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Original Research Article

Is calcium a concern in neonates undergoing phototherapy?

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ABSTRACT

Background: Neonatal hypocalcemia is defined as total serum calcium concentration of < 7 mg/dl or ionized calcium concentration of <4 mg/dl (<1 mmol/L). The current aim was to look the effect of phototherapy on ionized calcium levels before and after phototherapy in otherwise healthy term and late preterm (35 to 37 weeks) neonates.
Methods: The study group included 50 neonates. Measurement of serum ionized calcium levels was done before and at the end of phototherapy.
Results: At the end of phototherapy in study group, a significant fall in calcium level in 64% of term and 76% of late preterm neonates was observed, but almost all except one remained asymptomatic.
Conclusions: The efficacy of phototherapy in the prevention and treatment of hyperbilirubinemia in newborn infants has been well established. The mean duration of phototherapy in our study was 32 hours. Duration of phototherapy may influence the severity of hypocalcaemia. The regulation of calcium homeostasis in the newborn period has been of considerable interest. Phototherapy increases calcium absorption by the bones and leads to the reduction of melatonin levels. Changes in melatonin levels affect the incidence of hypocalcaemia-induced phototherapy. The mechanism of hypocalcaemia 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. It is suggested that serum calcium levels be assessed in neonates treated with phototherapy. Neonatal Jaundice is one of the most common problems that can occur in the newborn. Hypocalcaemia during phototherapy has been reported in literature.

Keywords: Asymptomatic, Hyperbilirubinemia, Hypocalcemia, Neonatal jaundice, Phototherapy

INTRODUCTION

Neonatal hypocalcemia is defined as total serum calcium concentration of <7 mg/dl or ionized calcium concentration of <4 mg/dl (<1 mmol/L). Ionized calcium is crucial for many biochemical processes, including blood coagulation, neuromuscular excitability, cell membrane integrity and function, and cellular enzymatic and secretory activity.[1,2] Romnagoli et al was the first to suggest the association of hypocalcaemia in newborn following phototherapy. Neonatal jaundice is an important problem in the first week of life. It is a cause of concern for the physician and a source of anxiety for the parents.[3,4] High bilirubin level may be toxic to the developing central nervous system and may cause neurological impairment even in term newborns. Nearly 60% of term newborn becomes visibly jaundiced in the first week of life. Phototherapy is the standard of care in the management of hyperbilirubinemia in neonates.[5,6] The predominant mechanism involves transforming unconjugated bilirubin into water-soluble isomers that can be eliminated without conjugation in the liver. Phototherapy is considered as a safe and effective therapeutic modality albeit has few side effects.[7,8] The

known side effects of phototherapy are loose stools, hyperthermia, dehydration due to increased insensible fluid loss, photo retinitis, bronze baby syndrome, and putative DNA damage A lesser known side effect, but a potential complication of phototherapy is hypocalcemia.[9,10]

The relation between hypocalcemia and phototherapy is not very well described in literature except for very few studies. Even though varying incidence ranging from 15 to 60% has been quoted in literature, hypocalcemia remains to be asymptomatic. In the present era of high prevalence of vitamin D deficiency hypocalcemia due to phototherapy may get exaggerated. Hence, the present study was carried out to evaluate the ionized serum calcium level in term and late preterm (35 to 37 weeks) newborns undergoing phototherapy for neonatal jaundice.[10,11]

METHODS

To evaluate the serum calcium levels in otherwise healthy term and late preterm neonates (35 to 37 weeks) receiving phototherapy for neonatal jaundice a tertiary care hospital at Hyderabad. Healthy term and late preterm neonates (35 to 37 weeks) receiving phototherapy for neonatal jaundice were included in the study. Neonates who were at risk of hypocalcaemia such as perinatal asphyxia, respiratory distress, small for gestational age (< 3rd centile on Fenton's charts), infant of diabetic mother and maternal history of consumption of anticonvulsant were excluded.

Those babies who were found to hypocalcaemia prior to phototherapy were excluded from the study. Neonates who were admitted in NICU only for jaundice were assessed and were enrolled in to the study if they satisfied the enrollment criteria. Written informed consent was taken from the parents prior to enrollment.

All the neonates included in the study group had significant hyperbilirubinemia. Evaluation and management with phototherapy was done as per American academy of pediatrics 2004 guidelines. Serum calcium was measured pre and post phototherapy. Convenient sample size of 50 neonates was chosen.

Thorough clinical examination was done for all enrolled neonates Serum bilirubin estimation was done as per the standard guidelines. Ionized serum calcium was done before and at the end of phototherapy.

Ionized serum calcium was determined by acid base analyser machine (ABG machine, Roche Cobas b 121). A level of 1.15 to 1.4 mmol/L and 0.9 to 1.1 mmol/L were considered normal for term and preterm respectively (AAP, 1994). All the neonates were clinically assessed for features of hypocalcaemia i.e. jitteriness, irritability/ excitability, letharginess and convulsion, as well as other complication like rash, loose stool, fever and dehydration during phototherapy.

RESULTS

50 neonates were enrolled in the study, among them 25 were term and 25 were late preterm neonates.

Table 1: Baseline variables.

Variable	Mean or Number (%)
Mean birth weight in gm	2978 (425)
Mean gestation in weeks	37.5 (1.2)
Late preterm group	25 (50%)
Term group	25 (50%)
Male	24 (48%)
Term (> 37 weeks)	25 (50%)
Late preterm (35 to 37 weeks)	25 (50%)
AGA	33 (66%)
SGA	17 (34%)
Mode of delivery	
LSCS	30 (60%)
Vaginal	17 (34%)
Forceps	3 (6 %)
Exlusively breast fed	32 (64%)
Age at the onset of hyperbilirubinemia (hours)	85 (56 to 96)
Duration of phototherapy (hours)	32 hours (SD 14)
Blood group incompatibility	
ABO	10(20%)
Rh	1 (0.5)
Mean TSB mg/dL	16 (1.6)

Table 2: Distribution of cases according to the age of onset of jaundice.

Age of onset (hours)	Term (n = 25)	Late preterm (n = 25)
<24	-	-
24-72	8 (32%)	10 (40%)
>72	17 (68%)	15 (60%)

Females outnumbered males (males 24, females 26) in the study group, none of the term babies developed jaundice before first 24 hours of life; 8 (32%) cases had onset of jaundice between 24 to 72 hours, while majority of cases 17 (68%) had onset of jaundice after 72 hours. In preterm's of study group, 10 (40%) developed jaundice between 24 to 72 hours and 15 (60%) after 72 hours.

In all, 19 (76%) of preterm neonates and 16 (64%) term neonates developed hypocalcaemia after exposure to phototherapy. The mean ionised calcium levels before the onset of phototherapy were significantly different between groups (term vs late preterm; 1.3 vs 1.0 mmol/L; p value <0.01).

Table 3: Ionised calcium levels.

	Late preterm	Term	95% CI	P value
Hypocalcaemia after phototherapy	19 (76 %)	16 (64 %)		
Ionised calcium level (before phototherapy)	1.0 (0.05)	1.3 (0.04)	0.19 to 0.40	<0.01
Ionised calcium lev (end of phototherapy)	0.81(0.2)	0.96 (0.3)	-0.00 to 0.28	0.05
Symptomatic hypocalcaemia	1 (seizures)	0		

Table 4: Ionised calcium, pre and post phototherapy.

	Before Phototherapy	After Phototherapy	Mean diff	P value
Late preterm Mean (SD)	1.0 (0.05)	0.81 (0.2)	0.19	0.000
Term group	1.3 (0.04)	0.96 (0.3)	0.34	0.000

Post phototherapy mean ionised calcium levels remained statistically significant between groups (term vs late preterm; 0.81 vs 0.96 mmol/L; p value <0.01). The fall in ionised calcium pre and post phototherapy was statistically significant in both late preterm and term groups.

DISCUSSION

The overall prevalence of hypocalcaemia was quite high in our study (70%) which is in tune with several reports available in the literature. The prevalence was higher in late preterm group in comparison with term group. Cortisol has a direct hypocalcaemia effect and increases bone uptake of calcium and induces hypocalcaemia. Kumar R et al has reported, a significant fall in calcium level in 66.6% of term and 80% of preterm neonates. Jain et al also observed hypocalcaemia effect of phototherapy, in 30% term and 55% preterm neonates.

Yadav observed that 66% of term and 80% of preterm's developed hypocalcaemia after phototherapy. Sethi et al has studied the effect of phototherapy in 20 terms and 20 preterm hyperblirubinemic neonates. They observed hypocalcaemia in 75% of term and 90% of preterm neonates after phototherapy.[7] Similarly, in 2006, Medhat from Cairo University observed 75% of term and 90% of preterm developed hypocalcaemia after phototherapy.[8] In all, 19 (76%) of preterm neonates and 16 (64%) term neonates developed hypocalcaemia after exposure to phototherapy. The mean ionised calcium levels before the onset of phototherapy were significantly different between groups (term versus late preterm; 1.3 versus 1.0 mmol/L; p value <0.01). Post phototherapy mean ionised calcium levels remained statistically significant between groups (term versus late preterm; 0.81 versus 0.96 mmol/L; p value < 0.01). The fall in ionised calcium pre and post phototherapy was statistically significant in both late preterm and term groups. In this study we also observed a significant fall in the ionised calcium levels before and after phototherapy in both late preterm and term group. Even though there was a biochemical fall in the ionised calcium levels this did not translate in to clinical symptomatology. Only one baby had seizures due to hypocalcemia which later turned out to be severe vitamin D deficiency.

CONCLUSION

The efficacy of phototherapy in the prevention and treatment of hyperbilirubinemia in newborn infants has been well established. The mean duration of phototherapy in our study was 32 hours. Duration of phototherapy may influence the severity of hypocalcaemia. The regulation of calcium homeostasis in the newborn period has been of considerable interest. We could not a detailed work up of babies who developed biochemical hypocalcaemia due to logistic reasons and also for the reason that babies remained asymptomatic. In the present era of high prevalence of vitamin D deficiency whether phototherapy was the principle reason for the fall in the calcium is debatable.

Phototherapy increases calcium absorption by the bones and leads to the reduction of melatonin levels. Changes in melatonin levels affect the incidence of hypocalcaemia-induced phototherapy. The mechanism of hypocalcaemia 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. We could not a detailed work up of babies who developed biochemical hypocalcaemia due to logistic reasons and also for the reason that babies remained asymptomatic. In the present era of high prevalence of vitamin D deficiency whether phototherapy was the principle reason for the fall in the calcium is debatable.

Other limitation of the study was that we did not look in to maternal calcium intake and her calcium status. In conclusion hypocalcemia is a significant concern in babies receiving phototherapy but seems to be asymptomatic. Larger studies are warranted to confirm these findings. The frequency of hypocalcemia is significant in the jaundiced neonates treated with phototherapy. One needs to be vigilant in dealing neonates in this context while serial monitoring for hypocalcemia and its complications should be considered in institutional policy and research priority. The frequency of hypocalcemia is significant in the jaundiced neonates treated with phototherapy. One needs to be vigilant in dealing neonates in this context while serial monitoring for hypocalcemia and its complications

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