

# Serum Calcium Levels in Preterm and Term Neonates on Phototherapy

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## Abstract

**Introduction:** In addition to known causes of hypocalcemia like, prematurity, Intrauterine growth retardation (IUGR), asphyxia, sepsis, infants of diabetic mothers (IDM), high phosphate formula, Magnesium deficiency, effect of phototherapy on serum calcium levels has caught attention of researchers from time to time. The objectives of this study were to evaluate serum calcium levels in relation to duration of phototherapy, single surface Vs double surface phototherapy in term and preterm neonates.

**Materials and Methods:** This study was done in a neonatal ICU of a tertiary care hospital. Hundred preterm and term neonates > 72 hrs of age with weight appropriate for gestational age were selected. Serum calcium levels were measured at the onset and after 24 hrs and 48 hrs of phototherapy and results were analyzed in both the groups. **Results:** Hypocalcemia was more frequently observed in term group as compared to preterm group. Hypocalcemia occurred more frequently after 48 hrs of continuous phototherapy in both groups. Hypocalcemia was more common under DSPT as compared to SSPT in both groups.

**Conclusion:** Hypocalcemia is a significant problem in neonates subjected to phototherapy.

**Key words:** Hyperbilirubinemia, Hypocalcemia, single surface phototherapy, double surface phototherapy, serum bilirubin.

## Introduction

Pathological hyperbilirubinemia with its neurotoxic complications is one of the reasons for admission of newborns to neonatal unit in addition to sepsis, perinatal asphyxia, prematurity, respiratory distress syndrome and metabolic derangements<sup>1</sup>. Phototherapy is a convenient and inexpensive modality for the treatment of neonatal hyperbilirubinemia which has revolutionized the management of jaundice thereby decreasing the number of exchange transfusions drastically<sup>2</sup>. It requires protection of eyes to prevent retinal damage, covering genitalia to prevent chromatid changes, maintenance of adequate hydration particularly in preterm babies due to large surface area and euthermia. Decreased activity of glutathione reductase in red blood cells and subsequent haemolysis and preventive role of vitamin B<sub>2</sub> was suggested by WuZL<sup>3</sup>. Green stools due to transient lactose intolerance and increased concentration of bile salts and unconjugated bilirubin in the bowel is common under phototherapy<sup>4</sup>.

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Hypocalcemia defined as total serum calcium level less than 8mg/dl in term and less than 7mg/dl in preterm babies is an important metabolic aberration in neonatal period due to its ill effects on neurological and cardiac functions<sup>5</sup>. Hypocalcemia may be asymptomatic particularly early onset hypocalcemia or symptomatic in the form of jitteriness, lethargy, apnea, hypotonia, high pitched cry, stridor, irritability and seizures. Uninhibited effect of corticosteroids due to decreased synthesis of melatonin from pineal gland under phototherapy is thought to be responsible for hypocalcemia.

Blue lamps with a peak output of 425-475nm at a distance of 18" (45cm) with irradiance of 6-12 $\mu$ w/cm<sup>2</sup>/nm constitutes conventional phototherapy whereas intensive phototherapy involves increasing irradiance to more than 25 $\mu$ w/cm<sup>2</sup>/nm<sup>6,7</sup>.

Because of widespread use of phototherapy for treatment of neonatal hyperbilirubinemia, present study was conducted to study the effect of phototherapy, its duration and single (SSPT) versus (vs) double surface phototherapy (DSPT) on serum calcium levels in term and preterm babies and its clinical implications if any.

## Materials and Methods

Study comprised of 100 inborn and out born newborns admitted in NICU of Sri Guru Ram Das Institute of Medical Sciences and Research for treatment of hyperbilirubinemia. 46 were preterms and 54 were term babies. They were subjected to single or double surface phototherapy depending upon serum bilirubin values. Phototherapy was given according to the American Academy of Pediatrics Subcommittee on hyperbilirubinemia guidelines in neonates 35 or more weeks of gestation<sup>8</sup>. In neonates <35 weeks gestation phototherapy was started when total serum bilirubin was 0.75% of birth weight in grams. Cut off values were 7-9mg/dl in 1000-1500 grams, 10-12 mg/dl in 1500-2000 grams, 13-15 mg/dl in 2000-2500 grams birth weight<sup>9</sup>. Single surface phototherapy was used for serum bilirubin level in the range 50-60% and double surface phototherapy for serum bilirubin level in the range of 60-70% of recommended value for exchange transfusion for different birth weights<sup>10</sup>. Babies with IUGR, IDM, prolonged and difficult labor, respiratory distress and those receiving cow's milk were excluded from study. Phototherapy units with four blue and two white lights with a wavelength of 420-480nm and irradiance of 6-12 $\mu$ w/cm<sup>2</sup>/nm were used placed at a distance of 45cm from skin surface. Serum calcium was measured at the onset and then at 24 and 48 hrs of phototherapy by OCPC method. In addition to CBC and blood group, serum bilirubin was estimated by Jendrassik and Grof method. Data was compiled and statistically analyzed with student's t test. t value was calculated and compared with table value for given degree of freedom and level of significance calculated for 95% confidence limit.

$T = \frac{\bar{d} (n)^{1/2}}{S} = \frac{[\sum d^2 - n(\bar{d})^2]^{1/2}}{(n-1)^{1/2}}$   $\bar{d} = \sum d/n$  and interpreted following t table.

## Results

All the 46 preterms and 54 term babies were appropriate for gestational age and more than 72 hrs of age. Majority of babies (preterm 78% and term 85%) were 72-96 hrs old at the initiation of phototherapy. Gestational age was 34-37 weeks in 28 preterms and 30-34 weeks in 18 preterm babies thus all were more than 30 weeks of gestation. Hypocalcemia was observed in 20 out of 46 preterms (43%) and 30 out of 54 term neonates (56%) after 48 hrs of continuous phototherapy.

At the end of 24 hrs four preterms (9%) developed hypocalcemia with number increasing to 20 (43%) at end of 48 hrs with a t value 9.786 and 11.443 respectively which is more than table value of t at 95% confidence level (t 0.05=2.000) which was statistically significant. 23 term babies (42%) developed hypocalcemia at the end of 24 hrs and number rose to 30 (56%) at the end of 48 hrs when three babies had serum calcium levels less than 7mg/dl. t value was 7.58 and 9.66 respectively which was statistically significant (Table 1).

Out of 24 preterms subjected to SSPT, none had hypocalcemia at end of 24 hrs while seven had hypocalcemia at the end of 48 hrs. t value was more than table value of t at 95% confidence level (t 0.05 = 2.069). On the other hand under DSPT four preterms (18%) out of 22 had hypocalcemia at the end of 24 hrs and 13 (59%) had serum calcium level below 7mg/dl at 48 hrs, t value higher than table value of t at 95% confidence level which is statistically significant (Table 2).

11 (33%) and 14 (42%) term babies developed hypocalcemia under SSPT at 24 and 48 hrs respectively. Fall in serum calcium level is statistically significant as t value is more than table value of t at 95% confidence level (t 0.05= 2.02). Under DSPT 12 (57%) term babies had hypocalcemia at 24 hrs and 16 (76%) term babies developed hypocalcemia at 48 hrs. Two term neonates had serum calcium level below 7mg/dl at 48 hrs. Fall in serum calcium level is statistically significant since t value is more than table value of t at 95% confidence level (t. 0.05 = 2.084) (Table 3).

On the whole, hypocalcemia occurred more commonly under DSPT than SSPT in both term and preterm babies. It was more frequently encountered in term as compared to preterm babies 14 (42%) vs 7 (29%) under SSPT and 16 (76%) vs 13 (59%) under DSPT (Table 4).

Symptomatic hypocalcemia was more common in preterm group than term group. Jitteriness was the commonest symptoms observed in 7 (35%) preterms and 3 (10%) term babies followed by lethargy in 2

(10%) preterms and 1 (4%) term baby. Symptoms like irritability, poor feeding and convulsions were not encountered in the present study (Table 5).

**Table 1:** Serum calcium levels after 24 hrs and 48 hrs of phototherapy

Serum Calcium mg/dl	Preterm (n=46)			Term (n=54)		
	0 hrs	24 hrs	48 hrs	0 hrs	24hrs	48hrs
< 7	--	4 (9)	20 (43)	-(-)	- (-)	3 (6)
7.1-8	10 (22)	21(46)	19(41)	-(-)	23(42)	27(50)
8.1-9	22 (48)	20(43)	7 (15)	39(72)	29(54)	24(44)
> 9	14 (30)	1 (2)	- (-)	15(28)	2(4)	(-)
t value		9.786	11.443	7.58	9.66	

Figures in paranthesis indicate percentage

**Table 2:** Effect of SSPT Vs DSPT on serum calcium level in preterm babies.

Serum Calcium levels mg/dl	SSPT (n=24)			DSPT( n=22)		
	0 hrs	24 hrs	48hrs	0 hrs	24 hrs	48 hrs
< 7	--	--	7 (29)	--	4 (18)	13 (59)
7.1-8	3 (13)	11 (46)	13 (54)	7 (32)	10 (46)	6 (27)
8.1-9	13 (54)	12 (50)	4 (17)	9 (41)	8 (36)	3 (14)
>9	8 (33)	1 (4)	-	6 (27)	-	-
t. value		5.856	7.65		8.895	9.02

Figures in paranthesis indicate percentage

**Table 3:** Effect of SSPT vs DSPT on serum calcium level in term babies.

Serum Calcium levels mg/dl	SSPT (n=33)			DSPT (n=21)		
	0 hrs	24 hrs	48hrs	0 hrs	24 hrs	48 hrs
< 7	--	--	1 (3)	--	-	2 (9)
7.1-8	--	11(33)	13 (39)		12(57)	14(67)
8.1-9	23(70)	20(61)	19(58)	16(76)	9 (43)	5 (24)
>9	10(30)	2(6)	-	5(24)		-
t. valve		5.3112	6.685		5.836	7.28

Figures in paranthesis indicate percentage

**Table 4:** Comparison of hypocalcemia in Preterm & term neonates under SSPT and DSPT.

	Total number	Number on SSPT	Hypocalcemic	Number on DSPT	Hypocalcemic
Preterm	46	24	7 (29%)	22	13 (59%)
Term	54	33	14(42%)	21	16(76%)

Figures in paranthesis indicate percentage

**Table 5:** Signs and symptoms of hypocalcemia.

	Preterm (n=20)	Term (n=30)
Lethargy	2 (10%)	1 (4%)
Irritability	--	--
Poor feeding	--	--
Jitteriness	7 (35%)	3 (10%)
Convulsions	--	

Figures in paranthesis indicate percentage

## Discussion

Forty six preterm >30 weeks of gestation and 54 term babies were enrolled for the present study. All the babies were more than 72 hrs of life to avoid effect of early onset hypocalcemia. Sethi et al (1993)<sup>12</sup> and Eghbalian F et al (2002)<sup>14</sup> excluded newborns with icterus in first 24 hrs of life. Sethi et al (1993)<sup>12</sup> and Karamifer H et al (2002)<sup>13</sup> selected preterms more than 31 weeks whereas Eghbalian et al (2002)<sup>14</sup> included only term neonates.

All the term and preterm neonates in the present study were appropriate for gestational age. Same was the case in the studies done by Romagnoli et al (1979)<sup>16</sup>, Sethi et al (1993)<sup>12</sup> and Jain BK et al (1998)<sup>15</sup>.

Hypocalcemia was more commonly encountered in term neonates 30 (56%) as compared to preterm neonates 20 (43%). Hypocalcemia was related to duration of phototherapy in both groups. It was detected in 4 (9%) and 20 (44%) preterm babies at 24 hrs and 48 hrs of phototherapy respectively. In term group hypocalcemia was detected in 23 (42%) and 30 (56%) babies at the end of 24 hrs and 48 hrs of phototherapy respectively. Hypocalcemia was more commonly observed under DSPT as compared to SSPT in both groups. In preterm group, hypocalcemia occurred in 13 (59%) neonates under DSPT as compared to 7 (29%) under SSPT. In term group, hypocalcemia occurred in 16 (76%) newborns under DSPT. versus 14 (42%) under SSPT. Higher incidence of hypocalcemia in term group was probably attributed to higher cut off value of serum calcium level of 8mg/dl as compared to 7mg/dl in preterm babies.

Much higher incidence of hypocalcemia was observed by Sethi et al<sup>12</sup> and lowest incidence was reported by Karamifer H et al<sup>13</sup>. Hypocalcemia was reported more frequently in preterm babies as compared to term babies, percentage being 90%, 55% and 22.6% in preterm group & 75%, 30% and 87% in term group by Sethi et al (1993)<sup>12</sup> Jain BK et al (1998)<sup>15</sup> Karamifer H et al (2002)<sup>13</sup>. Romagnoli et al (1979)<sup>16</sup> only studied preterm group and observed hypocalcemia in 52.3% babies.

The differential effect of single versus double surface phototherapy has not been studied by other workers. In present study symptomatic hypocalcemia was observed more frequently under DSPT as out of seven preterm having jitteriness six were under DSPT and two preterms had lethargy that too under DSPT. Jain BK et al<sup>15</sup> and Sethi et al<sup>12</sup> reported higher incidence of symptomatic hypocalcemia in preterm group (55% and

50% respectively) as compared to term group (30% and 15% respectively). Symptomatic hypocalcemia has not been reported by Karamifer H et al (2002)<sup>13</sup>. Jitteriness was observed in 90% and 64% and irritability in 40% and 27% by Sethi et al<sup>12</sup> and Jain BK et al<sup>15</sup> respectively in preterm group. In term neonates jitteriness was observed in all babies by Sethi et al<sup>12</sup> followed by irritability in 33%. Jitteriness, lethargy & irritability was noticed in 50%, 33% and 50% of hypocalcemic term babies by Jain BK et al.<sup>15</sup> In present study symptoms occurred only in term neonates under DSPT.

## Conclusion

Thus hypocalcemia is a significant problem in neonates subjected to phototherapy which is a commonly used modality of treatment for neonatal hyperbilirubinemia hence there is need for closed monitoring of serum calcium levels and prophylactic calcium supplementation in neonates subjected to phototherapy.

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**Conflict of Interest:** None

**Permission from IRB:** Yes

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