

THE EFFECT OF PHOTOTHERAPY ON SERUM IONIZED CALCIUM LEVELS IN NEONATES WITH UNCONJUGATED HYPERBILIRUBINEMIA

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ABSTRACT: AIM: To study the occurrence of hypocalcemia in neonates with hyperbilirubinemia after 48 hours of continuous phototherapy and to compare the results between term and preterm neonates. **METHODS:** This study was performed on 100 neonates with unconjugated hyperbilirubinemia, 55 term and 45 preterm, who were given phototherapy in neonatal intensive care unit. Serum ionized calcium levels were checked and after 48 hours of phototherapy. The prevalence of hypocalcemia after 48 hrs. of phototherapy was observed and compared between full term and preterm neonates. Neonates who had hyperbilirubinemia, asphyxia, respiratory distress, haemolytic anaemia sepsis were excluded from the study. **RESULTS:** 46/100 NEONATES, THAT IS 46% developed hypocalcemia. 22/55 full term neonates, that is 40% and 24/45 preterm neonates that is 53% developed hypocalcemia after 48 hrs. of phototherapy. **CONCLUSION:** significant decline in serum calcium level is observed in neonates receiving phototherapy for hyperbilirubinemia. **KEYWORDS:** Hypocalcemia, phototherapy, hyper bilirubinemia.

INTRODUCTION: Neonatal hyperbilirubinemia is one of the common conditions occurring in the neonatal period. It is commonly managed by phototherapy with its inherent complications. About 60% of term and 80% of preterm infants develop jaundice in the first week of life.¹ Hyperbilirubinemia leading to encephalopathy is a devastating brain injury, which can cause permanent neurodevelopmental handicap.² It is commonly managed by phototherapy with its inherent complications. It is very fortunate that a non-invasive and easily available, phototherapy, is effective in degrading unconjugated bilirubin.³

Pathophysiological basis of the jaundice is the same in term preterm infant, but premature babies are at a higher risk of developing hyperbilirubinemia. High bilirubin may cause neurological impairment even in term neonates.

When comparing blue, blue-green, green and white light, researchers found that blue light was the most effective in degrading bilirubin. Therefore phototherapy with blue light is widely used in the clinical practice.⁴ Blue lamp with a peak output of 425-475nm at a distance of 18" or 45cm with irradiance of 6- 12 μ w/cm²/nm constitutes conventional phototherapy. Phototherapy may also lead to undesired effects including skin rash, diarrhoea, dehydration, temperature instability, skin rashes, loose stools, retinal damage, hypocalcemia and bronze baby syndrome.⁵

Hypocalcemia is one of the known adverse effects. 90% of preterm and 75% full-term neonates develop hypocalcemia after being subjected to phototherapy.⁶ Jaundice occurs due to physiological immaturity of neonates to handle increased bilirubin production. Visible jaundice

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usually appears between 24-72hrs. Of age. Even though pathophysiology of jaundice is same in term and preterm neonates, premature babies are at a higher risk of developing hyperbilirubinemia. In preterm infants hypocalcemia is defined as total serum calcium of less than 7mg/dl or 1.75mmol/L., OR ionized calcium level less than 4mg/dl, or 1 mmol/L. in full-term infants total serum calcium level less than 8mg/dl (2mmol/L) or ionized calcium level less than 4.8mg/dl (1.2mmol/L).⁷ Ionized calcium is essential for many biochemical processes blood coagulation, cell membrane integrity and function, cellular enzymatic activity and neuromuscular excitability. The underlying mechanism for phototherapy induced hypocalcemia, although not yet well understood, but it seems that hypocalcemia is accompanied by a decrease in serum melatonin concentration which in turn is regulated by the pineal gland in normal humans. However, it is shown to be influenced by the diurnal variation.

Hypocalcemia can cause serious complications like convulsions, apnoea, irritability, jitteriness.⁸ Hence, phototherapy induced hypocalcemia is a significant problem. There are some reports on hypocalcemic effect of phototherapy especially in preterm neonates. There are still few studies on hypocalcemic effect of phototherapy on the term new-born's. Few recommend that in order to prevent hypocalcemia, babies should be given calcium as prophylaxis.⁹

Romagnoli et al (1979) for the first time suggested the association of hypocalcemia with phototherapy in preterm new-borns. So this study was undertaken to evaluate the occurrence of phototherapy induced hypocalcemia and to compare it between full-term and preterm neonates.

MATERIALS AND METHODS: The present study was carried out in Neonatal Intensive Care Unit of the department of Paediatrics, government general hospital, government medical college, Ananthapuram, from September 2014 to February 2015.

Total serum bilirubin estimation is a routine procedure in our hospital for all those babies receiving phototherapy for neonatal jaundice. No special consent was required for estimation of Total serum bilirubin as it is of patient care. There were no ethical issues involved and apart from blood sampling, no other invasive procedure was carried out on new borns as a part of the study. Serum calcium level was estimated in the same blood sample.

Hundred new borns, of which 55 full term and 45 preterm neonates admitted in the NICU at our hospital and fulfilling the criteria of jaundice and required phototherapy were included in the study. Neonates were classified on the basis of gestational age into full term and preterm with the help of the New Ballard's score. Neonates with conjugated hyperbilirubinemia birth asphyxia, septicaemia, renal failure and abnormal electrolyte status detected before phototherapy were excluded from these study. Detailed history and examination of neonates admitted with jaundice was carried out, according to a predesigned proforma. 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, septecemia, infants of diabetic mother or any other high risk factor, were excluded from the study.

The blood samples were drawn from the neonates for serum bilirubin estimation and serum ionized calcium estimation, before and after 48 hours of phototherapy. Total serum bilirubin was estimated by Diazo method ionized serum calcium was estimated by O-

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cresolphthalene complexone method. The neonates were clinically assessed for features of hypocalcemia that is jitteriness, irritability, excitability, letharginess and convulsions, and as well as other complications like rash, loose stools, fever and dehydration. Hypocalcemia in the neonate was managed with intravenous calcium.

The results were analysed using paired and unpaired students.

RESULTS: In the present study, all the cases had developed jaundice after 72 hrs of life.

TERM	Mean value of ionized calcium before 48 hrs of phototherapy(mmol/L)	Mean value of ionized calcium after 48 hrs of phototherapy(mmol/L)	P-value
Full term neonates	1.27±0.07	1.07±0.18	<0.0001
Preterm neonates	1.07±0.18	0.891±0.12	<0.0001

Table 1: Comparison of ionized calcium levels before and after phototherapy

Table 1 shows that after exposure to 48 hrs of continuous phototherapy, in preterm units, there was a significant fall in serum ionized calcium level($p<0.0001$). Similarly, in term neonates there was a significant fall in serum ionized calcium level ($p<0.0001$).

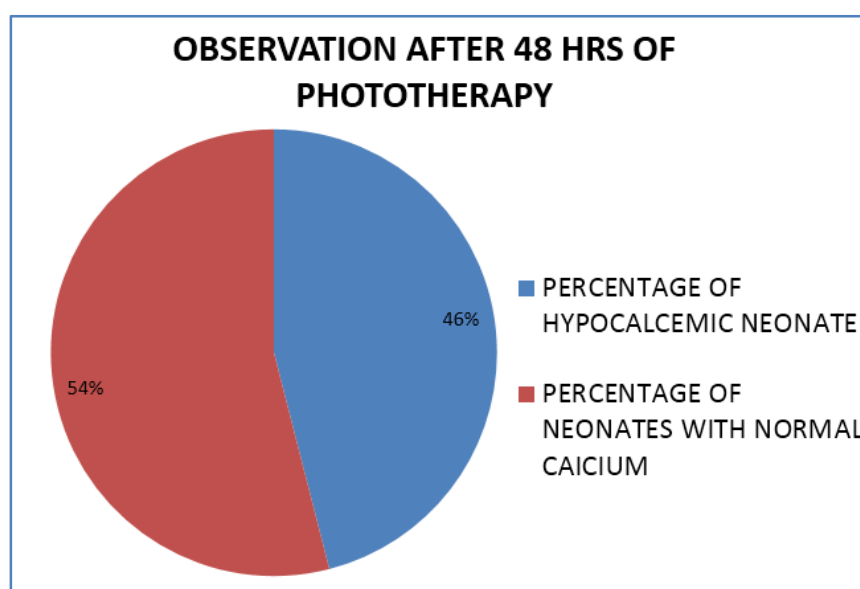


Fig. 1: Percentage of hypocalcemic neonates after 48 hrs of phototherapy

Above shows that 46/100(46%) neonates developed hypocalcemia.

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TERM	No. of hypocalcemic neonates after 48 hrs of phototherapy	Percentage of hypocalcemic neonates after 48 hrs of phototherapy
Full term (n=55)	22	40%
Preterm (n=45)	24	53%

Table 2: comparison of percentage of hypocalcemic term and preterm neonates after 48 hrs of phototherapy

Table 2 shows that 22/55(40%) term neonates, and 24/45 (53%) preterm neonates developed hypocalcemia after 48 hrs. of phototherapy. Thus, the percentage of hypocalcemia was statistically highly significant ($p < 0.048$) in preterm neonates units.

symptom	full-term	preterm	P-value
lethargy	6	4	0.47
jitteriness	7	8	0.034
convulsions	0	0	—

Table 3: comparison of symptomatic hypocalcemic neonates

Table 3 shows that of the 22 term neonates who had hypocalcemia, 13 were symptomatic. Out of them, 7 developed jitteriness, 6 were lethargic and none of them developed convulsions. Of the 24 preterm neonates who had hypocalcemia after exposure to phototherapy, 12 became symptomatic. Out of them, 8 developed jitteriness, 4 were lethargic and none of them developed convulsions.

DISCUSSION: This study shows significant decline in serum ionized calcium levels to the hypocalcemic level in neonates who had been given phototherapy. A higher percentage of preterm neonates were symptomatic showing the effect to be significantly more in them. Preterm neonates are physiologically prone for hypocalcemia. Thus, by subjecting them to phototherapy we put them at a higher risk for developing hypocalcemia eventually causing serious complications.

An older study¹⁰ had reported the effects of phototherapy in 20 term and preterm neonates with jaundice in which 75% term and 90% preterm neonates developed hypocalcemia after phototherapy. Another study¹¹ observed hypocalcemic effect of phototherapy in 30% term and 55% preterm neonates. A recent study¹² by Oden Bourgeois on 63 term neonates showed a statistically significant decline in serum calcium levels after phototherapy. Another recent study⁷ observed that after 48 hours of phototherapy given to 15 term neonates and 15 preterm neonates 66.6% of preterm neonates developed hypocalcemia.

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It has been shown that by covering the heads of the neonates during phototherapy, its effect on calcemia level is prevented significantly proving the effect of phototherapy on the pineal gland eventually causing hypocalcemia¹³. An earlier study showed a higher incidence of symptomatic hypocalcemia in preterm neonates mainly jitteriness and irritability¹⁰. Similarly another study recently reported a higher incidence of jitteriness and irritability in preterm neonates subjected to phototherapy¹⁴. We too have observed similar results among preterm neonates in our study though none of the neonates developed apnoea or convulsions. Correlating the findings of the present study with the previous few studies indicate that there is a significant decline in serum calcium to the hypocalcemic level in neonates subjected to phototherapy. Neonates requiring phototherapy are at a higher risk of developing hypocalcemia. Therefore, it is suggested that in neonates subjected to phototherapy administration of prophylactic calcium might be considered.

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