Research Article

Total and Ionic Serum Calcium Level in Icteric Newborn Receiving Phototherapy

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ABSTRACT

Jaundice is the most common condition that requires medical attention in newborns. The study was conducted on 100 neonates (42 preterm and 58 term) presenting with neonatal hyperbilirubinemia requiring phototherapy. Only normal neonates were included in study. Measurement of total and ionic serum calcium levels was done before and after 48 hours of institution of phototherapy. The sample collected before the start of phototherapy was taken as control. After 48 hours of phototherapy there was a statistically significant fall in total and ionic serum calcium levels in 54 % neonates. It was observed that hypocalcemia was more common in preterms (67%) than term (45%) neonates after receiving phototherapy for 48 hours. The present study shows hypocalcemia was more common in preterms and term newborns having higher total serum bilirubin levels. A statistically significant difference was observed in total calcium levels between TSB groups 15.1-20 and 20.1-30 mg/dl. The neonates were clinically assessed for features of hypocalcemia and it was found that preterms developed more symptoms of hypocalcemia than term neonates. Jitteriness was the most common symptom observed. It was concluded that phototherapy induced hypocalcemia is a significant problem. Thus, calcium supplementation may be considered especially in neonates with higher range to total serum bilirubin.

KEY WORDS: hyperbilirubinemia, hypocalcemia.phototherapy,

INTRODUCTION:

Neonatal hyperbilirubinemia is cause of concern for the parents as well as the paediatricians. Early discharge of healthy term newborns after delivery had become a common practice because of medical and social reasons and economic constraints. It is significant that most common cause of readmission during the early neonatal period is hyperbilirubinemia.[1]

Adults appear jaundiced when the serum bilirubin levels is >2mg/dl, and newborn appear jaundiced when it is >7 mg/dl.[2] However hyperbilirubinemia in the newborn period can be associated with severe illness such as haemolytic disease, metabolic and endocrine disorders, anatomic abnormalities of the liver and infection. Unconjugated hyperbilirubinemia is the most common form of jaundice encountered by doctors. Common risk factor for hyperblirubinemia include fetomaternal blood group incompatibility, prematurity and previously affected sibling. Cephalhemotomas, bruising and trauma from instrumental delivery may increase the risk for serum bilirubin elevation.[3]

The aim of phototherapy is to prevent potentially toxic bilirubin level to reach central nervous system and to decrease the need for exchange transfusion. Decision for therapy depends on factor such as actual bilirubin level and its rate of increase, weight and length of gestation at birth, post natal age and presence of factor that influence bilirubin albumin level. Phototherapy and, if it in unsuccessful, exchange transfusion remain the primary treatment modality.[4]

The commonly known side effects of phototherapy are loose stool, hyperthermia, dehydration, skin burn, photoretinitis, low platelet count, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency, and DNA damage.[2] A lesser known but potential complication of

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phototherapy is hypocalcemia.[4]

In 1979, Romagnoli et al suggested the association of hypocalcemia with phototherapy in preterm newborns.[5] In 1981, Hakanson and Bergstrom also observed hypocalcemia in newborn rats.[6] Sethi et al in 1993 observed decrease in total calcium levels in 90% preterm and 75% term neonates after 48 hours of phototherapy.[4]

Several studies showed hypocalcemic effect of phototherapy (Jain et al,1998; Eghbalian F and Moncef A, 2002; Karamifar et al, 2002; Medhat FB,2006; Yadav et al,2012; Sajjadian et al, 2013; Tehrani et al and Bahbah et al, 2014)[7-14].

Neonatal hypocalcemia is defined as total serum calcium concentration < 7 mg/dl or ionized calcium concentration < 4 mg/dl (<1mol/l). In VLBW infants ionized calcium values of 0.8 – 1 mmol/l are common and not usually associated with clinical symptom. Assessment of calcium status using ionized calcium is preferred, especially in first week of life. Correction nomogram used to convert total calcium into ionized calcium are not reliable.[2]

Hypocalcemia symptoms include neuromuscular irritability like myoclonic jerks, jitteriness, exaggerated startle and seizures. Hypoclacemia may cause tachycardia, heart-failure, prolonged QT interval, decreased contractility. Apnea, cyanosis, tachypnoea, vomiting and laryngospasms are other symptoms that are noted. Ionized calcium is crucial for many biochemical processes, including blood coagulation, neuromuscular excitability, cell membrane integrity and function, and cellular enzymatic and secretory activity.[2]

The decrease in calcium due to phototherapy can be explained by melatonin secretion. Melatonin stimulates secretion of corticosterone, which decreases calcium absorption by bones. Phototherapy leads to inhibition of pineal gland by transcranial illumination, resulting in decline of melatonin level and as a result, hypocalcemia develops.[9]

Cortisol exerts a direct hypocalcemic effect by decreasing the absorption of Calcium and phosphate ions from the intestine by antivitamin D action and by increasing the renal excretion of these ions and also accelerates the bone uptake of calcium.[15]

Most of the studies done till now had observed only serum total calcium levels. Only one study by Yadav et al. in 2012 considered changes in ionic calcium with phototherapy but they did not observed total calcium. Moreover, none of the studies had considered neonates with ABO-Rh incompatibility.

The present study was thus undertaken to include neonates with ABO-Rh incompatibility and to assess the effect of phototherapy on serum total and ionic calcium in preterm and term neonates with hyperbilirubinemia.

MATERIALS AND METHODS:

This study was conducted from July 2014 to October 2015 at Sick Newborn Care Unit (SNCU) of Department of Pediatrics , M.L.B. Medical College, Jhansi with active collaboration of Department of Obstetrics and Gynaecology, after taking approval from the institutional ethical committee. The study was conducted on 100 neonates (42 preterm and 58 term) presenting with neonatal hyperbilirubinemia requiring phototherapy.

Only normal neonates were included in study. Any neonate who had or developed complication during the course of study were excluded. Newborn infants with neonatal jaundice who were managed with exchange transfusion were also excluded.

All the neonates included in our study having Hyperbilirubinemia were managed with phototherapy (Decided on 'American Academy of pediatrics, 2004')(Table 1 and Table 2).[16]

All the cases were evaluated by detailed history, clinical examination and laboratory investigation. Every case was investigated for serum total and ionic calcium (at zero hour and at 48 hours of phototherapy), serum bilirubin, blood group, and Rh typing, reticulocyte count, Hemoglobin, peripheral blood smear, sepsis screen, other electrolytes and renal function tests. Mothers were examined for their blood group and Rh typing.

Both serum total and ionic calcium was determined by calorimetric method using standard calorimetric test kits (with the help of auto analyser Beckman Coulter AU analyser). The reagent used for estimating total calcium was Arsenazo III and for ionic calcium was o-cresolphthalein complexone forming coloured complexes. Conjugated and unconjugated serum bilirubin was estimated by Malloy and Evelyn method by using diazo reagent. Thereafter, all data were tabulated and analyzed statistically to detect hypocalcemia as a complication of phototherapy. Statistical presentation and analysis of the present study was conducted by Student t-test and paired t-test.

RESULTS :

This study was carried out on 100 neonates (42 preterm and 58 term) over a period of 16 months. Out of 42 preterm neonates 17 (41%) were males

Table 1: Management of Hyperbilirubinemia in healthy term newborn.

Total Serum Bilirubin (mg/dl)				
Age (Hours)	Consider Phototherapy	Phototherapy	Exchange transfusion if phototherapy fails	Exchange transfusion and phototherapy
< 24 hrs	-	-	-	-
25 – 48	≥ 12	≥ 15	≥ 20	> 25
49 – 72	≥ 15	≥ 18	≥ 25	≥ 50
≥ 72	≥ 17	≥ 20	≥ 25	> 30

Table 2: Management of Neonatal hyperbilirubinemia in very low birth weight babies based on bilirubin level (mg/dl)

Weight (g)	Phototherapy	Consider exchange transfusion
500-750	5-8	12-15
750-1000	6-10	7-15
1000-1250	8-10	15-18
1250-1500	10-12	17-20
1500-2500	15-18	20-25

Table 3: Pre study and post study values of total calcium (mg/dl) in preterm and term neonates.

	PRETERM - Total serum calcium (mg/dl) [Mean ± SD]			TERM - Total serum calcium (mg/dl) [Mean ± SD]		
Prestudy	9.5009 ± 0.6510			9.6456 ± 0.7422		
Poststudy	8.7777 ± 1.3359			9.1496 ± 1.0066		
Significance	p<0.05	df=82	t=3.15	p <0.05	df= 114	t=3.02

while 25 (59%) were females and out of 58 term babies 39 (67%) were males and 19 (33%) were females. The ratio of male:female among preterm neonates is 0.68:1 while it is 2:1 in term neonates. Overall the male:female ratio is 1.3:1. 57 neonates (57%) were weighing more than 2500 grams, 33 (33%) were low birth weight and 10 (10%) were very low birth weight. According to the mode of delivery 22 (52%) preterm neonates were born through normal vaginal route while 20 (48%) by LSCS. In term babies 34 (58%) were born by normal route while 24 (42%) by LSCS. Most of the neonates (66) were having TSB between 15.1 and 20 mg/dl while 11 neonates were in TSB range 10.1 and 15.0 mg/dl, 22 were in TSB range 20.1 and 30.0 and only one neonate was having TSB more than 30 mg/dl. 10 preterm (24%) out of 42 and 18 term (31%) neonates were having ABO or Rh incompatibility but none of the baby was having both types of incompatibility. Overall 28 (28%) of the neonates in our study was having either ABO or Rh incompatibility. Most of the cases, 24 (57%) preterm and 36 (62%) term have onset of jaundice after 72 hours while none of the cases presented before 24 hours.

Table 4: Pre study and post study values of Ionic calcium (mmol/l) in preterm and term neonates.

	Preterm - Ionic serum calcium (mmol/l) [Mean ±SD]			Term - Ionic serum calcium (mmol/l) [Mean±SD]		
Prestudy	1.0954 ± 0.1036			1.1053 ± 0.1182		
Poststudy	0.9819 ± 0.1323			1.0420 ± 0.1231		
Significance	p<0.05	df=82	t=4.37	p<0.05	df= 114	t=2.82

Table 5: Total serum calcium values before and after phototherapy in different TSB range.

TSB Range (mg/dl)	No of Neonates	Total Serum Calcium (mg/dl)		
		Before phototherapy	After phototherapy	p value (<0.05)
10.1 -15	11	9.540 ±0.548	8.257 ±1.128	0.0029
15.1 -20	66	9.312 ±0.631	8.611 ±1.302	0.0001
20.1 -30	22	9.641 ±0.744	7.814 ±1.570	0.0001
>30	01	10.9	6.8	

Table 6: Serum Ionic calcium values before and after phototherapy in different TSB range.

TSB Range (mg/dl)	No of Neonates	Ionic Calcium (mmol/l)		
		Before phototherapy	After phototherapy	p-value (<0.05)
10.1 -15	11	1.178 ±0.112	0.978 ±0.126	0.0008
15.1 -20	66	1.073 ±0.104	0.956 ±0.132	0.0001
20.1 -30	22	1.124 ±0.128	0.902 ±0.104	0.0001
>30	01	1.37	1.10	

Table 7: Distribution of cases according to symptoms in symptomatic hypocalcemic neonates.

Symptom	Preterm neonates having hypocalcaemia		Term neonates having hypocalcaemia	
	No	%	No	%
Jitteriness	14	50	10	38
Irritability/Excitability	6	21	6	24
Lethargic	6	21	4	15
Convulsion	0	0	0	0
Total	26	92	20	77

It was found that out of 42 preterm neonates 28 (67%) developed hypocalcemia. While out of 58 term neonates only 26 (45%) developed hypocalcemia. Overall 54 (54%) of icteric newborns developed hypocalcemia after 48 hours of phototherapy (Table 3 and Table 4).

It was observed that there was a statistically significant fall in total and ionic serum calcium levels in neonates in different total serum bilirubin range after phototherapy. Decrease in serum calcium (Total and Ionic) in all groups was found to be statistically significant (p<0.05) (Table 5 and Table 6).

The fall in serum total and ionic calcium among groups with TSB range 10.1-15 and 15.1-20 was not found to be significant (p=0.39) and (p=0.60). The fall in serum total calcium among groups with TSB range 15.1-20 and 20.1-30 was found to be significant (p=0.02) but fall in ionic calcium among these groups was not significant (p=0.08).

Further studies are needed to confirm significant difference in fall in ionic calcium among different TSB range groups. Out of 28 preterm neonates that developed hypocalcemia after exposure to phototherapy, 26 (92%) became symptomatic. Similarly, out of 26 term neonates that developed hypocalcemia 20 (77%) became symptomatic. Jitteriness was the most common symptom in both groups and none developed convulsions (Table 7).

DISCUSSION:

Jaundice is an important problem in the first week of life. Jaundice is attributable to physiological immaturity of neonates to handle increased bilirubin production. The use of phototherapy has decreased the need for exchange transfusion in term and preterm infants with hemolytic and nonhemolytic jaundice. When indication for exchange transfusion are present phototherapy should not be used as a substitute however, phtototherapy may reduce the need for repeated exchange transfusion in infants with hemolysis.[17]

Our study was carried out on 100 neonates (42 preterm and 58 term). The first samples collected before the start of phototherapy acted as control. Neonates presenting with hyperbilirubinemia were subjected to phototherapy for 48 hours and levels of serum total and ionic calcium were observed.

Jain BK et al. in 1998 studied 20 term and 20 preterm icteric neonates and observed hypocalcemia in 55% preterm and 30% term neonates after 48 hours of phototherapy.[7]

Study done by Medhat FB et al. in 2006 on 20 term and 20 preterm neonates observed hypocalcemia in 95% preterms and 75% term neonates after 48 hours of phototherapy.[10] Study done by Yadav RK et al. (2012) took 15 preterm and 15 term neonates and 20 neonates were taken as control (10 preterm and 10 term). They observed hypocalcemia in 80% preterm and 66.6% term neonates.[11]

Latest study was done in 2014 by Bahbah et al. at the Menaufia University, Egypt. They studied only 50 full term neonates with jaundice (25 males and 25 females) who received phototherapy for treatment of neonatal indirect hyperbilirubinemia and 25 neonates complaining of physiological hyperbilirubinemia taken as controls not exposed to phototherapy. After 48 hours of phototherapy hypocalcemia was found in 13 (26%) neonates and 37 cases (74%) had normal calcium levels.[18]

Study by Yadav et al. (2012) observed that all the hypocalcemic preterm neonates became symptomatic and 80% term babies became symptomatic while in our study 2 preterm hypocalcemic neonates remained asymptomatic, while 77% term neonates became symptomatic. Jitteriness remained the most common manifestation of hypocalcemia.[11] Study by Eghbalian F (2002) observed only one case of symptomatic hypocalcemia in the form of apnea in a term baby.[8] Study by Bahbah et al. (2014) showed jitteriness as the most common symptom of hypocalcemia while some cases developed convulsions.[18]

Hakanson DO et al. in 1987 reported that when young rats were exposed to white fluorescent light, the serum concentration of calcium did decrease. He showed that this calcium drop was accompanied by a decrease in serum melatonin concentration. This effect can be prevented by shielding the output, by inhibiting corticosterone synthesis, and by administration of endogenous melatonin. Light induced hypocalcemia may result from increased calcium uptake by bone when the blocking effect of melatonin decrease after pineal inhibition by transcranial illumination.[6]

The efficacy of phototherapy in prevention and treatment of hyperbilirubinemia in new born infants has been well established. In the present study all our neonates responded to management with phototherapy. All those neonates who were in need of exchange transfusion but could not be done due to unavailability of blood, also responded well to phototherapy. In this study a significant fall in total and ionic serum calcium levels was observed after phototherapy. Hypocalcemia was observed in larger percentage of preterm neonates as compared to full term neonates. The present study show that there is significant fall in total and ionic serum calcium levels in neonates in different TSB range groups after phototherapy. As the serum bilirubin increases there is a significant fall in total calcium levels among different TSB range groups (TSB 15.1-20 mg/dl and TSB 20.1-30mg/dl). But further studies are needed to confirm significant difference in fall in ionic calcium among different TSB range groups.

CONCLUSIONS:

A significant fall in total and ionized serum calcium levels was observed in icteric neonates after 48 hours of phototherapy. The present study shows hypocalcemia was more common in preterms than term newborns. There is greater fall in total and ionic serum calcium levels at higher total serum bilirubin levels. A statistically significant difference was observed in total calcium levels between TSB groups 15.1-20 and 20.1-30 mg/dl. On clinical assessment preterms developed more symptoms of hypocalcemia than term neonates. Jitteriness was the most common symptom observed. Hypocalcemia in neonates was managed with intravenous calcium gluconate and none required anticonvulsants. All of our neonates responded to management with phototherapy and none of them required exchange transfusion, got improved and discharged. This study shows that neonates under phototherapy are at high risk of hypocalcemia.

It is concluded that phototherapy induced hypocalcemia is a significant problem and hence calcium supplementation to these babies may be considered.

REFERENCES:

1. Taksande A, Vilhekar K, Atkari S .Prediction of development of neonatal hyperbilirubinemia. Ind Medica 2005 ;9(1):5-9.
2. Cloherty JP, Martin RC. Neonatal hyperbilirubinemia. In : Cloherty JP, Eichenwald EC, Stark AR, (Eds.),;. Manual of Neonatal Care.7th Edn.; Philadelphia: Lippincott Williams and Wilkins; 2012.
3. Dennery PA, Seidman DS, Stevenson DK. Neonatal Hyperbilirubinemia. N Engl J Med 2001; 344(8):581-590.
4. Sethi H, Saili A, Dutta AK. Phototherapy induced hypocalcemia. Indian Pediatr 1993;30(12):1403-1406.
5. Romagnoli C, Polidori G, Cataldi L, Tortorolo SG, Segni G. Phototherapy induced hypocalcaemia. J Pediatr 1979;94(5): 813-816.
6. Hakanson DO, Bergstrom WH. Phototherapy induced hypocalcaemia in newborn rats : prevention by melatonin. Science J 1981;214(4522):807-809.
7. Jain BK, Singh H, Singh D, Toor NS. Phototherapy induced hypocalcemia. Indian Pediatr 1998;35(6): 566-567.
8. Eghbalian F, Monsef A. Phototherapy-induced hypocalcemia in icteric newborn. Iran J Med Sci 2002;27(4):169-71.
9. Karamifar H, Pishva N, Amirhakimi GH. Prevalence of Phototherapy Induced Hypocalcemia. Iran J Med Sci 2002; 27(4):166-168.
10. Medhat FB: Assessment of phototherapy induced hypocalcemia. Thesis submitted for MSc. Pediatrics in Cairo University. Classification No.8461;2006.
11. Yadav RK, Sethi RS. The evaluation of the effect of phototherapy on serum calcium level. PJSR 2012;5(2):1-4.
12. Sajjadian N, Taheri PA, Eivazzadeh B. Prevelance of phototherapy induced hypocalcemia in term neonate. Iran J Pediatr 2013;23(6):710-711.
13. Tehrani FHE, Sabet Z, Kavehmanesh Z, Mirzaei M. The effect of phototherapy on serum calcium levels in full term neonates. JBCP 2014;2(2):57-60.
14. Bahbah MH, Nemr FME, Zayat RSE, Aziz EAK: Effect of phototherapy on serum calcium level in neonatal jaundice. Menoufia Med J 2015;28:426-430.
15. Zecca E, Romagnoli C, Tortorola G: Ineffectiveness of Vitamin 25(OH)D3 in the prevention of hypocalcemia induced by phototherapy. Pediatr Med Chir 1983;5(5):317-319.
16. American Academy of Pediatrics. Practice parameter- management of hyperbilirubinemia in healthy term and preterm newborn. Pediatric 1994;94:555-565.
17. Ambalavanan N, Carlo WA. Jaundice and hyperbilirubinemia in newborn. In: Kliegman RM, Stanton BF, Schor NF, Behrman RE, Geme JW (Eds.); Nelson textbook of paediatrics; First South Asia edition. India. Elsevier 2016.
18. Bahbah MH, Nemr FME, Zayat RSE, Aziz EAK. Effect of phototherapy on serum calcium level in neonatal jaundice. Menoufia Med J 2015,28:426-430.

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