International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 11; Issue 01 (A); January 2022; Page No.47-50
DOI: http://dx.doi.org/10.24327/ijcar.2022.50.0010

Research Article

CORRELATION BETWEEN PHOTOTHERAPY AND HYPOCALCEMIA IN TERM AND PRETERM NEWBORN WITH JAUNDICE: AN OBSERVATIONAL STUDY

Mrinal K Sana

Consultant Neonatologist, Department of Neonatology, Bal Gopal Children Hospital, Raipur 492001, Chhattisgarh, India

A R T I C L E I N F O

Article History:
Received 6th October, 2021
Received in revised form 15th November, 2021
Accepted 12th December, 2021
Published online 28th January, 2022

Key words:

Phototherapy, Hypocalcemia, Term newborns, Preterm newborns, Hyperbilirubenemia

A B S T R A C T

Introduction: Jaundice is amongst the most frequently encountered medical problems in newborns during the first week of life. A lesser known side effect, but a potential complication of phototherapy is hypocalcemia.

Aims and Objectives: To study the effect of phototherapy on serum total calcium levels in term and preterm newborns having pathological unconjugated hyperbilirubenemia at the end of 48 hours and to compare the effect of phototherapy on serum total calcium levels in these newborns with their respective controls.

Materials and Method: 100 term and 100 preterm newborns were selected including 50 controls in each group. Controls were the newborns having physiological jaundice and not underwent phototherapy. Blood sample for serum calcium level was sent at the time of starting phototherapy and at the end of 48 hours of phototherapy in cases and at the start of study and at the end of 48 hours in controls.

Results: Out of total term (50) and preterm newborn cases (50) exposed to phototherapy, 26% and 60% developed hypocalcemia respectively. Only 16% of newborns in preterm control group developed hypocalcemia. Mean total serum calcium levels (mg/dl) before starting phototherapy and after 48 hours of continuation of phototherapy were 8.712 ± 0.471 and 7.672 ± 0.622 respectively for term newborns and 8.118 ± 0.169 and 6.59 ± 0.83 respectively for preterm newborns. P value was found significant (<0.05) in both cases.

Conclusion: Serum calcium level falls to a significant level in both phototherapy treated term and preterm newborns, more so in preterm newborns.

INTRODUCTION

Jaundice is one of the most frequently encountered medical problems in newborns during their first week of life. It causes significant stress and anxiety to the parents in the immediate neonatal period. Nearly it affects about 60% of term newborns and 80% of preterm newborns in the first week of life.[1] Most of the time it is physiological and does not need any treatment but about 5-10% of them develop clinically significant jaundice and need intervention in the form of phototherapy.[2, 3] In the majority of cases, jaundice is due to the physiological immaturity of the newborns to manage increased bilirubin production and it usually appears between 24-72 hours of age.[4] Basic pathophysiology of jaundice is same in term and preterm neonates, but premature babies are at a higher risk of developing jaundice.[5] If left untreated, severe unconjugated hyperbilirubinemia may leads to potentially neurotoxic outcomes.[1]

Phototherapy is the most commonly used routine method for the management of icteric newborns. It mostly works by transforming the bilirubin into water soluble isomers that can be eliminated without conjugation in the liver.[6] Although, it is the most affordable and effective way of reducing serum bilirubin level in the newborns, some side effects are also associated with it like loose stools, hyperthermia, dehydration due to fluid loss, skin burn, photo retinitis, low platelet count, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency and DNA damage. A lesser known side effect, but a potential complication of phototherapy is hypocalcemia.[7]

It has been postulated that Melatonin stimulates secretion of corticosterone, which decreases calcium absorption by bones. Phototherapy leads to inhibition of pineal gland by transcranial illumination, resulting in a decline in melatonin level and as a result, hypocalcemia develops.[8] In a study conducted by Jain *et al*, the prevalence of phototherapy induced hypocalcemia was 55% in preterm and 30% in full term neonates, whereas in a study conducted by Yadav *et al* in 2012, 80% of preterm neonates and 66.6% of term neonates developed hypocalcemia after 48 hours of phototherapy.[9, 10]As suggested by previous studies, there is a varying prevalence of hypocalcemia in phototherapy treated term and preterm newborns, hence some

Corresponding author:* **Mrinal K Sana
Consultant Neonatologist, Department of Neonatology, Bal Gopal Children Hospital, Raipur 492001, Chhattisgarh, India

more studies are required in this direction to find out a definite association between phototherapy and hypocalcemia in icteric newborns.

Aims and Objective

1. To study the effect of phototherapy on serum total calcium levels in term and preterm newborns having pathological unconjugated hyperbilirubenemia at the end of 48 hours.
2. To compare the effect of phototherapy on serum total calcium levels in term and preterm newborns with their respective controls.

MATERIALS AND METHOD

This study was conducted in the Neonatal Intensive Care Unit of a tertiary level children hospital from April 2018 to September 2018. Ethical approval for the study was obtained from the Institutional Ethical Review Committee.

It was a prospective observational study, conducted with a sample size of 100 term and 100 preterm newborns, including 50 controls in each group based on the previous studies. Sampling technique was non probability consecutive sampling.

Inclusion Criteria: neonates who were icteric and stable, requiring phototherapy for >48 hours for management of hyperbilirubenemia, on either breast feeding, expressed Breast Milk (EBM) or formula feeding were included.

Cases

1. Healthy term (37 completed weeks to 41 completed weeks) newborns having pathological unconjugated hyperbilirubenemia requiring phototherapy.
2. Healthy preterm (32 completed weeks to <37 weeks) newborns having pathological unconjugated hyperbilirubenemia requiring phototherapy.

Controls

1. Healthy term (37 completed weeks to 41 completed weeks) newborns having physiological unconjugated hyperbilirubenemia, not requiring phototherapy.
2. Healthy preterm (32 completed weeks to <37 weeks) newborns having physiological unconjugated hyperbilirubenemia, not requiring phototherapy.

Any neonate in the control group, who developed critical level of bilirubin requiring phototherapy or exchange transfusion for management, was excluded from the study.

Exclusion Criteria: Following newborns were excluded from the study:

1. With onset of jaundice within 24 hrs of age
2. With perinatal asphyxia (Apgar score <4 at 1 minute of age)
3. With congenital malformations
4. With sepsis
5. Born to a Diabetic mother
6. Mother had history of taking Anticonvulsants
7. Fed with cow's milk
8. Who had exchange transfusion
9. With jaundice lasting more than 14 days of life
10. With hypocalcemia prior to the start of phototherapy
11. ABO or RH incompatibility, G6PD Deficiency, Hypothyroidism
12. IUGR babies
13. Requiring intravenous fluid therapy
14. Those who developed any significant illness or hypoproteinemia during the course of study were excluded both from cases and controls.
15. Those who required phototherapy less than 48 hrs

Neonates fulfilling the inclusion criteria were enrolled in the study as cases and controls after taking written informed consent from their parents in their preferred language. All details of procedure of phototherapy and adverse effects were discussed with the parents. Complete maternal history was taken to rule out the risk factors like Diabetes Miletus, Hypertension, Epilepsy, Oligohydraminos, Anemia, fever with rash of any kind and any drug intake apart from iron and folic acid supplementation. Complete history and physical examination of the neonates included in the study was also done and gestational age, birth weight, gender, mode of delivery, mode of feeding, time of appearance of icterus in hours were recorded in appropriate format. Anthropometric measurements in the form of weight, length and head circumference were taken and vitals were recorded.

Gestational age assessment was done by New Ballard scoring.[11] Requirement of phototherapy was assessed based on the hours of appearance of icterus after birth and gestational age and consulted in reference to American Academy of Pediatrics curves for hyperbilirubenemia 2004 for infants with gestational age 35 weeks or more and NICE guidelines for infants 34 weeks gestation or lower.[12, 13] Neonates were then divided into 2 groups-

Group A (cases): Term neonates from 37 completed weeks to 41 completed weeks having pathological uncongjugated hyperbilirubenemia requiring phototherapy.

Group A (controls): Term neonates from 37 completed weeks to 41 completed weeks having physiological unconjugated hyperbilirubenemia, not requiring phototherapy.

Group B (cases): Preterm neonates from 32 completed weeks to <37 completed weeks having pathological uncongjugated hyperbilirubenemia requiring phototherapy.

Group B (controls): Preterm neonates from 32 completed weeks to <37 completed weeks having physiological uncongjugated hyperbilirubenemia, not requiring phototherapy.

After enrollement, total serum bilirubin with direct and indirect fractions, serum albumin, ABO and RH typing of mother and baby, direct coombs test, G6PD, reticulocyte count and thyroid profile was sent in all neonates. Blood sample for serum calcium level was sent at the time of starting phototherapy and at the end of 48 hours of phototherapy in cases and at the start of study and at the end of 48 hours in controls. Serum bilirubin level was sent at the commencement of the study and every 24 hours in both cases and controls. Hypocalcemia was considered as total serum calcium level less than 8 mg/dl in term and less than 7 mg/dl in preterm newborns.

Estimation of serum calcium*:* Total serum calcium was estimated by Olympus AU 640 and Olympus AU 400 automated analyser, which provides the latest technology for calorimetric determination of calcium in biological sample.

Estimation of serum bilirubin*:* Serum bilirubin was estimated by Erba Mannheim automated CHEM -5 Plus analyser. Direct

and indirect bilirubin was estimated by Diazo method of Pearlman & Lee.

Phototherapy was given in continuous form with GE Healthcare Lullaby LED Phototherapy system which supply desired wavelength (450-465nm) and spectral irradiance level of 45µw/cm^2/nm. Naked infant was placed at a distance of 18 cm from phototherapy unit in a cot. Eyes and genitalia were covered appropriately and position of infant was changed from time to time.

Daily weight recording of the neonate was done with the same weighing machine and state of hydration was checked. Extra fluids in the form of more frequent feedings were given to offset the fluid losses. Temperature was noted every four hourly to assess hypo or hyperthermia. Neonates were assessed for features of hypocalcemia clinically like jitteriness, irritability, convulsions, apnea, increased extensor tone, clonus, hyperreflexia, stridor etc. Neonates in the control group were also assessed regularly for vitals and clinically for symptoms of of hypocalcemia.

Statistical Analysis: All observed data were recorded in pre designed proforma and statistical analysis was done with the help of SPSS 17 software. P value <0.05 was considered significant and <0.001 as highly significant.

RESULTS

The present study includes 50 cases and 50 controls in term newborns group (**Group A**) and 50 cases and 50 controls in preterm newborns group (**Group B**). There was equal distribution of male and female participants in each group. Mean gestational age and birth weight of term newborns was 38.5 ± 0.86 weeks and 2.59 ± 0.492 Kg in cases and 37.5 ± 1.59 weeks and 2.8 ± 0.292 Kg in controls respectively. Similarly, the mean gestational age and birth weight of preterm newborns was 33.5 ± 1.59 weeks and 1.76 ± 0.229 Kg in cases and 34.26 ± 1.45 weeks and 1.63 ± 0.189 Kg in controls respectively. In term newborns group, 68% of cases and 70% of controls developed jaundice between 48-72 hours of age and similar pattern was seen in preterm newborns where 70% of cases and 50% of controls developed jaundice.

Mean total serum calcium levels (mg/dl) before starting phototherapy and after 48 hours of continuation of phototherapy in term newborn cases and controls are depicted in table 1. Similarly, mean total serum calcium levels (mg/dl) before starting phototherapy and after 48 hours of continuation of phototherapy in preterm newborn cases and controls are depicted in table 2. Overall effect of phototherapy on serum total calcium levels in cases and controls are depicted in table 3.

Observation Tables

Table 1 Mean total serum calcium level before and after phototherapy in term newborn cases and controls

Timing	Cases	Controls (phototherapy not used)
Pre study mean ± SD S.Calcium	8.712 ± 0.471	9.07 ± 0.306
Post study(at the end of 48 hours) mean ± SD S.Calcium	7.672 ± 0.622	8.986 ± 0.271

Above table depicting mean ± SD total serum calcium levels (mg/dl) before starting phototherapy and after 48 hours of continuation of phototherapy in term newborn cases and mean ± SD total serum calcium levels (mg/dl) at an interval of 48 hours in term newborn controls where phototherapy was not used. P value was found to be <0.05 in term newborn case group, which was statistically significant

Table 2 Mean total serum calcium level before and after phototherapy in preterm newborn cases and controls

Timing	Cases	Controls (phototherapy not used)
Pre study mean ± SD S.Calcium	8.118 ± 0.169	8.85 ± 0.593
Post study (at the end of 48 hours) mean ± SD S.calcium	6.59 ± 0.83	8.59 ± 0.88

Above table depicting mean ± SD total serum calcium levels (mg/dl) before starting phototherapy and after 48 hours of continuation of phototherapy in preterm newborn cases and mean ± SD total serum calcium levels (mg/dl) at an interval of 48 hours in preterm newborn controls where phototherapy was not used. P value was found to be <0.05 in term newborn case group, which was statistically significant

Table 3 Effect of phototherapy on total serum calcium levels in newborns exposed to phototherapy

Subjects	Exposed to Phototherapy (Cases)	Developed Hypocalcemia after phototherapy	Not exposed to Phototherapy (Controls)	Developed Hypocalcemia after phototherapy
Term Newborns	50	13 (26%)	50	00
Preterm newborns	50	30 (60%)	50	8 (16%)

Out of total term (50) and preterm newborn cases (50) exposed to phototherapy, 26% and 60% developed hypocalcemia respectively and out of total term (50) and preterm newborn controls (50) not exposed to phototherapy, none of the newborn in term group developed hypocalcemia, whereas 16% of newborns in preterm group developed hypocalcemia.

DISCUSSION

Phototherapy is the most common and affordable way of treating neonatal hyperbilirubinemia in the NICU. It is widely accepted as a relatively safe and effective method for treatment of neonatal hyperbilirubinemia. Wide clinical experience suggests that long term adverse biological effects of phototherapy are absent, minimal or unrecognized.[1]

It was Romagnoli and colleagues in 1979, who first suggested an association between hypocalcaemia and phototherapy in preterm neonates and observed hypocalcemia in 52.3% babies.[14] Later Hakanson *et al* in 1981 reported hypocalcemia in young infant rats when exposed to white flourscent light.[15] Sethi *et al* in 1990 found 75% of term and 90% of preterm neonates out of 20 term and 20 preterm neonates to be hypocalcemic after phototherapy.[16] Jain *et al* in 1998 found 55% of preterm and 30% of term neonates to be hypocalcemic after treatment with phototherapy.[9] In a study in government medical college Bhopal by Jyotsana *et al* in 2015, 66.7% of preterm and 30% of term neonates developed hypocalcemia after 48 hours of phototherapy. There were 30 newborns in each term and preterm group and 15 newborns in each group served as control, however none of the newborn in the control group developed serum calcium below 7 mg/dl.[17] The results were comparable to the present study where 60% of preterm and 26% of term neonates developed hypocalcemia out of 50 preterm and 50 term newborns which were given 48 hours of phototherapy. However, none of the newborn in control groups developed serum calcium level below 7mg/dl during the study period. Mean serum calcium levels after 48 hours of phototherapy in above mentioned study were 6.64+ 1.03 in preterm neonates and 7.58+0.83 in term neonates respectively, whereas in the present study, mean serum calcium levels were found to be 6.59+0.83 in preterm neonates and 7.672± 0.622 mg/dl in term newborns respectively after 48 hours of phototherapy and p value was found to be significant (<0.05) in both preterm and term groups. These results were also in accordance with other previous studies like one conducted by Monica *et al*, where 55% of preterm and 30% of term neonates

developed hypocalcemia.[18] Some studies were conducted only of term newborns to see the effect of phototherapy on serum calcium level. In a study conducted by Rozurio *et al* in 2015-2016 on 100 term newborns, 67% of newborns developed hypocalcemia after 48 hours of double surface phototherapy.[19] Also some studies are there like conducted by Paymanesh *et al* and Srinivasa *et al*, where authors concluded that no significant hypocalcemia occurred after phototherapy.[20, 21]

CONCLUSION

Serum calcium level falls to a significant level in both phototherapy treated term and preterm newborns. Though fall is more significant in preterm newborns, term newborns are also at risk. It is recommended to check serum calcium levels before start of phototherapy and at subsequent intervals thereafter during the entire phototherapy period and also after stopping phototherapy to detect hypocalcemia. Newborns should also be monitored clinically for the signs of hypocalcemia. The limitation of the present study was its small sample size. Studies with larger sample size are needed to find out a clear association between phototherapy and hypocalcemia in newborns. Moreover, whether prophylactic calcium administration before start of phototherapy in icteric newborns has any role in the prevention of hypocalcemia is not clear and some more studies are also needed in this direction.

Acknowledgement

The authors would like to thank to the institutional ethical committee for giving permission for the commencement of the study. Also we would like to express our gratitude towards the Head of the Department of Neonatology, for proving all support for the study. Also we would like to thank all the parents for giving consent for participation in the study.

Funding: Nil

Conflict of interest: Nil

References

1. Anthony J, Piazza, Stoll BJ. Jaundice and hyperbilirubinemia in newborn. In: Kliegman, Behrman, Jenson, Stanton (eds) Nelson Text book of pediatrics. 20th ed. Philadephia: Elsevier. 2015: 871-875.
2. Dijk P, de Vries T, de Beer J. Guideline'Prevention, diagnosis and treatment of hyperbilirubinemia in the neonate with a gestational age of 35 or more weeks' Nederlands Tijdschrift Voor Geneeskunde. 2009; 153: 93.
3. Hansen TWR. Twists and turns in phototherapy for neonatal jaundice. Acta Paediatrica. 2010;99(8):1117–1118. doi:10.1111/j.1651-2227.2010.01898.
4. Khan M, Malik K A, Bai R. Hypocalcemia in jaundiced neonates receiving phototherapy. Pak J Med Sci. 2016 Nov-Dec; 32(6): 1449–1452.
5. Walsh S, Murphy J. Neonatal jaundice--are we over-treating? Iran Med J. 2010; 103(1): 28–29.
6. Stokowski LA. Fundamentals of phototherapy for neonatal jaundice. Adv Neonatal Care 2006; 6: 303–312.
7. Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care. Lippincott Williams & Wilkins; 2008.
8. Karamifar H, Pishva N, Amirhakimi GH. Prevalence of phototherapy induced hypocalcemia. IJMS 2002; 4:166–168.
9. Jain BK, Singh H, Singh D, Toor NS: Phototherapy induced hypocalcemia. Indian Pediatr 1998; 35(6):566-7.
10. Yadav R, Sethi RS, Sethi AS, Kumar L, Shankar Chauraisa O. The evaluation of effect of phototherapy on serum calcium level. PJSR. 2012; 5(2): 1-4.
11. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard score, expanded to include extremely premature infants. *J Pediatr* 1991; 119: 417-423.
12. American Academy of Pediatrics Subcommitte on Hyperbilirubinemia. Management of hperbilirubinemia in the newborn infant 35 weeks or more weeks of gestation. Pediatrics 2004; 114: 297-316.
13. National Institute for Health and Clinical Excellence. Neonatal Jaundice. National Institute for Health and Clinical Excellence, 2010, www.nice.org.uk/CG98.
14. Romagnoli C, Polidore G, Cataldi L, *et al*. Phototherapy- induced hypocalcemia. *J Pediatr*, 1979; 94(5): 815-6.
15. Hakanson D, Penny R, Bergstrom WH. Calcemic responses to photic and pharmacologic manipulation of serum melatonin. Pediatr Res., 1987; 22(4): 414-6
16. Sethi H, Saili A, Dutta AK: Phototherapy induced hypocalcemia. Indian Pediatr, 1993; 30(12): 1403-6
17. Shrivastava J, Singh A. Phototherapy Induced Hypocalcemia in Neonates. Sch. *J. App. Med. Sci*., 2015; 3(8C):2931-2933.
18. Tandon M, Nayar D, Ramachandran S, Kapil U; Phototherapy Induced Hypocalcemia. Indian Pediatr. 1998; 35(1): 566-67.
19. Rozario C I, Pillai P S, Ranamol T. Effect of phototherapy on serum calcium level in term newborns. *Int J Contemp Pediatr*. 2017 Nov; 4(6): 1975-1979.
20. Paymaneh AT, Sajjadian N, Eivazzadeh B; Prevalence of Phototherapy Induced Hypocalcemia in Term Neonate. *Iran J Pediatr*. 2013; 23(6): 710–711.
21. Srinivasa S, Renukananda S, Srividya GS; Effect of phototherapy on hypocalcemia. *J of Evolution of Med and Dent Sci*. 2015; 4(24): 4165-68.

How to cite this article:

Mrinal K Sana (2022) 'Correlation Between Hypocalcemia And Phototherapy In Term And Preterm Newborn With Jaundice: An Observational Study', *International Journal of Current Advanced Research,* 11(01), pp. 47-50.
DOI: http://dx.doi.org/10.24327/ijcar.2022.50.0010

****