

Hypocalcemia in Jaundiced Neonates Receiving Phototherapy

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ABSTRACT

Background: Hyperbilirubinemia is a common problem in neonates. Phototherapy and exchange transfusion are the primary treatment modalities. Less known, but one of the potential complications of phototherapy is hypocalcemia. Most of the neonates with hypocalcemia are asymptomatic. Though asymptomatic, treatment should be initiated immediately when serum calcium level is reduced. This study was conducted to detect the incidence of hypocalcemia in jaundiced neonates receiving phototherapy.

Methods: It is a hospital-based cross-sectional study conducted from May 2020 to December 2020 in the neonatal intensive care unit of Nepal Medical College Teaching Hospital. A total of 128 full-term neonates with jaundice and a normal serum calcium level before initiating phototherapy were enrolled in the study. Serum calcium level was measured before starting conventional phototherapy and after 48 hours of continuous phototherapy.

Results: Hyperbilirubinemia was present in 23.3% of neonates admitted to the neonatal unit. Hypocalcemia was seen in 26 (20.3%) of term jaundiced neonates receiving phototherapy. Signs of hypocalcemia were present only in 3 (2.3%) neonates.

Conclusions: Hypocalcemia is a common complication of phototherapy. Serum calcium levels should be monitored in all the full-term neonates receiving phototherapy.

Keywords: Hyperbilirubinemia; hypocalcemia; phototherapy

INTRODUCTION

Hyperbilirubinemia is a common problem in neonates, observed during the first week after birth in approximately 60% of term infants and 80% of preterm infants.¹ A study done in Nepal Medical College from 2005 to 2008 showed 10.5% of neonates admitted to NICU had significant hyperbilirubinemia.² Although bilirubin may have a role as an antioxidant, elevation of unconjugated bilirubin is potentially neurotoxic. Phototherapy and exchange transfusion are the primary treatment modalities. The common complications of phototherapy are loose stools, erythematous macular rash, overheating, dehydration, hypothermia, bronze baby syndrome, etc.¹ Less known, but potential complication of phototherapy is hypocalcemia.³ Incidence of hypocalcemia in jaundiced neonates receiving phototherapy was 22.8% and 14.4% in different studies.^{4,5} In many cases neonates with hypocalcemia are asymptomatic.³ Treatment should be initiated immediately even in asymptomatic patients to avert complications attributable to reduced calcium

level.⁶

This study was conducted to detect the occurrence of hypocalcemia in jaundiced neonates receiving phototherapy.

METHODS

It is a hospital-based cross-sectional study conducted from May to December 2020 in the neonatal intensive care unit of Nepal Medical College Teaching Hospital. A total of 128 newborn babies who fulfilled the inclusion criteria were enrolled in the study. They were the full-term neonates with jaundice requiring phototherapy and had a normal serum calcium level before initiating phototherapy. The preterm babies who were born before 37 weeks of gestation, the babies with birth asphyxia, sepsis, infants of the diabetic mother were excluded from the study. The gestational age was assessed using Modified Ballard Score. A sample of 3 ml of venous blood was sent to the laboratory for serum calcium level before

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initiating conventional phototherapy and after 48 hours of initiating phototherapy, irrespective of the duration of phototherapy. Hypocalcemia is defined as a total serum calcium concentration of less than 8mg/dL (2mmol/L) or an ionized calcium concentration of less than 4.4mg/dL (1.1mmol/L) for term neonates.⁶ Calcium concentration was measured using the dry chemistry method. Detail maternal and neonatal history was obtained. Complete physical examination of all the newborns including head-to-toe examination was done. Presence of any of the signs of hypocalcemia: jitteriness, convulsions, apnea, arrhythmia, and irritability in neonates during the period was recorded. Written informed consent was obtained from all the parents. Data of the patient was collected in a preformed proforma. Data was analyzed using SPSS 16 software applying the Chi-square test and p-value <0.05 was considered significant. Ethical clearance was obtained from the Institutional Review Committee of Nepal Medical College (Ref. no. 009-077-78; dated August 12, 2020).

RESULTS

A total of 128 neonates who fulfilled the inclusion criteria were included in the study. Out of them, 74 (57.8%) were male and 54 (42.2%) were female. The incidence of hyperbilirubinemia was 23.3%. After 48 hours of phototherapy, hypocalcemia was seen in 26 (20.3%) newborns with jaundice. Signs of hypocalcemia was present only in 3 (2.3%) neonates. Jitteriness was the only sign present in all the symptomatic cases.

The mean duration of phototherapy was 1.91 days and serum calcium level before and after phototherapy was 8.74 mg/dL and 7.19 mg/dL respectively. Statistical significance of hypocalcemia was not observed with gestational age (p=0.100), sex (p=0.990), duration of phototherapy (p=0.470), weight (p= 0.73) except with the age of newborn (p=0.04) (Table. 1).

Table 1. Frequency of hypocalcemia with respect to age, weight, gender, gestational age and duration of phototherapy.

	Hypocalcemia		Total	P-value
	Yes	No		
Age group (days)				
≤ 5	19 (24.0 %)	60 (75.9%)	79	0.04
5.1 to 10	4 (11.1%)	32 (88.8%)	36	
10.1 to 15	3 (25.0%)	9 (75.0%)	12	
15.1 to 20	0 (0%)	1 (100%)	1	
Gender				

Male	14 (18.9%)	60 (81.0%)	74	0.90
Female	12 (22.2%)	42 (77.8%)	54	
Gestational Age (weeks)				
37+1 to 40	24 (23.3%)	79 (76.7%)	103	0.10
> 40	2 (8.0%)	23 (92.0%)	25	
Duration of phototherapy (days)				
1	6 (35.3%)	11 (64.7%)	17	0.47
2 to 5	20 (18.9%)	86 (81.1%)	106	
> 5	0 (0%)	5 (100%)	5	
Weight (Kg)				
< 2.5	0 (0%)	3 (100%)	3	0.73
2.5 to 4	26 (21.3%)	96 (78.7%)	122	
> 4	0 (0%)	3 (100%)	3	

DISCUSSION

Neonatal jaundice accounts for one of the majority of admission in the Neonatal Intensive care unit. The incidence of neonatal jaundice in our study was 23.3% whereas the Incidence was only 12.46% at one of the tertiary care centers.⁷ The prevalence of neonatal jaundice was 31% in the mid-western part of Nepal and phototherapy is a very effective treatment modality to reduce the serum bilirubin in most cases.⁸ The variation in the incidence of jaundice noted in different studies may be due to inter-observer variation in detection of jaundice during clinical examination by the health care worker. Also, neonates would present to the hospital after being observed by the family members, that can also cause variability.⁹ In a hospital-based study, phototherapy was required in 95.5% and exchange blood transfusion in 4.6% of cases of neonatal jaundice, which demonstrated the effectiveness of phototherapy in the management of neonatal hyperbilirubinemia.² Although phototherapy is the most widely accepted and effective treatment method for hyperbilirubinemia, it is also associated with both short-term and long-term side effects. It may be associated with long-term side effects such as melanocytic nevi, allergic diseases, and retinal damage.¹⁰ Phototherapy may reduce the pineal secretion of melatonin which causes hypocalcemia due to the unchecked effect of cortisol.³

A study showed that phototherapy leads to a decrease in the level of serum calcium, magnesium, and sodium, where 26% of neonates developed hypocalcemia following phototherapy.¹¹ The result is similar to our study where 20.3% of neonates developed hypocalcemia after 48 hours of initiation of phototherapy. In another study, after 48 hours of phototherapy, 40.0 % of term neonates developed hypocalcemia.¹² The symptom of

hypocalcemia was present in only 3 (2.3%) cases in our study, which is similar to the findings of the study by Karamifar H, et al., where none of the neonates who developed hypocalcemia after phototherapy were symptomatic.⁵

Ionic calcium is crucial for many biochemical process including blood coagulation, neuromuscular excitability, cell membrane integrity, and many of the cellular enzymatic activities.¹³ The signs of hypocalcemia are usually nonspecific: apnea, seizures, jitteriness, increased extensor tone, clonus, hyperreflexia, stridor, etc.¹⁴ In our study, jitteriness was the only sign of hypocalcemia observed in all the neonates who are symptomatic. Neonates after being subjected to phototherapy, develop hypocalcemia which can cause serious complications like jitteriness, lethargy, convulsions, apnea, and irritability, so it requires close monitoring of calcium levels and timely supplementation of calcium to prevent hypocalcemia.¹²

We conducted the study in a single-center and enrolled only the term neonates with jaundice. We also did not evaluate the outcome benefit of detecting and treating hypocalcemia, consequent to phototherapy. Multicentric studies, enrolling both term and preterm neonates and a before and after study design to evaluate the benefit of treating hypocalcaemia, would be beneficial.

CONCLUSIONS

Hypocalcemia is a common complication observed in neonates with jaundice undergoing phototherapy. Monitoring of serum calcium level would be prudent for all the full-term neonates receiving phototherapy. That would facilitate early detection and treatment of hypocalcemia.

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REFERENCES

1. Shaughnessy EE, Goyal NK. Jaundice and hyperbilirubinemia in the newborn. In Kliegman RM, Blum NJ, Shah SS, ST Geme III JW, Tasker RC, Wilson KM, Behrman RE editors. Nelson Text Book of Pediatrics (21th ed). Philadelphia: Elsevier 2020: 953-7.
2. Rijal P, Biccha RP, Pandit BP, Lama L. Overview of neonatal hyperbilirubinemia at Nepal Medical College Teaching Hospital. Nepal Med Coll J. 2011;13(3):205-7. [\[PubMed\]](#)
3. Singh M. Care of the newborn. 5thed. New Delhi: Sagar Publications; 2002.
4. Khan M, Malik KA, Bai R. Hypocalcemia in jaundiced neonates receiving phototherapy. Pak J Med Sci. 2016;32(6):1449-52. [\[PMC\]](#)
5. Karamifar H, Pishva N, Amirhakimi GH. Prevalence of phototherapy-induced hypocalcemia. Iran J Med Sci. 2002;27(4):166-8. [\[Download PDF\]](#)
6. Vuralli D. Clinical approach to hypocalcemia in newborn period and infancy: Who should be treated? Int J Pediatr. 2019;2019:4318075. [\[PubMed\]](#)
7. Chapagain RH, Basaula YN, Kayastha M, Adhikari K, Shrestha SM. Disease profile and hospital outcome of newborn admitted to neonatal intermediate care unit at tertiary care center in Nepal. Kathmandu Univ Med J. 2017;58(2):126-9. [\[Download PDF\]](#)
8. Roma KM, Kanodia P, Pyakurel M, Gupta V. A study of neonatal hyperbilirubinemia in Mid-Western part of Nepal. Journal of Nepalgunj Medical College. 2017; 15(2):41-3. [\[Article\]](#)
9. Sharma S. Neonatal hyperbilirubinemia: Hospital based study in Western Region, Nepal. Janapriya Journal of Interdisciplinary Studies. 2017;5:75-82. [\[Article\]](#)
10. Taksande A, Selvam S. Side effects of phototherapy in neonatal hyperbilirubinemia. Acta Scientific Paediatrics. 2018;1(5): 24-30. [\[Download PDF\]](#)
11. Subhashini B, Vani SAV, Das P, Niranjana R. Adverse effects of phototherapy on calcium, magnesium and electrolytes levels in neonatal jaundice. Int J Clin Biochem Res. 2019;6(3):275-8. [\[Article\]](#)
12. Gusain P, Gupta VK, Gupta S, Natani BS, Agrawal S,

- Yadav N, et al. Comparative analysis of symptomatic hypocalcemia in term and preterm neonates undergoing continuous phototherapy. *J Dent Med Sci* 2017; 16:46-9. [\[Article\]](#)
13. Jain A, Agrawal R, Sankar MJ, Deorari A, Paul VK. Hypocalcemia in the newborn. *Indian J Paediatr.* 2010;77:1123-8. [\[PubMed\]](#)
14. Steve A, Abrams. Abnormalities of serum calcium and magnesium. In Cloherty JP, Eichenwald EC, Hansen AR, Stark AR, editors. *Manual of neonatal care* (7th ed). Philadelphia: Lippincott Williams & Wilkins 2012: 297-303.