

Effect of phototherapy on Urinary Calcium Excretion in neonates with Hyperbilirubinemia

Dr Lakshmi Ramya Gontla¹, Dr Amitha Rao Aroor², Dr Santosh T Soans³

¹Junior resident,, Department of Pediatrics A J Institute of Medical sciences , Mangalore

²Professor; Department of Paediatrics , AJ Institute of Medical sciences , Mangalore

³HOD & Professor; Department of Paediatrics , AJ Institute of Medical sciences , Mangalore

Abstract: Phototherapy is the most common, most effective, and least dangerous treatment method for neonatal hyperbilirubinemia and is the treatment of the first choice for neonatal icterus. Hypocalcemia is one of the lesser-known complications of phototherapy. Some studies have shown a relationship between increased urinary calcium excretion and phototherapy-induced hypocalcemia.

Aim Of The Study: We aimed to assess the effect of phototherapy on urinary calcium excretion in term neonates and possibility of detecting hypocalcemia and giving calcium supplementation. It could be used a noninvasive method for detecting hypocalcemia

This before-after study was performed on 57 term Neonates suffering from hyperbilirubinemia admitted in NICU(Neonatal intensive care unit) A.J Institute of medical sciences during the period of one year (2016-2017) . Blood and urine samples were taken from all neonates before and 24 h after phototherapy. Phototherapy was performed using four lamps with similar wavelengths from a distance of 20 cm. The serum and urinary calcium before and after phototherapy were measured and compared.

Results :It was found that there was significant increase in urine calcium excretion in 80% of the neonates , although it was not significantly causing hypocalcemia. Data was analyzed using SPSS software, version 16.

Conclusion: Phototherapy increases urinary calcium excretion although it may or may not cause hypocalcemia.

Date of Submission: 27-03-2018

Date of acceptance: 09-04-2018

I. Introduction

Hyperbilirubinemia is a common and often benign condition in neonates. It is seen in 60% of term neonates during the 1st week of life and 80% of premature neonates. It is usually caused by the dermal accumulation of lipid-soluble, non-polar unconjugated bilirubin pigments (indirect type)¹

Phototherapy is a commonly used method for the treatment and prophylaxis of unconjugated hyperbilirubinemia. Phototherapy can decrease Total bilirubin concentration in most neonates irrespective of their maturity, degree of dermal pigmentation, and hemolysis. Considering previous studies on phototherapy , it has been concluded that this treatment method is relatively safe and can reduce the need for exchange transfusion in infants.

Moreover, follow-up studies have not reported any serious complications in neonates who had undergone phototherapy. One of the less common complications of phototherapy is hypocalcemia. In animal studies, researchers have found that phototherapy might reduce melatonin levels which in turn decreases the glucocorticoid secretion thereby causing hypocalcemia by increasing calcium (Ca) resorption.⁵⁻⁷

In some studies, the mean urinary Ca excretion increased in several neonates after 48 h of phototherapy.^{8,9}

Urinary Ca excretion in the 1st week of life is directly dependent on the urinary sodium excretion as well as gestational age. Furthermore, glomerular filtration can affect Ca secretion by urinary excretion of cyclic 3',5'-adenosine mono-phosphate and potassium.^{10,11}

Whether hypocalcemia is the result of increased urinary Ca excretion is yet to be known and should be further studied. A limited number of studies have evaluated phototherapy as a risk factor for hypocalcemia.^{6,8,12.}

Hypocalcemia induced seizures could have a negative impact on the central nervous system (CNS) and intensify the damage to CNS possibly affected by jaundice itself. Since the main cause of hypocalcemia is still not well determined , evaluating the etiology of phototherapy-induced hypocalcemia is also important.

Therefore, we aimed to assess the effect of phototherapy on urinary Ca excretion in term neonates. In this study we aim at the identification of the effect of urinary excretion of calcium which maybe an indicator of the calcium loss which may further cause hypocalcemia. This could be further used as a noninvasive method for determination of hypocalcemia and requirement of calcium supplementation.

This before-after study was performed on 57 term neonates suffering from hyperbilirubinemia admitted in NICU(Neonatal Intensive Care Unit) of A.J Institute of Medical Sciences , Mangalore ; during the period of one year (sep2016-aug 2017)

All stages of the study were explained to the parents and their written informed consent was obtained.

Inclusion criteria

- We included neonates with a birth weight of >2500 g
- who were more than 48 hrs of life,
- who did not have a history of icterus during the 48 h after birth
- who had an indication for phototherapy (serum bilirubin: 15–19 mg/dL) and were breastfed.

Exclusion criteria

We excluded neonates who were on antibiotic therapy or candidates for exchange transfusion, hemolytic anemia, asphyxia, respiratory distress, sepsis, infants of diabetic mothers, and infants with a history of intravenous therapy and admission at birth because of disease. All the preterm neonates were excluded.

II. Material And Methods

Study place : NICU – A.J Institute of Medical Sciences Mangalore

Study period : September 2016 to august 2017

Sample size - 57

Blood and urine samples were drawn from all neonates before and 24 h after phototherapy. Phototherapy was performed using four lamps with similar wavelengths from a distance of 20 cm.

SEX

	Frequency	Percent
FEMALE	25	43.9
MALE	32	56.1
Total	57	100.0

The urine samples were collected within 2 hrs of admission. In case of no urination, phototherapy was not postponed, but the neonate was excluded from the study.

The serum and urinary Ca levels before and after phototherapy were measured and compared. Urine samples were collected from urine bags. Quick Wee method was also used to collect the urine.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
GESTATIONAL AGE	57	37.40	40.40	38.7930	.68082
BIRTH WEIGHT	57	2.50	4.00	3.0384	.32674

III. Results

The data was analysed with the paired t test and standard deviation analysis.

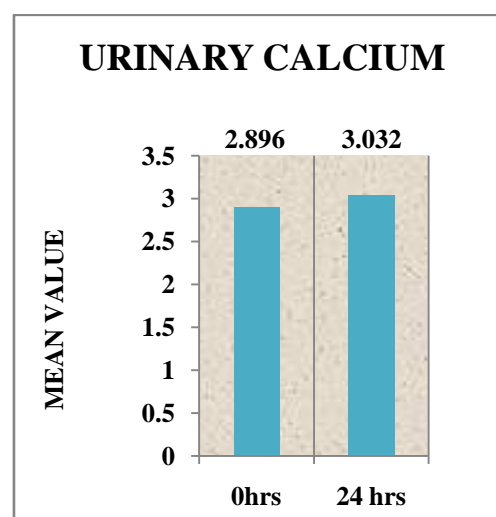
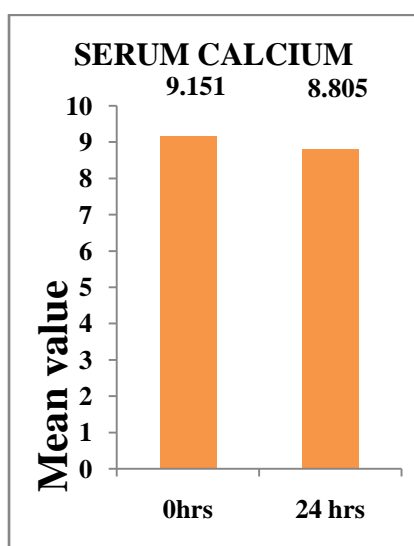
The urinary calcium excretion levels were significantly elevated in correlation with the serum calcium levels which were also reduced significantly. In 80% of the neonates there was significant increase in the calcium excretion.this was in positive correlation with the reduction of serum calcium. However not significant enough to cause hypocalcemia.

Paired Samples Test

	Paired Differences		t	p
	Mean	Std. Deviation		
TOTAL BILIRUBIN -0 hrs - TOTAL BILIRUBIN -24 hrs	4.465	2.161	15.601	<0.001 vhs
DIRECT BILIRUBIN -0 hrs - DIRECT BILIRUBIN -24 hrs	0.054	0.144	2.851	0.006hs
SERUM CALCIUM - 0 hrs - SERUM CALCIUM - 24 hrs	0.346	0.379	6.886	<0.001 vhs
URINARY CALCIUM - 0 hrs - URINARY CALCIUM - 24 hrs	-0.135	0.309	-3.306	0.002hs

Hs-highly significant ; vhs- very highly significant

Paired Samples Statistics			
	N	Mean	Std. Deviation
TOTAL BILIRUBIN -0 hrs	57	13.767	2.088
TOTAL BILIRUBIN -24 hrs	57	9.302	2.256
DIRECT BILIRUBIN -0 hrs	57	0.458	0.131
DIRECT BILIRUBIN -24 hrs	57	0.404	0.113
SERUM CALCIUM - 0 hrs	57	9.151	0.731
SERUM CALCIUM - 24 hrs	57	8.805	0.671
URINARY CALCIUM - 0 hrs	57	2.896	1.055
URINARY CALCIUM - 24 hrs	57	3.032	1.094



IV. Discussion

The regulation of Ca homeostasis in the newborn period has been of considerable interest. At birth, the plasma 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 that 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.

Phototherapy is an appropriate and safe measure to reduce indirect bilirubin level in newborns.

Although phototherapy is one of the relatively safe and uncomplicated treatment methods for curing neonatal jaundice, it could have several side effects such as skin rash, loose stools, hyperthermia, dehydration, DNA damage, chills, ophthalmic damage, nasal obstruction following eye coverage, and bronze baby syndrome.^{1,3}

One of the less frequent complications of phototherapy is hypocalcemia. The pathogenesis of phototherapy-induced hypocalcemia is still not fully understood.⁵ One study reported that Vitamin D does not have an important role in phototherapy-induced hypocalcemia because the administration of 25-hydroxy Vitamin D did not reduce the incidence of hypocalcemia in the studied premature neonates on phototherapy.¹⁴ Hakanson et al found that white fluorescent light beam led to reduced serum Ca levels in newborn mice. This study showed that the reduction of serum Ca levels was caused by the reduction of serum melatonin levels as a result of exposure of the pineal gland to phototherapy. Moreover, they concluded that administering melatonin exogene could prevent hypocalcemia.¹⁵ In a study on the effect of using hats on phototherapy-induced hypocalcemia in 120 newborns with icterus in Iran, the researchers found a significant difference in the amount of hypocalcemia in the group using hats compared with those receiving routine phototherapy (without hats). Head coverage in the occipital region was presented as a suitable, safe, and inexpensive method for preventing phototherapy-induced hypocalcemia.¹⁶

The prevalence of phototherapy-induced hypocalcemia and hyper-calciuria varies in different studies. In another study in Iran on 153 term and preterm neonates, the researchers found that 22 (14.3%) neonates had hypocalcemia and that the incidence of hypocalcemia was considerably higher in preterm neonates (22.6% vs.

8.7%)¹⁴. The increased urinary Ca excretion observed in our study did reduce the serum Ca levels, and we found significant difference between serum Ca levels before and after phototherapy.

Our analysis was performed 24hrs after phototherapy but some studies performed after 24 – 36 hrs of phototherapy 12 .Since we did not include preterm neonates, this lack of significance cannot be generalized to preterm neonates.⁶

We did not assess albumin levels which are influential in ionized Ca levels because the aim of sampling in this study was to assess total Ca levels in which evaluating albumin levels was not important and would increase costs. Moreover we did not find any case of symptomatic hypocalcemia which was in line with another study⁶ and different from the findings of one other study¹² that showed one neonate with apnea induced by hypocalcemia

In our study on 57 neonates, the effect of phototherapy on increased urinary Ca excretion was confirmed. However, since the reduction in serum calcium is not sufficient in a range to cause hypocalcemia ,prophylactic use of calcium should be based on baseline serum calcium. However due to the high significance of the calcium excretion cannot be neglected and can be an important parameter to determine the cause of hypocalcemia in neonates with phototherapy

V. Conclusion

On the basis of this study, phototherapy could increase urinary Ca excretion although it may or maynot cause hypocalcemia. Therefore, we do not advice routine Ca prophylaxis before and during phototherapy in term neonates but should be done with significant urine calcium loss and if baseline calcium is low. It could be used as a noninvasive method if the baseline calcium is already low and excessive urinary calcium excretion is observed.

References

- [1]. Stoll BJ, Kliegman RM. Jaundice and hyperbilirubinemia in the newborn. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson Textbook of Pediatrics. 19th ed. Philadelphia: WB Saunders Co.; 2011. p. 603-12.
- [2]. Gartner LM, Green HL. Effect of milk feeding on intestinal bilirubin absorption in the rat. *J Pediatr* 1983;103:464.
- [3]. Kaplan M. Neonatal jaundice and liver disease. In: Fanaroff AA, Martin RJ, eds. Neonatal-Perinatal Medicine: Disease of the Fetus and Infant. 9th ed. Elsevier Mosby; 2011. p. 1470-6.
- [4]. Tan KL, Stocker R, Swinney DC, et al. The pattern of bilirubin response to phototherapy for neonatal hyperbilirubinemia. *Pediatr Res* 1982; 16:670.
- [5]. Romagnoli C, Polidore G, Cataldi L. Phototherapy- induced hypocalcemia. *J Pediatr* 2006; 94:815-6.
- [6]. Ozkaya O, Buyan N, Erol I, et al. The relationship between urinary calcium, sodium, and potassium excretion in full-term healthy newborn. *Turk J Pediatr* 2005;47:39-45.
- [7]. Hakanson DO, Bergstrom WH. Phototherapy induced hypocalcemia in newborn rats: Prevention by melatonin. *Science* 1981;214:807-9.
- [8]. Hooman N, Taheri Derakhsh N, Samaii H, Mohammad Hoseini AA. Blood level and urinary excretion of calcium in neonates with non physiological hyperbilirubinemia under phototherapy. *RJMS* 2009;16:195-202.
- [9]. Karamifar H, Pishva N, Amirkhani GH. Prevalence of phototherapy – Induced hypocalcemia. *IJMS* 2002;27:166-8.
- [10]. Hooman N, Honaripisheh A. The effect of phototherapy on urinary calcium excretion in newborn. *Pediatr Nephrol* 2005;20:1363-4.
- [11]. Aladangady N, Coen PG, White MP, Rae MD, Beattie TJ. Urinary excretion of calcium and phosphate in preterm infants. *Pediatr Nephrol* 2004;19:1225-31.
- [12]. Bert S, Gouyon JB, Semama DS. Calcium, sodium and potassium urinary excretion during the first five days of life in very preterm infants. *Biol Neonate* 2004;85:37-41.
- [13]. Eghbalian F, Monsef A. Phototherapy – Included hypocalcemia. *Indian Pediatr* 2008;35:566-7.
- [14]. Ahmadzadeh A, Hakimzadeh M, Safa Abedi A. Idiopathic hypercalciuria in Iranian children. *Iran J Pediatr* 2008;18:163-6.
- [15]. Zecca E, Romagnoli C, Atalay Y, et al. Ineffectiveness of vitamin 25(OH) D3 in prevention of hypocalcemia induced by phototherapy. *Pediatr Med Chir* 1993;5:317-9.
- [16]. Ehsanipour F, Khosravi N, Jalali S. Hat effect in relation to neonatal jaundice phototherapy\ induced hypocalcemia. *RJMS* 2009;15:25-9.
- [17]. Gutcher GR, Odell GB, Klein RZ, et al. Hypocalcemia and hypernatremia associated with phototherapy in newborn rats. *Photochem* 1993;37:177-80.
- [18]. Tan KL, Jacob E. Effect of phototherapy on neonatal fluid and electrolyte status. *Acta Paediatr Acad Sci Hung* 1981;22:187-94.
- [19]. Jain BK, Singh H, Singh D, Toor NS. Phototherapy induced hypocalcemia. *Indian Pediatr* 1998;35:566-7.
- [20].

Dr Lakshmi Ramya Gontla "Effect of phototherapy on Urinary Calcium Excretion in neonates with Hyperbilirubinemia."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 4, 2018, pp 15-18.