symptomatic in 80% of the full-term neonates and in 100% of the pre-term neonates.¹² Another study was performed by Tehari A et al in 2008 and 2009 in Tehran, and the results showed that, after 48 hours of phototherapy, 7% newborns developed hypocalcemia.¹³ Some other studies are also available concerning the prevalence of hypocalcemia in neonates after phototherapy, but the results varied based on where the studies were conducted. 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. So, more studies are required to reach a definite conclusion. Through this study our aim was to evaluate whether significant change in serum calcium level occurs in term newborns who are undergoing phototherapy and to find out the association between effect of phototherapy on serum calcium level and birth weight, postnatal age, type of feeding and blood group incompatibility.

METHODS

This cross-sectional study was conducted from January 2015 to June 2016 at Government TD Medical college Alappuzha. The study was approved by the institutional research committee and the ethical committee.

All full-term newborns in the inborn nursery, outborn nursery and the special newborn care unit with hyperbilirubinemia undergoing double surface phototherapy for a duration of atleast 48 hours with blue

light were included in the study. Infants of diabetic mothers and those with mothers having a history of taking anticonvulsants were excluded. Babies with APGAR of less than 7 at 5 minutes, those who had exchange transfusion, with jaundice lasting more than 14 days, babies with sepsis and those with serum calcium less than 7 mg/dl before phototherapy were also not included.

Sample size was calculated to be 99 based on previous studies and expecting a non responsive state of 25%. Hence sample size was taken as 100.

After getting written consent from one of the parents, all babies fulfilling the inclusion criteria were enrolled in the study. Complete history and appropriate physical examination was done in all selected cases. Birth weight, age in hours at the time of diagnosis of hyperbilirubinemia, type of feed, and blood group incompatibility were noted. 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. Those babies who needed less than 48 hours phototherapy and those who developed sepsis during phototherapy, were also excluded from the study. 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 is considered as hypocalcemia. 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 Social Sciences (SPSS). Data was expressed in frequency and percentage as well as mean and standard deviation. To elucidate the associations and comparisons between different parameters, Chi square (χ^2) test was used as nonparametric test. Student's t test was used to compare mean values between two groups. For all statistical evaluations, a two-tailed probability of value, <0.05 was considered significant.

RESULTS

Study was done in 100 term newborns. Out of these 59 babies were males and 41 babies were females. 63 babies were born via normal vaginal delivery and 33 via cesarean section and 4 via assisted vaginal delivery. Majority of babies (49%) had a birthweight between 2.6-3 kg and most of them (60%) developed jaundice at 25-48 hours of age.

Table 1: Frequency distribution table of serum calcium values before PT.

S. calcium before PT	Frequency	Percent
7.0 - 7.9	1	1
8.0 - 8.9	38	38
9.0 - 9.9	42	42
10.0 - 10.9	19	19
Total	100	100

After phototherapy about 67% of babies had a decrease in serum calcium level from the initial value.

Out of these, 32% had a 5-9% reduction in serum calcium value and 20% had greater than 10% reduction in serum calcium value. This reduction in serum calcium was found to be statistically significant (p value<0.001).

Figure 1: Frequency distribution of S. Calcium levels after PT.

Even though 67% babies had reduction in calcium value only 3% of babies developed hypocalcemia (serum calcium <7 mg/dl).

Table 2: Frequency distribution showing change in serum calcium value after phototherapy.

Effect of PT on S. Calcium	Frequency	Percent
No Change	9	9
Decrease	67	67
Increase	24	24
Total	100	100

None of these babies were symptomatic and they were started on oral calcium supplement. The repeat serum calcium value at 24hr after stopping phototherapy was normal in all of them.

Figure 2: Frequency distribution showing percentage reduction in s. calcium value after phototherapy.
Table 3: Comparison of mean S. calcium (mg/dL) before and after phototherapy.

Parameter	Observation	Mean	+SD	t value	p value
S. Calcium	Before PT	9.27	0.73	6.551	< 0.001
	After PT	8.88	0.70		

Table 4: Frequency table showing comparison of distribution of S. Calcium before and after PT

S. calcium: before PT	S. calcium: after PT					Total
	6.0 - 6.9	7.0 - 7.9	8.0 - 8.9	9.0 - 9.9	10.0 - 10.9	
7.0 - 7.9	1					1
	33.30%					1.00%
8.0 - 8.9	2	4	26	6		38
	66.70%	100.00%	54.20%	15.40%		38.00%
9.0 - 9.9			18	24		42
			37.50%	61.50%		42.00%
10.0 - 10.9			4	9	6	19
			8.30%	23.10%	100.00%	19.00%
Total	3	4	48	39	6	100
Chi Square: 82.361; P <0.001						

The mean value of calcium before phototherapy was 9.27 ± 0.73 and mean value of serum calcium after phototherapy was 8.88 ± 0.70 . This reduction in serum calcium level after phototherapy was found to be statistically significant (p value < 0.001).

Table 5: Association between birth weight and effect of PT on S.Ca.

Birth weight (Kg)	Effect of PT on S.Ca			Total
	No change	Decrease	Increase	
2.1 - 2.5	1 11.10%	5 7.50%		6 6.00%
2.6 - 3.0	4 44.40%	34 50.70%	11 45.80%	49 49.00%
3.1 - 3.5	4 44.40%	22 32.80%	11 45.80%	37 37.00%
3.6 - 4.0		6 9.00%	2 8.30%	8 8.00%
Total	9	67	24	100
Chi Square: 3.954; $P > 0.05$				

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

Figure 3: Association between and BG incompatibility and effect of PT on S.CA.

DISCUSSION

Neonatal jaundice is one of the leading causes of NICU admission. And phototherapy is one of the best and safe method as a treatment option in neonatal jaundice as described by Cremer et al in 1953. Every safe method has its own side effects and so also phototherapy. One of the known side effects of phototherapy is hypocalcaemia.

Romagnoli was the first to suggest the association of hypocalcaemia and phototherapy in preterms.⁸ Hakinson and Hunter hypothesized that phototherapy inhibits pineal secretion of melatonin which blocks the effect of cortisol on bone calcium.^{9,10} So, cortisol increases bone uptake of calcium and induces hypocalcaemia.

In present study, it was found that after phototherapy about 67 % babies had a decrease in serum calcium level from the initial value. Out of these 32% babies had a 5-9% reduction and 20 % babies had $>10\%$ reduction in serum calcium value. This reduction in serum calcium level was found to be statistically significant (p value < 0.001). Even though 67% babies had a reduction in calcium value only 3% babies developed hypocalcaemia after phototherapy. These results are comparable 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.¹³ Another study done by Karamifar et al in Iran also reported that out of 91 term babies 8.7% had developed hypocalcaemia after 48 hrs of phototherapy.¹⁴ Out of 3 babies who developed hypocalcaemia in our study no one was symptomatic. Similar results were found in Karamifar's study, 8.7% babies developed hypocalcaemia but none of the babies developed symptoms.¹⁴ But in Eghbalian's study, one of the hypocalcaemic newborns had apnea.¹⁵ In Yadav's study 80% of hypocalcaemic term neonates became symptomatic, the most common sign being jitteriness.¹²

In present study, the mean value of serum calcium before phototherapy was 9.27 ± 0.73 and mean value of calcium after phototherapy was 8.88 ± 0.70 . This reduction in mean serum calcium value was found to be statistically significant based on t-test (p value < 0.001). Similar result was shown in study done by Tehari et al.¹³

However, the reported prevalence of hypocalcaemia in some other studies was more than our study. Arora et al reported that 56% term babies developed hypocalcaemia.¹⁶ Yadav et al reported 66% term babies had hypocalcaemia and Jain B K et al also observed hypocalcaemic effect of phototherapy in 30% term and 55% preterm neonates. Similarly, in 2006, Medhat from Cairo University observed 75% of term and 90% of preterm developed hypocalcaemia after phototherapy.¹⁷

Observation of the present study and some Iranian studies like Thehari et al and Karamafir et al was much lower than the above-mentioned studies.¹⁴ The exact reason for this difference is not known. One reason could be that some studies like Arora et al and Manoj GM et al taken serum calcium value < 8 mg/dl as hypocalcaemia, so they got a higher prevalence of hypocalcaemia.^{16,18}

Also, Arora et al have done their study in 54 term babies, Yadav et al in 15 term babies, Jain BK et al in 20 term babies. The small sample size could be the reason why they got a high prevalence of hypocalcaemia.

In some studies, like Yadav et al the ionized calcium level was measured and they got a higher prevalence.¹² In the present study, we examined total serum calcium and not ionized calcium. Ionized calcium is the active component which is kept under control by the various

physiological mechanisms involved in calcium homeostasis. Albumin and pH may influence the distribution of total serum calcium level. Hence the use of total serum calcium rather than ionized calcium can be considered as one of the limitations of present study.

It is not known whether other factors like the type of fluorescent tube used, method of estimation of serum calcium level etc have also affected the results.

In present study, there was no significant association between reduction in serum calcium level and other parameters like, birthweight, postnatal age, type of feeding and blood group incompatibility. Similar results were reported by Manoj GM et al and Karamafir et al in their studies.^{14,18}

Based on this study it is suggested that, even though the prevalence of hypocalcemia is less there is significant reduction in serum calcium level in term newborns undergoing phototherapy, so it is better to monitor S. calcium level in newborns treated with phototherapy for 48 hrs or more. We recommend further and larger studies for estimation of prevalence of hypocalcemia in phototherapy.

CONCLUSION

There is significant reduction in serum calcium level after phototherapy but risk of hypocalcemia is low in healthy full-term neonates. No significant association was found between reduction in serum calcium level and birth weight, postnatal age, type of feeding and blood group incompatibility. Therefore, we do not recommend using prophylactic calcium in healthy, full-term neonates with hyperbilirubinemia during phototherapy. However, we recommend monitoring serum calcium concentrations during and after phototherapy in all term babies.

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