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Prevalence of hypocalcemia after phototherapy among neonates who underwent phototherapy in Koodakan Hospital in Bandar Abbas in 2013

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Abstract

Introduction: Hyperbilirubinemia is one of the most common problems in newborns, and it is reported in about 60% of infants. Phototherapy is used extensively to treat these patients, and hypocalcemia is one important side effect of the phototherapy. The aim of this study was to determine the prevalence of hypocalcemia after phototherapy in full-term newborns that underwent phototherapy in Koodakan Hospital in Bandar Abbas in 2013.

Methods: This cross-sectional study was conducted on 100 neonates admitted to Koodakan Hospital in Bandar Abbas. All of the newborns were full-term, healthy, weighed more than 2,500 g, and were candidates for phototherapy. The newborns were divided into two groups, i.e., 1) those who were more than three days old and 2) those who were less than three days old. Serum bilirubin and calcium levels were measured for each newborn before phototherapy and 48 hours after phototherapy, and the before and after levels were compared. The data were analyzed using IBM SPSS 21.0 statistical software. The Fisher Exact test, the independent samples t-test, and the paired t-test were used to test the research hypothesis.

Results: Among the 100 newborns studied, 54% had decreased calcium levels after phototherapy. The prevalence of hypocalcemia was 9% in this study, and the prevalence was not significantly different in the two age groups (P = 0.217).

Conclusion: Phototherapy does not increase the risk of hypocalcemia in healthy, full-term neonates. Therefore, prophylactic calcium is not recommended for healthy, full-term neonates who have undergone phototherapy.

Keywords: hypocalcemia, phototherapy, hyperbilirubinemia, newborns

1. Introduction

Hyperbilirubinemia is one of the most common problems in newborns during their first week of life, and it is a cause of concern for parents (1). Although the etiologies of neonatal jaundice are different, they usually are benign and do not require intervention (2). Jaundice occurs in the first week of life in 60% of full-term and 80% of pre-term neonates (2), and pre-term neonates and those who only are breast fed are at higher risk for jaundice (3). In approximately 5 to 10% of neonates, bilirubin increases significantly and requires intervention (2). Untreated hyperbilirubinemia may develop into acute encephalopathy (2). Untreated non-conjugated, high-level hyperbilirubinemia is severely neurotoxic (4), and it can lead to kernicterus as an early complication with hyperbilirubinemia as a later complication, which can result in mental retardation, deafness, and cerebral palsy that can result in lifetime disability (5). Beginning about 50 years ago, phototherapy has been performed with the goal of preventing the neurotoxic complications of indirect hyperbilirubinemia (6). Phototherapy leads to changes in the structure of bilirubin, and the resulting isomers can be excreted in bile and urine (7). Acute changes in the

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temperature of inside the room may lead to insensible water loss in neonates (3). Significant complications of phototherapy are rare, but they may include dehydration, oxidative injury, hyperthermia, chill, hypocalcemia, fecal incontinence, and injuries to DNA (6). The mechanism of hypocalcemia is uncertain, but it probably depends on changes in the melatonin level that is modulated by the pineal gland, which is affected by cycles between light and darkness. Recently, in limited studies, phototherapy was reported to be a risk factor for hypocalcemia (8). Hypocalcemia is defined as a level of serum calcium less than 8 mg/dl in a full-term neonate and less than 7 mg/dl in a pre-term neonate (9). Hypocalcemia in neonates present with tetanus, spasms of the larynx, dysfunction of myocardia and apnea (10), myoclonic seizure, jerking, chills, tachycardia, heart failure, and decreased contractility of the heart (11). Hypocalcemia is a common cause of seizure in neonates during their first five days of life (10). In 2012, Kumar et al.'s study showed that hypocalcemia occurred in 80% of pre-term neonates and in 66.6% of full-term neonates. The occurrences were symptomatic in 80% of the full-term neonates and in 100% of the pre-term neonates (1). Another study was performed by Alizadeh et al. in 2008 and 2009 in Tehran, and the results showed that, after 48 hours of phototherapy, hypocalcemia occurred in 56% of neonates, with 7% of those being symptomatic (12). Also, a high prevalence of hypocalcemia has been reported by other similar studies (13-15). Also, some other studies are available concerning the prevalence of hypocalcemia in neonates after phototherapy, but the results varied based on where the studies were conducted (11-15). Studies from Hamadan, Shiraz, and Tehran have shown a high prevalence of hypocalcemia after phototherapy (12-14). No study conducted in Bandar Abbas has reported a prevalence of hypocalcemia in neonates after phototherapy. Therefore, we aimed to assess the frequency of hypocalcemia after phototherapy in neonates admitted to Koodakan Hospital in Bandar Abbas in 2013.

2. Material and Methods

2.1. Study setting, sampling, and selection criteria

In this cross-sectional study, we evaluated 100 neonates who were admitted for phototherapy in the neonatal ward at Koodakan Hospital in Bandar Abbas in 2013. Considering the type I error of 0.05, a power of 80%, a 15% prevalence of hypocalcemia, and an accuracy of 7%, a sample size of 100 was obtained using MedCalc version 13.3.3.0. Thus, 100 neonates were included in the study using a simple sampling method in a 3-month duration. The neonates were divided into two age groups, i.e., 1) those less than three days old and 2) those more than three days old. Healthy, full-term neonates who had normal examinations and normal birth weights (i.e., more than 2500 g) were selected as candidates for phototherapy. The exclusion criteria included the following: 1) the neonate's mother has diabetes mellitus, 2) Apgar score below 7 in 5 min, 3) pre-term neonates, 4) blood exchange, 5) neonate dependent on dried milk, 6) sepsis, 7) respiratory distress, 8) jaundice more than 14 days after birth, 9) use of anti-convulsion drugs in the neonate or the mother, 10) hypocalcemia before phototherapy, and 11) jaundice on the day the neonate was born.

2.2. Measurement tool and data collection

A 5-cc blood sample was taken 48 hr before and 48 hr after phototherapy, and the neonates' calcium levels were measured. For all of the neonates, phototherapy was conducted using standard phototherapy with four 40-W lamps with blue light, 410-470 nm at a distance of 30-40 cm from the neonate. A checklist including demographic factors and the concentration of calcium in the serum before and after phototherapy was completed for each patient.

2.3. Research ethics

The study protocol was approved by the Research Ethics Committee at Hormozgan University of Medical Sciences. The patients were not charged for the laboratory tests. The patients' information was kept confidential.

2.4. Statistical analysis

Data were analyzed by IBM SPSS 21.0 using descriptive statistics (frequency, percentage, mean, and standard deviation), Fisher`s exact test, independent samples t-test, and paired t-test. A P value less than 0.05 was assumed to be significant.

3. Results

3.1. Before phototherapy

We studied 100 full-term neonates. Among the neonates studied 55 (55%) were male and 45 were female. Also 28 were less than three days old and 72 were more than three days old. All of the neonates had normal calcium levels (> 8mg/dl) at the time of the study. The neonates who were less than three days old had a mean calcium level of 9.16 ± 0.61 mg/dl before phototherapy, and the neonates who were more than three days old has a mean calcium level of

9.08 ± 0.61. The results of the independent samples t-test showed that the difference between the mean calcium levels in the two groups was not statistically significant (P = 0.578).

3.2. After phototherapy

3.2.1 Prevalence of hypocalcemia

Among the 100 neonates, 54 (54%) had decreased calcium concentrations in their serum after phototherapy, but the prevalence of hypocalcemia was only9%. Table 1 provides the results of Fishers Exact Test, and the results indicated that the prevalence of hypocalcemia after phototherapy was not statistically significant between the two groups of neonates (P = 0.217).

Table 1. Prevalence of hypocalcemia among neonates according their age group

Calcium level	≤ 3 days old	> 3 days old	Total	P value
Ca ≥ 8 mg/dl	4 (14.3%)	5 (6.9%)	9 (9%)	0.217
Ca < 8 mg/dl	24 (85.7%)	67 (93.1%)	91 (91%)	
Total	28 (100%)	72 (100%)	100 (100%)	

3.2.2 Mean calcium level

The mean calcium level was 9.1 ± 0.61 mg/dl before phototherapy, and it was 9.02 ± 0.6 after phototherapy. The results of paired Samples t-test showed that the difference in the mean calcium level before and after phototherapy was not significant (P = 0.35). Also, Table 2 shows that, based on the results of the paired samples t-test, the difference in the mean calcium level before and after phototherapy was not statistically significant according to the age group.

Table 2. Mean calcium level before and after phototherapy by age group

Age group	Before phototherapy	After phototherapy	P value
≤ 3 days old	9.16 ± 0.62	8.9 ± 0.72	0.13
> 3 days old	9.09 ± 0.62	9.07 ± 0.67	0.86

4. Discussion

In this study, we reported a decrease in the serum calcium concentration in 54% of full-term neonates after phototherapy. However, the rate of hypocalcemia was not high. These results are discussed below. According to these results, a large percentage of our study population had decreased serum calcium concentrations, which is common in neonates after phototherapy. In a similar study, Jain et al. reported decreases in the serum calcium concentration in 55% of pre-term neonates and in 30% of full-term neonates. Our results were essentially in good agreement with their results. Despite the decrease in the serum calcium concentration in more than half of the patients in our study, hypocalcemia was reported in only 9% of the patients. This finding was different from that of Jain et al., who reported a high prevalence of hypocalcemia in their study population (16). This difference could be due to the differences in the study populations. We only included full-term neonates in our study, but Jail et al. included both full-term and pre-term neonates. Based on the results of Karamifar et al., the prevalence of hypocalcemia is greater among pre-term neonates after phototherapy (4). Also, Eghbalian et al. reported a significant incidence of hypocalcemia in their study, which may have been due to the longer duration of phototherapy that they used. Also, we determined the serum calcium concentrations 48 hr after phototherapy, whereas they determined these concentrations 72 hours after phototherapy (14). Also in contrast to our study, significant hypocalcemia was reported in a study conducted by Alizadeh et al. The difference between the results of our study and theirs may have been due to the greater sample size and the lower distance between the neonates and the phototherapy lamp in their study (20 cm as opposed to 30 cm in our study) (12). Our study had some limitations that should be considered in the interpretation of the results. We excluded pre-term neonates from our study, and it seems that the prevalence of hypocalcemia is greater for this category. Also, we did not determine in our study population the relationship between hypocalcemia and serum bilirubin concentration.

5. Conclusions

The risk of hypocalcemia after phototherapy is low in healthy, full-term neonates, and the risk is not related to the neonates' ages. Therefore, we do not recommend using prophylactic calcium in healthy, full-term neonates with hyperbilirobinemia during phototherapy. However, we recommend checking serum calcium concentrations during and after phototherapy in all patients.

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Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.

References

1) kumar Yadav R, Sethi R.S, Sethi A.S, Kumar L, Shankar Chauraisa O. The evaluation of effect of phototherapy on serum calcium level. PJSR. 2012; 5 (2):1-4.
2) Kliegman R, Stanton B, Behrman R, Geme J, Schor N. Nelson text book of pediatric.19th ed. 2012.
3) Jeffrey Maisels A, McDonagh A.F. Phototherapy for neonatal jaundice. NEJM. 2008; 358: 920-8. doi: 10.1056/NEJMct0708376.
4) karamifar H, pishva N, Amirhakimi GH. Prevalence of phototherapy induced hypocalcemia. Iran J Med Sci. 2002; 27 (4):166-8.
5) A joint statement with the College of Family Physicians of Canada. Approach to the management of hyperbilirubinemia in term newborn infants. Paediatr Child Health. 1999; 4 (2): 161–70. PMID: 20212978, PMCID: PMC2828212.
6) Tatli M, Minnet C, Kocyigit A, Karadag A, Ahmet Karadag. Phototherapy increase DNA damage in lymphocytes of hyperbilirubinemic neonates. Mutat Res-Gen Tox En. 2008; 654 (1): 93-5. doi: 10.1016/j.mrgentox.2007.06.013.
7) Stokowski L.A .Fudamentals of phototherapy for neonatal jaundice. Adv neonatal car. 2011; 11 (5):10-21. doi: 10.1097/ANC.0b013e31822ee62c.
8) Habibzadeh F, Karamizadeh Z. Phototherapy-induced hypocalcemia. IJMS. 2002; 27 (4):151.
9) Eghbalian F. The Study of Early Neonatal Hypocalcemia in the Educational Hospitals of Hamadan University of Medical Sciences. Scientific Journal of Hamadan University of Medical Sciences and Health Services. 2004; 11 (3): 48 To 52.
10) Borkenhagen JF, connor EL, Stafstrom CE. Neonatal hypocalcemic seizure due to excessive maternal calcium ingestion. Pediatr Neurol. 2013; 48 (6): 469-71. doi: 10.1016/j.pediatrneurol.2013.02.010. PMID: 23668874.
11) Korkmaz H.A, Ozkan B, Terek D, Dizdarer C, Arslanoğlu S. Neonatal seizure as a manifestation of unrecognized maternal hyperparathyroidism. J Clin Res Pediatr Endocrinol. 2013; 5 (3): 206-8. doi:10.4274/Jcrpe.1037. PMID: 24072092, PMCID: PMC3814538.
12) Alizadeh-Taheri P, sajjadian N, Eivazzadeh B. Prevalence of phototherapy induced hypocalcemia in term neonate. Iran J pediatr. 2013; 23 (6): 710-11.
13) Ehsanipoor F, Khosravi N, Jalali S. The effect of Hat on phototherapy induced hypocalcemia in icteric newborn. The Razi J Med Sci. 2008; 15 (58): 25-9.
14) Eghbalian F, monsef A. phototherapy induce hypocalcemia in icteric newborn. Iran J Med Sci. 2002; 27 (4): 169-71.
15) Hooman N, Honarpisheh A. The effect of phototherapy on urinary calcium excretion in newborn. Pediater Nephrol. 2005; 20 (9): 1363-4.
16) jain A, Agarwal R. Shankar M.J, Deorari A, Paul V.K. Hypocalcemia in the newborn. Indin J Pediater. 2010; 77 (10): 1123-8. doi: 10.1007/s12098-010-0176-0. PMID: 20737250