Research Article

The Evaluation of Effect of Phototherapy on Serum Calcium Level

Rajesh Kumar Yadav, R.S. Sethi, Anuj S. Sethi, Lalit Kumar, Om Shankar Chaurasia

Department of Paediatrics, M.L.B. Medical College, Jhansi - 284128 (Uttar Pradesh).

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Abstract:

Jaundice is one of the most common problem that can occur in the newborn. The study group included 30 neonates (15 term and 15 preterm) and control group included 20 neonates (10 terms & 10 preterm). All had hyperbilirubinemia. The controls were fully matched with the study group. All the neonates included in the study group required management with phototherapy. The neonates in the control group were managed without phototherapy. Measurement of ionized serum calcium level was done before and after 48 hours of institution of phototherapy in study groups and controls. Before phototherapy, there was no statistical significant difference in mean serum calcium level in term & preterm neonates of both study & control group. After 48 hours of phototherapy in study group, a significant fall in calcium level in 66.6% of term & 80% of preterm neonates was observed. Whereas, no difference was observed in control group. It is suggested that calcium level be assessed in neonates treated with phototherapy for more then 48 hours and managed accordingly.

Key Words: Hyperbilirubinemia, Phototherapy, Hypocalcemia.

Introduction:

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. 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 new borns become visibly jaundiced in the first week of life. In most of cases, it is benign and no intervention is required. Approximately 5-10% of them have clinically significant hyperbilirubinemia in whom the use of phototherapy becomes mandatory.

Jaundice is attributable to physiological immaturity of neonates to handle increased bilirubin production. Visible jaundice usually appear between 24-72 hours of age. Basic pathophysiology of jaundice is same in term and preterm neonates, but premature babies are at a higher risk of developing hyperbilirubinemia.

The commonly known side effects of phototherapy are loose stools, hyperthermia, dehydration fluid loss, skin burn, photoretinitis, low platelet count, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency and DNA damage. A lesser known side effect, but potential complication of phototherapy is hypocalcemia (Hunter, 2004).

Neonatal hypocalcemia is defined as total serum calcium concentration of < 7 mg/dl or ionized calcium concentration of < 4mg/dl (<1mol/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.

Romagnoli et al (1979) for the first time suggested the association of hypocalcemia with phototherapy in preterm newborns. Similarly Hakanson & Bergstrom (1981) documented this observation in newborn rats. There are few studies on hypocalcaemic effect of phototherapy (Tan, 1991; Sethi et al, 1993; Hakanson & Bergstrom, 1981).

Hence, the present study was carried out to evaluate the ionized serum calcium level in newborns who had undergone phototherapy.

Material and Methods:

The study was carried out in the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics, M.L.B. Medical College, Jhansi from February 2009 to April 2010 after taking approval from the institutional ethical committee. Study group included 30 neonates while 20 neonates served as a control. In the study group, 15 neonates were term (>37 weeks) and 15 neonates were preterm (>32 weeks and <37 weeks). Ten neonates each, acted as a control for the

Corresponding Author: Dr. Rajesh Kumar Yadav, Room No. 144, S.B.H. C.V. Raman Hostel, M.L.B. Medical College, Jhansi - 284128 (Uttar Pradesh)
Phone No.: 09452119483
E-mail : drrajesh.yadav71@gmail.com

two groups of study subjects. The controls were fully matched with the study group with respect to age, sex, period of gestation and birth weight.

All the neonates included in the study group had hyperbilirubinemia which required management with phototherapy (AAP, 1994; Cashore, 2000).

Table I: Phototherapy in term neonates as per age (hours) and serum bilirubin level

Age	Consider phototherapy	Phototherapy
	(serum bilirubin level)	
24 hours	-	-
25-48 hours	>12 mg/dl	>15 mg/dl
49-72 hours	>15 mg/dl	>18 mg/dl
>72 hours	>17 mg/dl	>20 mg/dl

Table II: Phototherapy in preterm neonates as per weight and serum bilirubin level

Weight	Phototherapy (serum bilirubin level)
1000-1250 gm	8-10 mg/dl
1250-1500 gm	10-12 mg/dl
1500-2500 gm	15-18 mg/dl

Complete history and thorough physical examination was carried out in all the cases of study and control group. Besides routine investigation, ionized serum calcium and total serum bilirubin levels, before and after 48 hours of phototherapy were estimated. Total serum bilirubin was estimated by Malloy & Evelyn method using diazo reagent. Ionized serum calcium was determined by acid base analyzer machine (ABG machine, Roche Cobas b 121). A level of 0.9 to 1.1 mmol/L and 1.15 to 1.4 mmol/L were considered normal for preterm and term respectively (AAP, 1994).

The neonates in the control group were babies who had hyperbilirubinemia but were managed without phototherapy. Any neonate who had or developed a complication during the course of study i.e. birth asphyxia, respiratory distress, septicemia, infants of diabetic mother or any other high risk factor, were excluded from the study.

The neonates were clinically assessed for features of hypocalcemia i.e. jitteriness, irritability/ excitability, letharginess and convulsion, as well as other complication like rash, loose stool, fever and dehydration. Hypocalcemia in the neonate was managed with intravenous calcium; none of them required anticonvulsant drug.

The results were analyzed using paired and unpaired students *t* test.

Results:

In the study group, none of the term cases developed jaundice before first 24 hours of life; 20% of cases had onset of jaundice between 24 to 72 hours, while majority of cases (80%) had onset of jaundice after 72 hours. Whereas in control group, all the cases developed jaundice after 72 hours. In preterms of study group, 5 (33.3%) developed jaundice between 24 to 72 hours and 10 (66.66%) after 72 hours whereas 2 (20%) of control group developed jaundice between 24 to 72 hours and rest of the 8 (80%) cases after 72 hours (Table III).

All the cases of study group had serum bilirubin level (SBL) of more than 15 mg/dl whereas in control group none of the case had SBL more than 15 mg/dl (Table IV).

After exposure, there was no significant difference in serum calcium level in study and control group before phototherapy. After 48 hours of phototherapy in preterm neonates of the study group, there was significant fall in calcium level ($p<0.0001$). Similarly, in term neonates there was significant fall in serum calcium level after phototherapy ($p<0.005$;Table V).

In all, 12 (80%) of preterm neonates and 10 (66.6%) term neonates developed hypocalcemia after exposure to phototherapy. None of the neonates in control group developed hypocalcemia.

Of the 10 term neonates that developed hypocalcemia, 8 became symptomatic; 3 (30%) developed jitteriness, 2 (20%) developed irritability/excitability, 3 (30%) developed letharginess and none of the neonate developed convulsion. All the preterm neonates who developed hypocalcemia after exposure to phototherapy, became symptomatic; 6 (50%) developed jitteriness, 3 (25%) irritability/excitability, 3 (25%) letharginess and none of the neonate developed convulsions (Table VI).

Discussion:

The efficacy of phototherapy in prevention and treatment of hyperbilirubinemia in newborn infants has been well established. Romagnoli et al (1979) was the first to suggest the association of hypocalcaemia in the phototherapy in preterm newborn. Similarly, Hakanson & Bergstrom (1981) documented this observation in newborn rats. Gutcher & Odell (1983) observed

Table-III : Distribution of cases according to the age of onset of jaundice

Age of onset (hours)	Study group (n=30)		Control Group (n=20)	
	Term (n=15) (>37 weeks)	Preterm (n=15) (< 37 weeks)	Term (n=10) (>37 weeks)	Preterm (n=10) (< 37 weeks)
< 24	-	-	-	-
24-72	3 (20%)	5 (33.33%)	0	2 (20%)
>72	12 (80%)	10 (66.66%)	10 (100%)	8 (80%)

Table IV: Distribution of cases according to total serum bilirubin level and birth weight

Total serum bilirubin (mg/dl)	Study Group (weight)		Control Group (weight)	
	>2.5kg (Term) mean weight (2.72kg)	>1.5kg-2.5kg (Preterm) mean weight (2.23kg)	>2.5kg (Term) mean weight (2.76kg)	>1.5kg-2.5kg (Preterm) mean weight (2.09kg)
<10mg/dl	0	0	2 (20%)	3 (30%)
10-15mg/dl	0	0	8 (80%)	7 (70%)
>15mg/dl	15	15	0	0

Table V: Serum ionized calcium level (mmol/l) before & after 48 hours of phototherapy.

	Preterm ionized calcium level (mmol/l; mean ± SD)		Term ionized calcium level (mmol/l; mean ± SD)	
	Prestudy	Poststudy	Pretstudy	Poststudy
Cases	1.0387±0.6139	0.75±0.1367	1.196±0.0548	0.98±0.1426
Control	1.007±0.0458	098±0.0479	1.193±0.0380	1.77±0.0357
Significance	p=0.171	p<0001	p=0.81	p<005

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

Symptoms	Term	Preterm	Controls
Jitteriness	3	6	0
Irritability/ excitability	2	3	0
Lethargic	3	3	0
Convulsion	0	0	0

significant decrease in serum calcium level in newborn rats after exposure to fluorescent daylight.

Ionized calcium is crucial for many biochemical processes including blood coagulation, neuromuscular excitability, cell membrane integrity and function and cellular enzymatic and secretory activity.

Hypocalcaemia increases cellular permeability to sodium ions and increased cell membrane excitability. The signs are usually non-specific like apnea, seizure, jitterness, increased extensor tone, clonus, hyperreflexia, and stridor (Laryngospasm).

Sethi et al (1990) has studied the effects of phototherapy in 20 term & 20 preterm hyperblirubinemic neonates. They observed that 75% of term & 90% of preterm neonates developed hypocalcaemia after phototherapy. Similarly, Medhat (2006) of Cairo University observed that 75% of term & 90% of preterm developed hypocalcaemia after phototherapy. Observation of the present study are in agreement with the above studies.

Jain et al (1998) also observed hypocalcaemic effect of phototherapy, in 30% term and 55% preterm neonates, which is much lower than the above mentioned studies.

Hunter (2004) hypothesized that phototherapy inhibits pineal secretion of melatonin which blocks the effect of cortisol on bone calcium. Cortisol unchecked exerts a direct hypocalcemic effect and increases bone uptake of calcium as well.

Neonates requiring phototherapy are at a higher risk of developing hypocalcemia. Therefore, it is

suggested that newborn requiring phototherapy administration of calcium may be considered in them.

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