TAJ June 2020; Volume 33 Number-1

ISSN 1019-8555
The Journal of
Teachers Association
RMC, Rajshahi

Original Article

Effects of Phototherapy on Hyperbilirubinemia and Serum Calcium Level in Neonates Admitted in a Tertiary Care Hospital

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Abstract

Background: Jaundice is most common problem in neonatal period. It is commonly managed by phototherapy. However, phototherapy may cause hypocalcaemia and create serious complications like convulsion. So, neonatal hyperbilirubinemia associated with hypocalcaemia has increased risk of neurotoxicity.

Objective: To determine the effects of conventional single surface phototherapy on serum calcium and serum bilirubin in neonatal hyperbilirubinemia.

Methodology: This longitudinal type of descriptive study was conducted in the neonatal unit of Rajshahi Medical College Hospital during January 2016 to December 2017. One hundred forty neonates both term and preterm with jaundice were included into this study. Conjugated hyperbilirubinemia, blood group, Rh incompatibilities, jaundice on 1st day, very LBW babies and very sick neonates were excluded from this study. All neonates were under conventional single surface phototherapy. Total calcium, direct and indirect serum bilirubin were estimated before starting phototherapy and serum calcium level and total bilirubin estimated every 24 hours interval . Results were analyzed statistically by paired student t' test and z' test.

Results: Total serum bilirubin and calcium level fall significantly and among all groups after phototherapy. Mean SD of serum bilirubin 17.14±4.20 mg/dl before phototherapy and 13.37±3.80 mg/dl after receiving (p <0.001). Mean SD of serum calcium level significantly decreased from baseline value of 9.45±10 mg/dl and 9.24±1.24 mg/dl after phototherapy. Analysis of complications revealed 19(13.6 %) developed hypocalcaemia and has significant difference between serum calcium level before and after phototherapy (p<0.04).

Conclusion: Total serum bilirubin and calcium level was reduced by single conventional phototherapy. Phototherapy causes hypocalcaemia in neonate but phototherapy associated hypocalcaemia causing convulsion was not noted.

Key wards: Phototherapy, Hyperbilirubinemia and Hypocalcaemia.

TAJ 2020; 33: No-1: 05-10

Introduction

Neonatal jaundice is one of the most Prevalent clinical Problems observing during the first week of life affecting approximately 60% of healthy term and 80% preterm babies. The commonest cause of neonatal jaundice is prematurity,

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physiological Jaundice, ABO incompatibility, RH incompatibility.[1,2,3,4,5] Harmful effect of bilirubin on the central nervous system especially in newborn as it can cause cerebral dysfunction leading to permanent neurological damage or death.[6] About 5-10% of term infants have clinically develop extreme hyperbilirubinemia.

Phototherapy plays a significant role in the treatment and prevention of hyperbilirubinemia in neonate. Phototherapy may also lead to undesired effect including skin rash diarrhoea body temperature chills trauma to the eye nasal obstruction bronze baby and DNA damage.[8] Jaundice due to hemolysis or cholestasis phototherapy less effective. The underlying mechanism for conventional phototherapy induced hypocalcaemia although not yet well understood. Phototherapy effectively reduce neonatal hyperbilirubinemia has been proved in several recent prospective studies.[9]

However this treatment modality may itself result in the development of Hypocalcaemia and create serious complications including convulsion and related conditions.[10] Neonatal hypocalcaemia is defined as a total serum calcium concentration of less than 1.75 mmol/L (7.0 mg/dl) and an ionized calcium concentration of less than 10 mmol/L (4.0 mg/dl).[11]

Phototherapy may also lead to undesired effects including skin rash, diarrhea, rise of body temperature, chills, trauma to the eye, bronze baby, DNA damage, hypocalcaemic tetany and convulsion.[12] Nonetheless, no change in blood ions/metabolites has been reported except for calcium concentration, a drop is serum calcium has been noticed in patients undergo phototherapy.[13] The underlying mechanism for phototherapy induced hypocalcaemia occurs due to decrease in serum melatonin concentration in turn regulated by pineal gland. Pineal gland is influenced by the diurnal light dark cycle.[14]

The aim of this study is to assess the prevalence of phototherapy induced hypocalcaemia and its effects among the neonates.

Materials and Methods

This is a hospital based longitudinal type of descriptive study, conducted in neonatal ward of Rajshahi Medical College Hospital on January 2016 to December 2017. Total sample size was 140. Data was collected on the basis of a structured questionnaire. The quantitative data from the survey were entered into Statistical Package for Social Science (SPSS) 16 for windows software programs. Informed consent was taken from each parent before enrolling in the study. There was minimal ethical issue and confidentiality of patients was maintained strictly.

Inclusion criteria : 1. Neonates (aged 3-14 days)**,** 2. Unconjugated hyperbilirubinemia. 3. Total serum bilirubin 10 mg/dl or more than 10 mg/dl in preterm baby 4. Total serum bilirubin 12 mg/dl or more than 12 mg/dl in term baby 5. Birth weight. (1-4 kg).

Exclusion Criteria: 1. Hypocalcaemic patient, 2. Conjugated hyperbilirubinemia 3. Extreme low birth weight baby (weight <1000 gm) 4. Rh incompatibility 5. Very sick neonates 6. Jaundice on first day of life 7. Serum bilirubin reaching critical level of exchange transfusion.

Results

The study populations were 140 neonates, 94 male, 46 females, with the mean chronological age and weight of 5.26±1.9 days and 2.54±0.543 kg respectively. 74(52.9%) of neonates had normal vaginal delivery and 66(47.1%) delivered by cesarean section. Mean±SD of serum bilirubin level was 17.14±4.20 mg/dl at admission and 13.37±3.80 mg/dl after receiving 48 hour phototherapy ($p<0.001$). Mean±SD of serum calcium level significantly decreased from baseline values of 9.45±1.0 mg/dl to 9.24±1.24 mg/dl after 48 hour phototherapy. Overall, 19 neonates 13.6% developed hypocalcaemia (calcium concentration less than 8 mg/dl). There was a significant difference between serum calcium level before and after phototherapy ($p<0.04$). Only 5 hypocalcaemic neonates were clinically symptomatic.

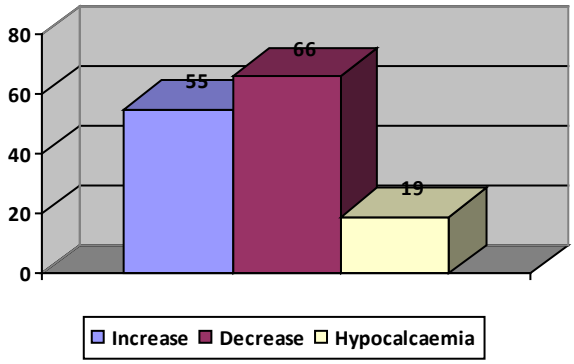

Figure-1: Frequency distribution of 140 neonates on the basis of calcium level (increase, decrease and hypocalcaemia) from initial base line.

Table-1: Laboratory changes before and after receiving phototherapy.

Test	Admission time	After 48 hours	p-value
Total bilirubin level (mg/dl)	17.14±4.20	13.37±3.80	0.001
Total calcium level (mg/dl)	9.45±1.0	9.24±1.24	0.043

Table-2: Calcium status after 48 hours phototherapy.

		Birth Weight group			
		<1.5 kg (very low BW)	1.5-2.5 kg (Low BW)	>2.5 kg (Normal)	Total
Calcium level at 48 hours	1-7.99 mg/dl	0(00%)	8 (7.4%)	9 (8.3%)	17 (15.7%)
	8-25 mg/dl	5 (4.6%)	41(38.9%)	44 (40.7%)	91 (84.3%)
Total		5 (4.6%)	50 (46.3%)	53 (49.1%)	108 (100%)

χ^2=0.998 df=2 p=0.607

Discussion

Phototherapy plays a significant role in the treatment and prevention of neonatal hyperbilirubinemia. Mean age and weight of 140 neonate was 5.26±1.9 day and 2.54+-.543 kg respectively. Male to female ratio was 2:1. Moreover, the health seeking behavior of our common people attaches greater importance to male child as compared to female ones. Male predominance was also observed in studies by other authors.[15] Term neonates were 105 (75.0%) and preterm 35(25.0%).

In this study significant percentage of neonates 71(50.7%) were in the normal birth weight (NBW) group followed by low birth weight (LBW) and very low birth weight (VLBW). This study corroborates with the studies of other authors.[15]

Causes of hyperbilirubinemia were neonatal sepsis jaundice of prematurity, perinatal asphyxia, and infant of diabetic mother, Rh and ABO incompatibility. On the basis of study findings of neonatal sepsis was lower and birth asphyxia higher. Greater numbers of asphyxiated babies were usually admitted in this hospital.[16]

This study represented that mean total serum bilirubin in NBW, LBW and VLBW group were 12.09±4.00 mg/dl, 11.67±4.62 mg/dl and 14.50±1.84 mg/dl respectively. The study findings are in agreement with the work of several authors.[17]

Initial mean TSB of term and preterm were 17.05±4.20 mg/dl and 16.14±3.16 mg/dl respectively, which were similar to other studies.[17]

In this study NBW neonates mean serum bilirubin levels before and after phototherapy was 17.14±4.20 mg/dl and 13.37±3.8 mg/dl respectively. Decrease was significant ($p<0.001$). Which were documented similar observations in Paul et al., and Barua et al.

Phototherapy was also effective in LBW neonates. In LBW mean serum bilirubin level before and after phototherapy were 16.14±3.16 mg/dl and 13.63±3.65 mg/dl respectively which was supported by Paul et al and Barua et al. studies.

So phototherapy is also effective in VLBW neonate. In this study mean serum bilirubin levels before and after phototherapy were 14.50±1.84 mg/dl and 11.76±4.62 mg/dl respectively closely similar to Paul et al. and Barua et al. studies.

After 24 hours phototherapy decline in bilirubin level was significantly higher in NBW neonates followed by VLBW and in LBW. Significant decrement was occurs among the three groups. Other authors observed the similarity (Barua et al., 2007 and Silva et al., 2009).

Mean bilirubin level after 48 hours phototherapy in NBW was 13.29±2.90 mg/dl, LBW 13.63±3.65 mg/dl and VLBW 11.76±4.53 mg/dl respectively. Similar observations were demonstrated in several studies (Paul et al., 2010 and Barua et al., 2007).

During phototherapy only 2(10.53%) neonates developed transient rash which disappeared after cessation of phototherapy. This is alike the study by Maisels et al (2008). In this study, 12(63.16%) neonates developed transient loose stool and others 5(26.31%) neonates developed hypocalcaemic tetany which was treated with medication. In this study, mean length of hospital stay was highest 3.629±1.51 (LBW) days, 3.49±1.3 day (NBW) and 3.14±0.69 (VLBW). The LBW neonates took longer time for recovery during phototherapy and from primary illness. This is similar to results in a study by Miliyana et al (2011).

The regulation of calcium homeostasis in the newborn period has been of considerable interest. At birth, the plasma calcium level in cord blood exceeds that in maternal blood. During the early days of life, the plasma calcium level progressively decreases in normal infants, so by the second or third day of life, the level is lower than that found in older infants and children. In most normal full-term infants the plasma calcium level returns to normal by 10 days of life (Altirkawi, K. and H.J. Rozycki, 2008). Phototherapy is an appropriate and safe measure to reduce indirect bilirubin level in newborns. Roming et al was the first to suggest the association of hypocalcaemia in newborn following phototherapy (Romagnoli, C.,1976).

The mechanism of hypocalcaemic effect of phototherapy was reported by inhibition of pineal gland via transcranial illumination, resulting to decline of melatonin secretion; which blocks the effect of cortisol on bone calcium. Cortisol has a direct hypocalcaemic effect and increases bone uptake of calcium and induces hypocalcaemia (Hakanson, Penny, and Bergstrom, 1987).

In neonatal study population receiving 48 hours of phototherapy, a significant decrease in serum calcium was observed (p 0.04). However, only 19

neonates developed hypocalcaemia below the acceptable threshold after 48 hours of phototherapy. Only five newborns had symptomatic hypocalcaemia.

In another Iranian study, between 7% - 15% of term newborn receiving phototherapy developed hypocalcaemia. Alizadeh, Sajjadian and Eivazzadeh, (2013) reported only ten (7%) newborns (4.2% females, 10.4% males) developing hypocalcaemia after 48 hours of phototherapy (Alizadeh, Sajjadian and Eivazzadeh, 2013). Ehsanipour, Khosravi and Jalali, (2008) and Karamifar, Pishva and Amirhakimi (2002) reported 15% and 8.7% hypocalcaemia are respectively in newborns receiving phototherapy.

However the reported prevalence of hypocalcaemia in other countries was more than Iranian newborn reports. Yadavs, Sethi and Sethi (2012) reported 66% and Jain (1998) also observed hypocalcaemic effect of phototherapy in 30% term and 55% preterm neonates. Sethi et al has studied the effect of phototherapy in 20 term and 20 preterm hyperblirubinemic neonates. They observed hypocalcaemia in 75% of term and 90% of preterm neonates after phototherapy (Sethi, Saili and Dutta 1993).

Similarly, in 2006, Medhat from Cairo University observed 75% of term and 90% of preterm developed hypocalcaemia after phototherapy (Medhat 2006). Observation of the present study and another Iranian study is much lower than the above -mentioned studies from other countries. The reason for this difference is not clear. However the type of fluorescent tube, serum vitamin D, bilirubin levels and also the patients skin color may play a role. Mutlu et al (2013) reported a significant difference in the serum 25(OH) vitamin D levels between newborns suffering from hyperbilirubinemia and control groups (Mutlu et al 2013). In a study done by Jain, the prevalence of hypocalcaemia was higher in newborns with higher concentration of serum bilirubin (Jain, 1999). In addition it might also be due to the fact that this study examined total serum calcium and not ionized calcium. Ionized calcium is the active component which is kept under control by the various physiological mechanisms involved in calcium homeostasis. Albumin and pH may influence the distribution of total serum calcium level, either bound or free and ionized calcium. Then, it can be considered one of the limitations of our study.

These findings justify further prospective studies in infants that would include concurrent measurements of ionized calcium and serum 25 (OH) vitamin D. Some reports recommend prescription of calcium to prevent early onset hypocalcaemia in premature newborns. Other similar advices are observed in sick infants of diabetic mothers and those with severe prenatal asphyxia (Jain, 2010).

In conclusion, although phototherapy induces hypocalcaemia in term and preterm infants, but the incidence of phototherapy associated hypocalcaemia is not too high. Then we can just advise check of calcium level in symptomatic newborns that have suggested hypocalcaemia signs.

Conclusion

Neonatal sepsis, perinatal asphyxia, preterm infants and ABO and Rh incompatible infant are prone to develop significant hyperbilirubinemia. Side effects of single surface phototherapy are hypocalcaemia, dehydration, greenish stool in all infants. Although phototherapy induces hypocalcaemia in neonates but the incidence of phototherapy induced hypocalcaemia is not too high. We can advise frequent monitoring of calcium level in symptomatic newborns.

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