

A comparative study of occurrence of phototherapy induced hypocalcemia in preterm and fullterm neonates with unconjugated hyperbilirubinemia



Pediatrics

KEYWORDS: Neonatal hyperbilirubinemia; Phototherapy; Hypocalcemia

Dr. Jitendra Prasad Bhatnagar

Assistant Professor, Department Of pediatrics, NIMS University, Jaipur (INDIA)

Dr. Virendra Kumar Gupta

Assistant Professor, Department Of pediatrics, NIMS University, Jaipur (INDIA)

Dr. Shagun Gupta

Assistant Professor, Department Of Obstetric & gynaecology, NIMS University, Jaipur (INDIA)

Dr. Preeti Gusain

Resident, Department Of pediatrics, NIMS University, Jaipur (INDIA)

ABSTRACT

Unconjugated hyperbilirubinemia is one of the most common problem that can occur in the newborn. This prospective cross sectional study was conducted in NIMS Medical College, Jaipur, Rajasthan, India, during period from 1st feb 2015 to 31st July 2016. The study group included 200 neonates (155 term and 45 preterm), fulfilling the criteria of jaundice and requiring phototherapy. Measurement of serum calcium level was done before and after 48 hours of initiation of phototherapy in these two groups. Out of 200 neonates, 86 (43%) developed hypocalcemia after 48 hours of phototherapy. Out of 45 preterm 24 (53.33%) and 155 term 62 (40%) neonates ($p=0.156$) developed hypocalcemia. Mean $\pm$ SD serum calcium levels were significantly lowered in both preterm ($p<0.001$) and term neonates ($p<0.001$), while no significant difference was found between these two groups ($p<0.247$). Of the 62 term neonates who had hypocalcemia, 13 (20.96%) were symptomatic and of the 24 preterm neonates who had hypocalcemia, 12 (50%) were symptomatic i.e. jitteriness, irritability/excitability, letharginess etc. **Conclusion:** Phototherapy induced hypocalcemia is a significant problem and there is a need for close monitoring of calcium levels in neonates subjected to phototherapy. Provision of calcium supplementation as prophylaxis and head covering may be considered in neonates subjected to phototherapy.

Introduction

Neonatal hyperbilirubinemia is a common and in most cases benign clinical condition in neonates, affecting approximately 60% of term and 80% of preterm infants first week after birth [1].

Pathophysiological basis of the jaundice is the same in term and preterm neonates, but premature babies are at a higher risk of developing hyperbilirubinemia.

Phototherapy having a significant role in the prevention and treatment of unconjugated hyperbilirubinemia in neonates. Continuous Phototherapy may also lead to undesired effects including skin rash, diarrhea, body temperature rise, chills, trauma to the eye, nasal obstruction, bronze baby and DNA damage [2].

Nonetheless, no change in blood ions/metabolites has been reported except for calcium concentration; a drop in serum calcium has been noticed in patients undergoing phototherapy [3].

Incidence of hypocalcemia proving the effect of phototherapy on the pineal gland eventually causing hypocalcemia which can be declined by covering of head of the neonate while giving phototherapy [4]. Hence, phototherapy induced hypocalcemia is a significant problem. A few studies recommend that in order to prevent hypocalcemia due to phototherapy, babies should be given calcium as prophylaxis [5,6].

1.1 Aims and objectives:

- 1) To study the change in serum calcium levels in neonates with unconjugated hyperbilirubinemia before and after 48 hours of continuous phototherapy
- 2) To compare the occurrence of phototherapy induced hypocalcemia between preterm and fullterm neonates with unconjugated hyperbilirubinemia.

2. Methods and Materials

This is hospital based prospective cross sectional study conducted in Departments of Pediatrics & Obstetrics & Gynaecology in NIMS Medical College, Jaipur, Rajasthan, India, during period from 1st feb

2015 to 31st July 2016.

A total of two hundred neonates (155 term and 45 preterm neonates) aged less than 2 weeks, all were AGA (Appropriate for Gestational Age) who developed hyperbilirubinemia after 72 hours of life, required phototherapy according AAP guidelines [7] included in this study. Neonates who had Conjugated Hyperbilirubinemia, any congenital anomalies or any co-morbidities like: Birth asphyxia, Septicemia, Renal failure were excluded from the study.

Detailed history and examination of neonates with hyperbilirubinemia developing after 72 hours of life was carried out, according to a predesigned proforma. After obtaining written and informed consent from parents or guardians, blood samples from the neonates fulfilling the above mentioned criteria were drawn from a peripheral vein for the estimation of serum bilirubin and serum calcium levels. Total serum bilirubin was estimated by using Jendrassik-Grof's method. Serum calcium was determined by Calcium Arsenazo III method [8].

Continuous phototherapy for 48 hours from a distance of 45cm from the skin using a phototherapy unit comprising of 10 LED lamps with a wavelength range of 450-465nm and a spectral irradiance between $45\mu\text{w}/\text{cm}^2/\text{nm}$ to $22\mu\text{w}/\text{cm}^2/\text{nm}$. The eyes of the neonates were shielded to prevent retinal damage and groin of male neonates were covered to protect the genitalia and head was covered during the procedure.

After 48 hours of continuous phototherapy, blood samples for total serum bilirubin and serum calcium were repeated. The results of serum calcium before and after 48 hours of phototherapy were analyzed.

Hypocalcemia was considered with serum calcium less than 7 mg/dl in preterm infants and less than 8mg/dl in term neonates [9]. The neonates were clinically assessed for features of hypocalcemia i.e. jitteriness, lethargy, apnea and convulsions. All neonates having hypocalcemia were treated as per the AIIMS-NICU protocol for hypocalcemia in neonates [9].

2.6 Statistical analysis

It was performed using Quickcal (Instat) software. Paired t-test was used for comparing the calcium levels before and after 48 hours of phototherapy whereas Z-test for proportion was used to compare the various percentages of hypocalcemic neonates.

3. Observations and Results

The study was done on 200 neonates (155 were term and 45 were preterm infants). None of the cases developed jaundice before 72 hours of life. Both term and preterm neonates having mean chronological age was 5 days. The mean±SD weight of preterm neonates was 2.02±0.15 kilogram and the mean±SD weight for full term neonates was 2.66±0.17 kilogram.

Out of 200 neonates, 86(43%) developed hypocalcemia after 48 hours of phototherapy. Out of 45 preterm 24 (53.33%) and 155 term 62 (40%) neonates (p=0.156) developed hypocalcemia.

The mean±SD serum calcium level in admission and 48 hours after phototherapy in term neonates were 8.62±0.24 mg/dl and 7.95±0.36mg/dl respectively (p<0.001). The mean±SD serum calcium level in admission and 48 hours after phototherapy in preterm neonates were 7.41±0.17 mg/dl and 6.81±0.44mg/dl respectively (p<0.001). While the mean ±SD of decline of serum calcium level after 48 hours after phototherapy in preterm and Post term neonates were 0.6677±0.2892 and 0.6044±0.4167mg/dl respectively which is non-significant (p<0.247) (Table 1).

Of the 62 hypocalcemic term neonates, 13(20.96%) were symptomatic and of the 24 hypocalcemic preterm neonates, 12(50%) were symptomatic (p=<.001). i.e. jitteriness, irritability/ excitability, letharginess etc.

4. Discussion

The calcium homeostasis regulation in the neonatal period has been of interest. At birth, the plasma level of calcium (Ca) in cord blood exceeds that in maternal blood. The level of plasma Ca progressively decreases in early days of life in normal infants, so by the second or third day of life, the level is lower than that found in older infants and children. In most normal fullterm infants the plasma Ca level returns to normal by 10th day of life [10].

Cord serum bilirubin level ≤ 2mg/dl are considered safe while ≥2.1mg/dl are highly suggestive of babies who will develop neonatal hyperbilirubinemia [11].

Phototherapy is an appropriate and safe measure to reduce unconjugated bilirubin level in neonates. Roming et al was the first to suggest the association of hypocalcaemia in newborn following phototherapy [12].

In the present study, 45 preterm and 155 term babies enrolled were subjected to phototherapy. All the babies were more than 72 hrs of life to avoid the effect of early onset hypocalcemia. All the term and preterm neonates in the present study were appropriate for gestational age. Same was the case in the studies done by Sethi et al (1993) [13] and Jain BK et al (1998) [14] and Arora et al (2014) [15].

Serum calcium levels were significantly lowered in both preterm (p<0.001) and term neonates (p<0.001) after 48 hours of continuous phototherapy. No significant difference was found between these two groups (p<0.247).

Table no. 2 shows that in the present study hypocalcemia occurred in 40% of term neonates after 48 hours of phototherapy which is comparable to the study done by Jain et al (1998) [14] and is lower than those observed by Yadav et al (2012) [16] and Arora et al (2014) [15]. This difference in incidence could be attributed to our larger sample size.

In the present study 53.33% preterm neonates developed hypocalcemia after 48 hours of phototherapy which is comparable to the study done by Jain et al (1998) [14]. Much higher incidence of hypocalcemia was noted in the present study among preterm neonates than reported by Arora et al (2014) [15].

5. Conclusion

Neonatal hyperbilirubinemia is one of the common conditions confronting neonatologists in their day to day practice.

Phototherapy is commonly being used in practice for the treatment of unconjugated hyperbilirubinemia.

Hence, phototherapy induced hypocalcemia is common problem and therefore calcium levels in neonates subjected to phototherapy should be checked.

Neonates after being subjected to phototherapy, develop hypocalcemia which can cause serious complications like convulsions, apnea, irritability and jitteriness.

Provision of calcium supplementation as prophylaxis and head covering may be considered in neonates subjected to phototherapy.

Acknowledgement:

Source(s) of support in the form of grants, equipment, drugs or all of these: NONE Declaration on competing interests: competing interests: NONE

Funding: NONE

Table: 1-COMPARISON OF DECREASE IN MEAN±SD VALUES OF SERUM CALCIUM (MG/DL) BETWEEN TERM AND PRETERM NEONATES BEFORE AND AFTER PHOTOTHERAPY

GESTATIONAL AGE	MEAN±SD VALUE OF SERUM CALCIUM AFTER 48HRS OF PHOTOTHERAPY (Mg/dL)	P – VALUE
TERM (n=155)	0.6677±0.2892	<0.247
PRETERM (n=45)	0.6044±0.4167	<0.247

Table: 2- COMPARISON OF RESULTS BETWEEN THE PRESENT STUDY AND OTHER STUDIES AFTER 48 HRS OF PHOTOTHERAPY.

STUDY	PERCENTAGE OF HYPOCALCEMIC TERM NEONATES	PERCENTAGE OF HYPOCALCEMIC PRETERM NEONATES
Jain et al (1998) [14]	30%	55%
Yadav et al (2012) [15]	66.6%	80%
Arora et al (2014) [5]	56%	43%
Present study	40%	53.33%

References:

- Rennie J, Burman-Roy S, Murphy MS. Neonatal jaundice: summary of NICE guidance. BMJ. 2010;340:c2409.
- Kliegman M. The fetus and the neonatal infant, in: Behrman R, Nelson textbook of pediatrics. 19th ed. Saunders Philadelphia 2011; 603-612.
- Xiong T, Qu Y, Cambrier S, et al. The side effects of phototherapy for neonatal jaundice: What do we know? What should we do? Eur J Pediatr 2011; 170(10):1247-55.
- Ehsanipour F, Khosraui Nastaran, Jalalisamaneh. The effect of Hat on phototherapy induced Hypocalcemia in icteric newborns. Journal of Iran University of Medical Sciences. 2008; 15(58). p.25-9
- Yadav RK, Sethi RS, Sethi AS, Kumar L, Chaurasia OS. The Evaluation of Effect of Phototherapy on Serum Calcium Level. People's J of Scientific Res. 2012; 5(2): 1-4.
- Karamifar H, Pishva N, Amirhakimi GH. Prevalence of Phototherapy Induced Hypocalcemia. Iran J Med Sci. 2002; 27(4): 166-168.
- Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Pediatrics 2004; 114: 297-316.
- Janssen JW et al. Arsenazo III: an improvement of the routine calcium determination in serum. Eur J Clin Chem Clin Biochem. 1991 Mar; 29(3): 197-201.
- Jain AJ, Agarwal RA, Sankar MS, et al. Hypocalcemia in the Newborn. AIIMS-NICU Protocols. 2010
- Altirkawi, K. and H.J. Rozycki, Hypocalcemia is common in the first 48 h of life in ELBW infants. Journal of Perinatal Medicine 2008; 36: 348-353.

- [11] Gupta S, Gupta V et al. Neonatal hyperbilirubinaemia after induction of labour with oxytocin and cord serum albumin is compared with cord serum bilirubin as a risk indicator International Journal of Biomedical Research 2016; 7(7): 435-438.
- [12] Romagnoli, C., et al., Phototherapy-induced hypocalcemia. Journal of Pediatrics 1979; 94:815-816.
- [13] Sethi H, Saini A, Dutta AK. Phototherapy induced hypocalcaemia. Indian Pediatr. 1993;30:1403-6
- [14] Jain BK, Singh H, Singh D, Toor NS. Phototherapy induced Hypocalcaemia. Indian Pediatr. 1998;35(6):566-7.
- [15] Arora SA, Narang GS, Singh GS. Serum Calcium Levels in Preterm and Term Neonates on Phototherapy. J. Nepal Paediatr. Soc. January-April, 2014; 34(1):24-28.