

Phototherapy Induced Hypocalcaemia in Neonates with Jaundice

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ABSTRACT

Introduction: Neonatal hyperbilirubinemia is seen mainly in the first week of life and in many of the cases it is only in physiological range which requires no intervention. Approximately 5-10% of them have clinically significant jaundice that requires phototherapy and even exchange transfusion. Phototherapy can produce various adverse effects; hypocalcaemia is one of the lesser known effects. So, estimation of calcium levels before and after phototherapy should be done in neonates with jaundice. **Aims:** The aim of this study is to determine hypocalcaemia, in neonates receiving phototherapy, by measuring serum calcium levels. **Methods:** This cross sectional study was conducted, from February 2020 to August 2020, on 50 neonates admitted in Neonatal Intensive Care Unit of Nepalgunj Medical College, Kohalpur with unconjugated hyperbilirubinemia requiring phototherapy. Serum calcium levels were evaluated before and after phototherapy. Neonates were assessed for clinical features of hypocalcaemia i.e. jitteriness, irritability/ excitability and convulsions. Data were analyzed using SPSS version 25. P value <0.05 was taken as significant. **Results:** Frequency of hypocalcaemia after phototherapy was 26%. There was significant change in serum calcium levels before and after phototherapy ($p < 0.01$). Among hypocalcaemic neonates, 56% were symptomatic; 38% developed jitteriness, 18% developed irritability / excitability and none of them developed convulsions. **Conclusion:** Neonates undergoing phototherapy are at increased risk for hypocalcaemia. Monitoring for hypocalcaemia and its complications should be considered. However, universal recommendation of calcium supplementation is yet to be established but seems reasonable.

Keywords: Hypocalcaemia, Jaundice, Neonates, Phototherapy

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INTRODUCTION

Jaundice is a common cause of morbidity encountered in neonates, mainly in the first week of life. It is an utmost concern for physicians and source of anxiety for parents.¹ Jaundice in newborns occurs when the level of bilirubin rises more than 5-6 mg/dl. It is observed in 60% of term and 80% of preterm neonates.² In majority of cases, it is benign and no intervention is required. Approximately 5-10% of them have clinically significant jaundice that requires treatment.³ High bilirubin level may be toxic to the developing central nervous system and may elicit neurological impairment.⁴ Phototherapy is one of the modalities for management of hyperbilirubinemia in neonates which is convenient and readily available.⁵ Phototherapy may lead to various complications including skin rashes, diarrhea, hyperthermia, dehydration, retinal degeneration, bronze baby syndrome especially in cholestatic jaundice, opening of patent ductus arteriosus in low birth weight neonates and hypocalcemia.⁶

Neonatal hypocalcaemia is defined as total serum calcium concentration < 7 mg/dl or ionized calcium concentration < 4 mg/dl. Ionized calcium is crucial for many biochemical processes, including blood coagulation, neuromuscular excitability, and cellular enzymatic activities.⁷ The overall prevalence of hypocalcaemia in neonates receiving phototherapy was 8.7% in full-term newborns.¹ In another investigation, 90% of the preterm and 75% of term neonates experienced hypocalcaemia after phototherapy.⁸ Hypocalcaemia can cause serious manifestations like convulsions, apnea, laryngospasm, irritability, and jitteriness.⁹ Hence, phototherapy-induced hypocalcaemia can be a significant problem. This study was undertaken to determine hypocalcaemia, in neonates receiving phototherapy, by measuring serum calcium levels.

METHODS

The cross sectional study was carried out in the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics,

Nepalgunj Medical College, Kohalpur from February 2020 to August 2020. Ethical clearance was obtained from the institutional Review Committee, Nepalgunj Medical College and Teaching Hospital. Study included 50 neonates who were admitted for phototherapy. Selection of cases was done by convenient sampling method. Neonates were divided in two groups- preterm and term. Informed consent was taken from their parents/guardians. Complete history and thorough physical examination was carried out in all the cases. Serum calcium was measured at initiation of phototherapy and 24 hours after completion of phototherapy. Neonates with jaundice requiring exchange transfusion, birth asphyxia, sepsis, and conjugated hyperbilirubinemia, infants of diabetic mother and with congenital anomalies were excluded from the study.

Requirement of phototherapy was decided based on American Academy of Pediatrics (AAP) Guidelines and according to birth weight in preterm neonates.¹⁰ The neonates were clinically assessed for features of hypocalcaemia i.e. jitteriness, irritability/excitability and convulsions, as well as other complications like rashes, loose stool, fever and dehydration. Hypocalcaemia in the neonates was managed with intravenous calcium supplementation.

Data were analyzed using statistical software SPSS 25. The results were calculated as mean ± standard deviation and compared based on the paired t-test. P <0.05 was considered statistically significant.

RESULTS

In the study, 50 neonates admitted in NICU for phototherapy were evaluated for hypocalcaemia. Among them 25(50%) were preterms and terms were 25(50%). Male newborns were 28(56%) and 22(44%) were females. Most of the neonates were exclusively breastfed 23(46%), 11(22%) of them were under lactogen feeding because of inadequate milk let down in mothers, and rest 16(32%) were under mixed feeding (mother’s milk and lactogen).

	Preterm (Mean±SD) (n=25)	Term (Mean±SD) (n=25)	p-value
Serum calcium before phototherapy (mg/dl)	8.42±0.9	9.90±3.1	<0.01
Serum calcium after phototherapy (mg/dl)	8.12±3.4	8.73±4.2	<0.01

Table I: Comparison of serum calcium level before and after phototherapy.

Frequency of hypocalcaemia after phototherapy was 20% and 32% in preterms and terms respectively. Mean serum calcium level before and after phototherapy was 8.42±0.9 mg/dl and 8.12±3.4 mg/dl in preterms, whereas it was 9.90±3.1 mg/dl and 8.73±4.2 mg/dl in term neonates. Statistical analysis showed hypocalcaemia was significant in both the groups, preterms and terms (p<0.01). (Table I).

Total serum calcium level (mg/dl)	Before Phototherapy (n=50)		After Phototherapy (n=50)		p- value
	Mean	SD	Mean	SD	
	9.1	2.3	8.9	3.8	<0.01

Table II: Change in serum calcium level with phototherapy.

In the present study, there was a significant decrease in serum calcium levels after phototherapy (p<0.01). The mean values of serum calcium before and after phototherapy were 9.1±2.3 mg/dl and 8.9±3.8 mg/dl respectively (Table II). Of the 50 neonates in the study, 13(26%) showed hypocalcaemia after phototherapy; among those 13 neonates, 56% developed hypocalcaemia symptoms; 18% developed irritability/excitability, 38% developed jitteriness and none of them developed convulsions.

DISCUSSION

Neonatal jaundice is a frequent cause of morbidity in newborns worldwide and significant cause of hospitalization, mainly in the first week.¹ Efficacy of phototherapy in treatment of hyperbilirubinemia in newborns has been well established. The efforts made around the globe recognize it as a potential complication with variable results, some showing severe hypocalcemia.⁷ Romagnoli et al. was the first to suggest the association of hypocalcaemia in a newborn following phototherapy.¹¹ Abrams SA hypothesized that phototherapy inhibits pineal secretion of melatonin which blocks the effect of cortisol on bone calcium. Cortisol unchecked exerts a direct hypocalcaemia effect and increases bone uptake of calcium as well.¹² In a study by Khan et al. there were 62.6% males and 37.4% females.¹ Also in a study by Alizadeh TP there were 49% female neonates and 51% were males.¹³ Observation in our study is similar to the above studies where number of male neonates is higher than that of females. Yadav et al observed that 66% of term and 80% of preterms developed hypocalcaemia after phototherapy.⁷ Sethi et al. reported that 90% of preterm neonates and 75% of full-term neonates developed hypocalcaemia after being subjected to phototherapy.⁸ This is in contrast to the present study where terms were 50% and preterms were also 50%. The selection method being convenient sampling method is attributed for this contrast. In the present study, mean serum calcium level before and after phototherapy was 8.42±0.9mg/dl and 8.12±3.4mg/dl respectively in preterms, whereas it was 9.90±3.1mg/dl and 8.73±4.2mg/dl respectively in term neonates. Statistical analysis showed hypocalcaemia was significant in both the groups, preterms and terms (p<0.01). Similar to the study by Shrivastava J *et al.* where the serum calcium level before and after phototherapy in preterm babies was 8.82 ±0.59 mg/dl and 6.64 ± 1.03 mg/dl respectively, whereas in term neonates it was 9.32 ± 0.99 mg/dl and 7.58 ± 0.83mg/dl respectively. Hypocalcaemia after phototherapy was statistically significant (p<0.001).¹⁴ Also in a study by

Singh PK et al. the mean serum calcium level in the preterm neonates before and after phototherapy was 8.41 mg/dl \pm 0.466 and 7.1 mg/dl \pm 0.793 respectively. In term neonates the mean serum calcium level was 9.52mg/dl \pm 0.53 and 8.42mg/dl \pm 1.1 respectively. Change in calcium level was statistically significant ($p < 0.05$).¹⁵

In a study by Goyal S et al. mean serum calcium levels before phototherapy was 9.14 \pm 0.78mg/dl and it reduced to 8.53 \pm 0.77mg/dl after phototherapy. The reduction was statistically significant ($p < 0.001$).¹⁶ Alizadeh TP et al. in their study found the mean serum calcium levels before and after phototherapy were 9.8 \pm 0.8 mg/dl and 9.5 \pm 0.9 mg/dl respectively. The difference in serum calcium level before and after phototherapy was statistically significant ($p = 0.03$).¹³ Similar to the present study where mean values of serum calcium before and after phototherapy were 9.1 \pm 2.3 mg/dl and 8.9 \pm 3.8 mg/dl respectively. Also there was a significant decrease in serum calcium levels after phototherapy ($p < 0.01$). In the present study, 13 out of 50 neonates showed hypocalcaemia after phototherapy. Among them 56% were symptomatic; 38% developed jitteriness, 18% developed irritability/excitability, and none of them developed convulsions. Similar to the study by Yadav RK et al. where 30% of hypocalcaemia neonates developed jitteriness, 20% developed irritability/excitability, 30% developed letharginess and none of the neonate developed convulsions.⁷ In a study done by Jain BK et al. 63.6% of hypocalcaemia preterm newborns had jitteriness and 27.3% had irritability whereas 50% of hypocalcaemia term neonates had jitteriness and 16.7% were irritable.¹⁷

LIMITATIONS

Duration of phototherapy is not constant for all the neonates which might have affected the results. In the same manner, age at initiation of phototherapy is also not same in all cases, there might be exaggeration of physiological hypocalcaemia in some neonates. Also the number of cases taken in the current study is small, larger case number would have given more precise and more reliable results.

CONCLUSION

Phototherapy induced hypocalcaemia is a significant finding in neonates with jaundice. Therefore, estimation of calcium levels before and after phototherapy and close monitoring of neonates for signs of hypocalcaemia should be done as well as treated accordingly. A universal recommendation of calcium supplementation in neonates undergoing phototherapy is yet to be established but seems reasonable taking into account the evidence in various studies.

REFERENCES

1. Khan M, Malik KA, Bai R. Hypocalcemia in jaundiced neonates receiving phototherapy. *Pak J Med Sci.* 2016;32(6):1449-52.
2. Imani M, Sadeghi-bojd S, Falahati KF, Moghadam AA. Effect of Phototherapy Treatment on Urinary Calcium Excretion in Neonates with Jaundice in Zahedan, Iran. *Iranian Journal of Neonatology IJN.* 2018;9(4):61-5.
3. Hansen TWR. Twists and turns in phototherapy for neonatal jaundice. *Acta Paediatrica.* 2010;99(8):1117-8.
4. Kaplan M, Bromiker R, Hammerman C. Severe neonatal hyperbilirubinemia and kernicterus: Are these still problems in the third millennium? *Neonatology.* 2011;100(4):354-62.
5. Pal S, Kalra BP, Kalra V. A study of serum-ionized calcium in neonates with unconjugated hyperbilirubinemia on phototherapy. *Indian J Child Health.* 2018;5(4):284-8.
6. Xiong T, Qu Y, Cambrier S, Mu D. The side effects of phototherapy for neonatal jaundice: What do we know? What should we do? *Eur J Pediatr.* 2011;170(10):1247-55.
7. Yadav RK, Sethi RS, Sethi AS, Kumar L, Chaurasia OS. The evaluation of the effect of phototherapy on serum calcium level. *People's J Sci Res.* 2012;5(2):1-4.
8. Sethi HA, Saili AR, Dutta AK. Phototherapy induced hypocalcemia. *Indian pediatrics.* 1993;30(12):1403-6.
9. Maisels MJ. Jaundice. In: *Avery's Neonatology Pathophysiology and management of the Newborn.* McDonald MG, Mullet MD, Seshia MMK. 6th ed. Lippincott Williams & Wilkins; 2005. p. 768-846.
10. American Academy of Pediatrics Subcommittee on hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics.* 2004;114:297-316.
11. Romagnodi C, Polidori G, Cataldi L, Tortorolo G, Segni G. Phototherapy-induced hypocalcemia. *J Pediatr.* 1979;94(5):815-6.
12. Abrams SA: Abnormalities of serum Calcium and Magnesium. In: Cloherty JP, Eichenwald EC, Hansen AR, Stark AR, editors. *Manual Of Neonatal Care.* 7th ed. New Delhi: Lippincott Williams & Wilkins; 2015. p.297-303.
13. Alizadeh TP, Sajjadian N, Eivazzadeh B. Prevalence of Phototherapy Induced Hypocalcemia In Term Neonate. *Iran J Pediatr.* 2013; 23(6):710-1.
14. Shrivastava J, Singh A. Phototherapy Induced Hypocalcemia in Neonates. *Sch. J. App. Med. Sci.,* 2015;3(8C):2931-3.
15. Singh PK, Chaudhuri PK, Chaudhuri AK. Phototherapy induced hypocalcemia in neonatal hyperbilirubinemia. *IOSR-JDMS.* 2017;16:35-8.
16. Goyal S, Srivastava A, Bhattacharjee P, Goyal I, Malhotra K. Effect of phototherapy on serum calcium levels in neonates receiving phototherapy for neonatal jaundice. *Int J Res Med Sci.* 2018;6:1992-5.
17. Jain BK, Singh H, Singh D, Toor NS. Phototherapy induced hypocalcemia. *Indian pediatrics.* 1998;35(6):566.