



## OBSERVATIONAL STUDY OF CLINICAL COMPLICATIONS AND HYPOCALCEMIA ASSOCIATED WITH PHOTOTHERAPY IN PRE TERM NEONATES

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**ABSTRACT** *Introduction:* Phototherapy is an appropriate and relatively safe measure in reducing indirect bilirubin levels in newborn. The commonly known adverse effects of phototherapy are loose green stools, hyperthermia, insensible water loss and dehydration, skin rashes and skin burns, photo-retinitis, bronze baby syndrome, hemolytic anemia due to photo-oxidation of red cells, tanning of skin, and DNA damage. A lesser known and studied but potential adverse effect of phototherapy is hypocalcemia. *Aim:* The present study aimed at detecting the effect of phototherapy on total serum calcium level and other short term clinical side effects in preterm neonates. *Materials and Methods:* This institutional based observational study was conducted at neonatal unit of Zanana Hospital, RNT Medical College, Udaipur, Rajasthan during June 2018 TO December 2018 with approval of Institutional Ethics Committee. Total n=214 neonates were enrolled for the study after taking written consent from their parents. Cases were divided in study group n=116 which required phototherapy and control group n=98 which did not required the same. Clinical and laboratory data assessed in the starting and after 48-72 hrs. *Results:* Clinical complications of phototherapy in study group were rashes in 32(27.59%), loose stools in 26(22.41%), dehydration in 14(12.07%) and fever in 11(9.48%). 54(46.55%) neonates did not showed any clinical complications. Study group showed significant weight loss than control group. Significant mean bilirubin level reduction seen in study group as compare to control group. Fall in Mean total serum calcium level in study group was observed as compare to control group which is statistically significant (p<.001). In study group 38(32.8%) neonate developed hypocalcemia after phototherapy. Out of these 21(55.3%) neonates had symptom of hypocalcemia and 17(44.7%) neonate were asymptomatic. Most common symptom was jitteriness 11(52.4%), followed by irritability & jitteriness 7(33.3%) and irritability 3(14.3%). Among control 1(1.72%) neonate developed hypocalcemia and was asymptomatic. *Conclusion:* Hypocalcemia is a common adverse effect of phototherapy in pre term infants. Jitteriness and irritability are initial clinical manifestations of hypocalcemia. There are very less serious side effects of phototherapy if given with precautions.

**KEYWORDS :** hyperbilirubinemia, phototherapy, preterm, hypocalcemia.

### INTRODUCTION

Phototherapy is now the most commonly used method of treatment of hyperbilirubinemia [1]. Safety and efficacy of phototherapy in prevention and treatment of neonatal hyperbilirubinemia has been well established by several control trials [2][3]. The commonly known adverse effects of phototherapy are loose green stools, hyperthermia, insensible water loss and dehydration, skin rashes and skin burns, photo-retinitis, bronze baby syndrome, hemolytic anemia due to photo-oxidation of red cells, tanning of skin, and DNA damage [4][5][6].

Different studies found that phototherapy influence the level of electrolytes and other ions especially on serum calcium and sodium levels during initial 24-72 hours of life [7]. A lesser known and studied but potential adverse effect of phototherapy is hypocalcemia. Hakanson and Bergstrom in 1980 found that hypocalcemia was accompanied with decreased in serum melatonin level. Based on this observation they proposed that probably light induced hypocalcemia may result from increased calcium uptake by bone when blocking effect of melatonin decreases [8]. Sethi et al (1993) reported 90% pre-term and 75% full-term and Jain et al (1999) 55% pre-term & 30% full-term developed hypocalcemia after subjected to phototherapy [9][10]. Till date not much data are available, only few studies have documented the effect of phototherapy on serum calcium level in newborn. So this study aimed at detecting effect of phototherapy on total serum calcium level and other short term clinical side effect in preterm newborns who are receiving phototherapy.

### MATERIAL AND METHODS

This institutional based observational study was conducted at neonatal unit of Zanana Hospital, RNT Medical College, Udaipur, Rajasthan during June 2018 TO December 2018 with approval of Institutional Ethics Committee. Total n=214 neonates were enrolled for the study after taking written consent from their parents as per following inclusion criteria defined below.

#### *Inclusion Criteria:*

Preterm neonates delivered vaginally or by caesarean section with

gestational age >32weeks to <37 weeks having jaundice clinically within one week of age (2-7 days) and did not required Neonatal Intensive Care Unit (NICU) admission for other causes.

#### *Exclusion Criteria:*

Neonates having history of birth asphyxia, Onset of jaundice within 24 hours of life, Septicemia, Congenital malformation, Rh incompatibility, infants with documented hypocalcemia at the time of enrollment, Respiratory distress syndrome, Large for gestational age babies, history of diabetes, hypo/hyperthyroidism in mother, Prolonged or difficult labour.

The neonates fulfilling the indications to treat with phototherapy as per curves of American Academy of Pediatrics 2004 (taking into account total bilirubin level) constituted the study group and those neonates who did not require phototherapy were allocated into control group. n=98 neonates kept as controls which were fully matched with the study group comprising of n=116 neonates. Study group and control group were matched and comparable.

A detailed history of all these neonates was taken from relatives or mother. A thorough general physical and systemic examination was performed of all neonates. Anthropometric measurement was also recorded. Gestational age was determined by New Ballard Score. All observed data were recorded on a pre designed Performa.

All neonates in the study group were kept under the special blue standard tube light (STL) phototherapy units (supplied by MEDITRIN INSTRUMENT, Mumbai). It was ensured that minimum 6-10 $\mu$ W/cm<sup>2</sup>/nm spectral irradiance must available and maintained at the level of infant's skin. The eyes of neonates were covered with eye pads and genitalia were also covered. Position of neonates was changed every two hourly under phototherapy. All neonates in study group received continuous phototherapy; babies were removed out only while feeding or for changing diaper. The state of hydration of child as well as temperature was regularly assessed and maintained.

Initial blood samples for total serum calcium, serum bilirubin,

complete blood counts, peripheral blood film, reticulocyte count, blood group, hematocrit, direct coomb's test and for other routine laboratory investigation were collected from peripheral vein in two separate vials (EDTA vial and plane vial) with taking all aseptic precautions. Repeated samples for serum bilirubin and hemoglobin was taken daily and repeat sample for serum total calcium was taken after 48-72 hours of initial sample.

**Ethical considerations:**

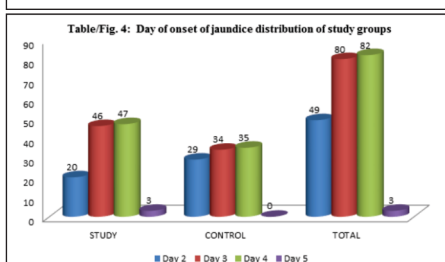
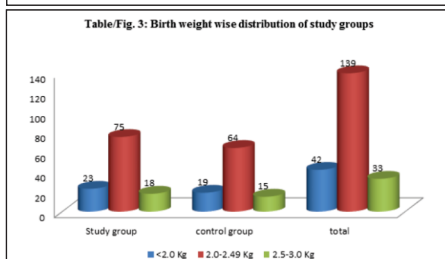
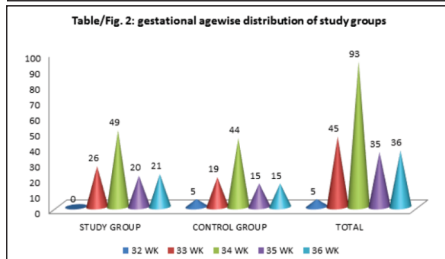
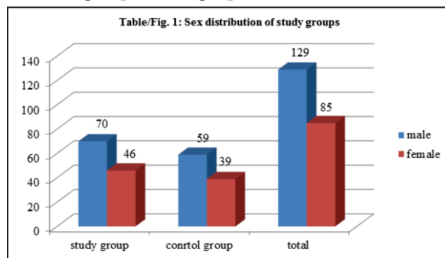
Permission of institute ethical committee (IEC) was taken. Written informed consent was obtained from parents/representatives before enrolling to this study.

**Statistical Analysis:**

All the data was collected in predesigned format. This data was entered to Microsoft Office Excel which was used for various calculations. Statistical analyses were performed using the software Statistical Package for the Social Sciences (SPSS) version 10.0 for MS-Windows. Descriptive frequencies were expressed using mean±Standard Deviation.

**RESULTS**

All the neonates included in this study were within one week of age (2-7 days). Gestational age, sex, birth weight and age of onset of jaundice were matched between study and control group [Table/Fig. 1] [Table/Fig. 2] [Table/Fig. 3] [Table/Fig. 4]. In study group n=70(60.34%) were male and n=46(39.66%) were female, in control n=59(60.20%) were male and n=39(39.80%) were female. Mean gestational age in pre term study was 34.15±1.08 weeks and control group was 34.3±1.08 weeks respectively. Mean bilirubin level in study group was 14.56±1.801 mg/dl at starting of phototherapy and after 48-72 hours of phototherapy it was 9.52±1.98 mg/dl while in control group initial bilirubin was 9.97±2.22 mg/dl and after 48-72 hours it was 9.05±2.33 mg/dl [Table/Fig. 5].



In the study group clinical complications of phototherapy observed were rashes in 32(27.59%), loose stools in 26(22.41%), dehydration in 14(12.07%) and fever in 11(9.48%). 54(46.55%) neonates did not showed any clinical complications. In study group mean weight loss was from 2.103±0.242 kg to 2.038±0.243 kg and in control group also weight loss noted from 2.164±0.251 kg to 2.125±0.256 kg. The fall in weight in neonates under phototherapy was statistically significant higher in study group than their respective control (P<0.001).

[Table/Fig. 5] Represent serum calcium level pre-study and post-study in the neonates. There is significant lower calcium level post- study in neonates requiring phototherapy compared to control group (p< 0.001).

**Table/Fig. 5: Pre And Post Study Levels Of Sr. Bilirubin and Sr. Calcium (Mean±SD)**

Measurements	Study Group (N=116)		Control Group (N=98)		P-Value
	Pre-Study	Post-Study	Pre-Study	Post-Study	
Sr. Bilirubin (mg/dl)	14.56 ±1.80	9.52 ±1.98	9.97 ±2.22	9.05±2.33	P<0.001
Sr. Calcium (mg/dl)	8.09±1.39	7.05±1.27	7.99±1.27	8.21±0.47	P<0.001

38 (32.8%) neonate in study group developed hypocalcemia (total serum calcium level <7 mg/dl) after phototherapy. Out of these 21 (55.3%) neonates had symptom of hypocalcemia and 17(44.7%) neonate were asymptomatic. Among symptomatic most common symptom was jitteriness which was present in 11(52.4%) newborns followed by irritability & jitteriness both in 7(33.3%) and 3(14.3%) had irritability. Among control 1(1.72%) neonate developed hypocalcemia and was asymptomatic.

**DISCUSSION**

Jaundice is the most common abnormal physical finding during first week of life. Efficacy of phototherapy in prevention and management of neonatal hyperbilirubinemia has been well established by several controlled studies [2][3]. Statistically significant fall in serum bilirubin observed in neonates under phototherapy (P<0.001). In this study no serious untoward side effects of phototherapy was reported. Appearance of rashes was most common clinical side effect followed by loose stools, dehydration and fever in neonates subjected to phototherapy. Maisels et al 2008 also noticed the same adverse effects of phototherapy which are rashes, loose stools, fever and dehydration [11]. Drew et al (1976) reported fever was (50%) most common feature followed by loose stools (27%), rashes (12%) and dehydration [12]. Bakken (1977) observed temporary lactase deficiency and proposed that diarrhoea attributed to this by osmotic mechanism[13]. Curtis et al (1989) rejected osmotic mechanism and proposed that pathogenic mechanism of diarrhoea to be traced in secretory nature [14]. Whittington et al (1981) showed that unconjugated bile act in intestine as secretagogue [15]. Significant increase in skin temperature as result of increased heat production from phototherapy was also noted by Glass L[16].

The fall in weight in neonates under phototherapy was statistically significant higher in study group than their respective control (P<0.001). This may be because of increased insensible water loss under phototherapy which is normally expected.

Phototherapy is affecting the serum electrolytes including serum calcium. Pathogenesis of hypocalcemia due to phototherapy is not clear exactly. After birth calcium level in newborn falls and nadir of low serum calcium is reached by 36-48 hours. The fall in total calcium level in the study group was statistically significant as compared to control group. Jitteriness and irritability are common symptoms but none of the subject had convulsions due to hypocalcemia. Romagnoli et al (1979) noted hypocalcemia in 52.3% neonates in study group while in 12.2% neonates in control group [7]. Sethi et al reported hypocalcemia in 90% pre term and 75% in full term receiving phototherapy, 0% in control group; Jitteriness was commonest symptom of hypocalcemia observed and none hypocalcemic neonate developed convulsion [9]. Study done by Hakanson D et al (1980) showed when young rats were exposed to white fluorescent light, the serum calcium concentration was decreased. They reported prevention of hypocalcemia by shielding of occiput in both newborn and rat pups. They also found that this effect can be prevented by administration of melatonin and proposed that light induced hypocalcemia may result from increased calcium uptake by bone when blocking effect of

melatonin decrease after inhibition by transcranial illumination [8]. As mentioned in above studies hypocalcemia is important complication of phototherapy. This study has also observed the same and further strengthening the previous studies. Monitoring of serum calcium level in babies under phototherapy is warranted.

#### **Limitations:**

As this study only includes preterm without any complications so we could not comment over birth weight below 1.8kg or gestational age below 32weeks. Different lab methods and phototherapy machines could grant different results. Also ionic calcium could not be measured due to some limitations.

#### **CONCLUSION:**

Phototherapy is a safe and effective method for management of neonatal hyperbilirubinemia with no serious untoward side effects. Hypocalcemia is a common and lesser observed adverse effect of phototherapy in pre term infants. We recommend monitoring of serum calcium levels and clinical symptoms of hypocalcemia in neonates under phototherapy. And also oral supplementations of extra calcium in neonates who receive phototherapy particularly for pre term babies routinely which check phototherapy induced hypocalcemia and also prevent osteopenia of prematurity.

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