

The Effect of Phototherapy on Serum Calcium Level in Full Term Neonates

Fatemeh HajiEbrahim Tehrani¹, Zari Sabet^{2*}, Zohreh Kavehmanesh³, Mohammad Mirzaei⁴

1. Associate Professor of Neonatology, Department of Pediatrics, Faculty of Medicine, Shahed University, Tehran, Iran.
2. Assistant Professor of Endocrinology, Department of Internal Medicine, Faculty of Medicine, Shahed University, Tehran, Iran.
3. Professor of Pediatric Gastroenterology, Department of Pediatric, Baqiyatallah University of Medical Sciences, Tehran, Iran.
4. MD. Student, Faculty of Medicine, School of Medicine, Shahed University, Tehran, Iran.

Article info

Received: 29 May 2014

Revised: 27 Aug 2014

Accepted: 07 Sep 2014

Key Words:

Hyperbilirubinemia

Phototherapy

Hypocalcaemia

A B S T R A C T

Background: Jaundice is one of the most common problems occurring in the neonatal period. It is commonly managed by phototherapy with its inherent complications. However, this treatment modality may itself result in the development of hypocalcaemia and create serious complications including convulsion and related conditions.

Objective: To determine the effect of phototherapy on serum calcium level in full-term hyperbilirubinemic neonates.

Materials and Methods: This study was performed on 198 full-term jaundiced neonates (113 males and 85 females) receiving phototherapy. These neonates had complete normal physical examination. Plasma bilirubin and calcium levels were determined before and after 48 hours of phototherapy.

Results: Fifteen neonates (7.5%) developed hypocalcaemia. After 48 hours of phototherapy, there were significant differences between serum calcium levels from baseline values of 9.46 ± 0.8 mg/dL to 9.12 ± 0.83 mg/dL after 48 hours of phototherapy ($p < 0.05$). None of the hypocalcaemic neonates were clinically symptomatic.

Conclusion: Although phototherapy induces hypocalcaemia in term infants, but the incidence of phototherapy-associated hypocalcaemia is not too much.

1. Introduction

Neonatal jaundice is one of the most prevalent clinical problems observed during the first week of life affecting approximately 60% of term and 80% of preterm infants (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. High bilirubin

level may cause neurological impairment even in term neonate. Approximately 5-10% of them have clinically significant hyperbilirubinemia.

Phototherapy plays a significant role in the treatment and prevention of hyperbilirubinemia in neonates. 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).

*Corresponding Authors: Zari Sabet, M.D

Assistant Professor of Endocrinology, Department of Internal Medicine, Endocrine Unit, Shahed University, Tehran, Iran. P.O. Box: 14166

Tel: +98 21 88966130; Fax: +98 21 88963739, E-mail: sabet@safineh.net

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). Ionized calcium is essential for many biochemical processes including blood coagulation, cell membrane integrity and function, cellular enzymatic activity and neuromuscular excitability. The underlying mechanism for phototherapy induced hypocalcaemia, although not yet well understood; but it seems that hypocalcaemia is accompanied by a decrease in serum melatonin concentration, in turn is regulated by the pineal gland. Pineal gland in normal human, however, is shown to be influenced by the diurnal light-dark cycle (4). There are some reports on hypocalcaemic effect of phototherapy especially in preterm neonates. There are still few studies on hypocalcaemic effect of phototherapy on the term newborns. Then, the aim of this study was to assess the prevalence of phototherapy induced hypocalcaemia among term neonates.

2. Methods and Subjects

This study was a cross-sectional study performed on 198 healthy term newborns over 2.5 kg of weight. These neonates were admitted to the neonatal ward of Shahid Mostafa Khomeini hospital of Tehran from October to February 2012 because of indirect hyperbilirubinemia who were managed with phototherapy. Neonates who were at risk of hypocalcaemia such as neonatal asphyxia, respiratory distress, sepsis, infant of diabetic mother and maternal consumption of anticonvulsant were excluded. Excluded were also premature newborns, apgar score

parenteral nutritional therapy. Serum calcium and bilirubin levels were measured on arrival and 48 hours after receiving phototherapy. Serum calcium level was measured via colorimeter using the Kavoshyar enzyme kit (Kavoshyar, Iran). Hypocalcaemia was considered as total serum calcium of $< 8 \text{ mg/dL}$. The study was approved by Ethics Committee of Shahed University of Medical Sciences.

2.1. Statistical analysis

Data were analyzed and assessed for normality using SPSS version 18. Descriptive data are presented as mean \pm SD or percentage. We used student's t – test to compare means. A value less than 0.05 were considered significant.

3. Results

The study populations were 198 term neonates (113 male, 85 females), with the mean chronological age and weight of 6.24 ± 2.91 days and 3226 ± 377 grams, respectively.

22.2% of neonates had normal vaginal delivery and 77.8% delivered by cesarean section.

Mean \pm SD of serum bilirubin level was $17.59 \pm 2.24 \text{ mg/dL}$ at admission and 13.76 ± 2.51 after receiving 48-hour phototherapy ($p < 0.001$). Mean \pm SD of serum calcium level significantly decreased from baseline values of $9.46 \pm 0.8 \text{ mg/dl}$ to $9.12 \pm 0.83 \text{ mg/dl}$ after 48-hour phototherapy. Overall, 15 neonates (7.5%) developed hypocalcaemia (calcium concentration less than 8 mg/dl). There was a significant difference between serum calcium level before and after phototherapy ($p < 0.03$). Fortunately, none of the hypocalcaemic neonates were clinically symptomatic.

Table 1. Demographic features of the newborns

variable	Mean & Number (percentage)
N=198	
Sex (male/female)(%)	113/85 (57.1%/42.9%)
Age at sampling (day)	6.24 ± 2.91
Age at the onset of hyperbilirubinemia (day)	3.57 ± 1.91
Weight at sampling (gram)	3226 ± 377
Type of delivery	
NVD (%)	44 (22.2%)
C/S (%)	154 (77.8%)

Table 2. Laboratory changes before and after receiving phototherapy

Test	Admission time	After 48 hours	p-value
Total bilirubin level (mg/dl)	17.59±2.24	13.76±2.51	0.001
Total calcium level (mg/dl)	9.46±0.8	9.12±0.83	0.03

4. Discussion

The regulation of calcium homeostasis in the newborn period has been of considerable interest. At birth, the plasma calcium (Ca) level in cord blood exceeds that in maternal blood. During the early days of life, the plasma Ca level progressively decreases 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 full-term infants the plasma Ca level returns to normal by 10 days of life (5). Phototherapy is an appropriate and safe measure to reduce indirect bilirubin level in newborns. Roming et al was the first to suggest the association of hypocalcaemia in newborn following phototherapy (6).

The mechanism of hypocalcaemic effect of phototherapy was reported by inhibition of pineal gland via transcranial illumination, resulting to decline of melatonin secretion; which blocks the effect of cortisol on bone calcium. Cortisol has a direct hypocalcemic effect and increases bone uptake of calcium and induces hypocalcaemia (4).

In our term neonatal study population receiving 48 hours of phototherapy, a significant decrease in serum calcium was observed. (p < 0.03). However, only 15 neonates (7.5%) developed hypocalcaemia below the acceptable threshold after 48 hours of phototherapy. Nevertheless none of our newborns had symptomatic hypocalcaemia.

In another Iranian study, between 7% - 15% of term newborn receiving phototherapy developed hypocalcaemia. Alizade et al reported only ten (7%) newborns (4.2% females, 10.4% males) developing hypocalcaemia after 48 hours of phototherapy (7). Ehsanipoor et al (8) and Karamifar et al (9) reported 15% and 8.7% hypocalcaemia respectively in newborns receiving phototherapy. However the reported prevalence of hypocalcaemia in other countries was more than Iranian newborn reports. Yadavs (10) reported 66% and Jain et al (11) also observed

hypocalcaemic effect of phototherapy in 30% term and 55% preterm neonates. Sethi et al has studied the effect of phototherapy in 20 term and 20 preterm hyperbilirubinemic neonates. They observed hypocalcaemia in 75% of term and 90% of preterm neonates after phototherapy (12). Similarly, in 2006, Medhat from Cairo University observed 75% of term and 90% of preterm developed hypocalcaemia after phototherapy (13). Observation of the present study and another Iranian study is much lower than the above-mentioned studies from other countries. The reason for this difference is not clear. However the type of fluorescent tube, serum vitamin D, bilirubin levels and also the patient's skin color may play a role. Muta et al reported a significant difference in the serum 25(OH) vitamin D levels between newborns suffering from hyperbilirubinemia and control groups (14). In a study done by Jain, the prevalence of hypocalcaemia was higher in newborns with higher concentration of serum bilirubin (15). In addition it might also be due to the fact that this study 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, either bound or free and ionized calcium. Then, it can be considered one of the limitations of our study.

These findings justify further prospective studies in infants that would include concurrent measurements of ionized calcium and serum 25(OH) vitamin D. Some reports recommend prescription of calcium to prevent early onset hypocalcaemia in premature newborns. Other similar advices are observed in sick infants of diabetic mothers and those with severe prenatal asphyxia (16).

In conclusion, although phototherapy induces hypocalcaemia in term infants, but the incidence of phototherapy associated hypocalcaemia is not too high. Then we can just advise check of calcium level in symptomatic newborns that have

suggested hypocalcaemia signs.

Acknowledgements

The authors would like to thank the members of Department of Neonatal ICU, Shahid Mostafa Khomeini hospital.

References

1. Rennie, J., et al., Neonatal jaundice: summary of NICE guidance. *British Medical Journal* 2010;340: 240-2499.
2. Kliegman M. The fetus and the neonatal infant, in: Behrman R, Nelson textbook of pediatrics. 19th ed. Saunders ,Philadelphia 2011; 603-612.
3. Xiong, T., et al., The side effects of phototherapy for neonatal jaundice: what do we know? What should we do?. *European Journal of Pediatrics* 2011; 170: 1247-1255.
4. Hakanson, D.O., R. Penny, and W.H. Bergstrom, Calcemic responses to photic and pharmacologic manipulation of serum melatonin. *Pediatric Research* 1987;22: 414-416.
5. 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.
6. Romagnoli, C., et al., Phototherapy-induced hypocalcemia. *Journal of Pediatrics* 1979; 94: 815-816.
7. Alizadeh-Taheri, P., N. Sajjadian, and B. Eivazzadeh, Prevalence of phototherapy induced hypocalcemia in term neonate. *Iran Journal Pediatrics* 2013; 23: 710-718.
8. Ehsanipour F, Khosravi N, Jalali S. The Effect of Hat on Phototherapy-Induced Hypocalcemia in Icteric Newborns. *Iran University of Medical Science Journal*. 2008; 15: 25-29
9. Karamifar H, Pishva N, Amirhakimi GH. Prevalence of Phototherapy-Induced Hypocalcemia. *Iran University of Medical Science Journal* 2002 ; 27:169-171.
10. Yadav RK, Sethi RS, Sethi AS. The evaluation of the effect of phototherapy on serum calcium level. *People's Journal Science Research* 2012; 5:1-4.
11. Jain, B.K., et al., Phototherapy induced hypocalcemia. *Indian Pediatrics* 1998;35: 566-567.
12. Sethi, H., A. Saili, and A.K. Dutta, Phototherapy induced hypocalcemia. *Indian Pediatrics* 1993;30: 1403-1406.
13. Medhat FB: Assessment of phototherapy induced hypocalcaemia. Thesis submitted for M.Sc. Pediatrics in Cairo University. Classification Number 8461; 2006.
14. M Mutlu, AÇayir, Y Çayir, B Özkan, Y Aslan. Vitamin D and Hyperbilirubinaemia in Neonates. *Hong Kong Journal of Paediatrics* 2013; 18:77-81
15. Jain, B.K., et al., Hypocalcemic effect of phototherapy - reply. *Indian Pediatrics* 1999;36: 208-209.
16. Jain, A., et al., Hypocalcemia in the newborn. *Indian Journal Pediatrics* 2010;77: 1123-1128.