Original Article

Effect of Phototherapy on Serum Calcium Level in neonatal hyperbilirubinemia

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ABSTRACT:

Background: Neonatal hyperbilirubinaemia or jaundice is most common morbidity seen in first week of life. Approximately 60% of term and 80% of preterm newborn develop clinical jaundice. Phototherapy is one of the therapy methods for jaundice. It has few side effects, one of them is hypocalcemia. This study was done to see the effect of phototherapy on serum calcium level on jaundiced neonates.

Methods: This was a prospective cross-sectional study, conducted from May 2020 to April 2021 at the Neonatal Intensive Care Unit and Special Newborn Care Unit of Karnali Academy of Health Sciences (KAHS), Jumla. A total of 40 neonates either male or female who had jaundice and placed under phototherapy were enrolled for this study. Blood sample for total serum bilirubin levels and serum calcium levels were sent. They were measured before starting and after stoppage of phototherapy. All the data were recorded in the preformed proforma. It was then, analyzed with the help of SPSS version 16. p-value< 0.05 was considered statistically significant.

Results: The mean age and mean gestational age of the neonates was found to be 4.12±1.09 days and 38.55 ± 2.34 weeks respectively. The mean age at which jaundice was noticed in the neonates was 4.13 ± 1.4 days. Pre-phototherapy and post phototherapy level of total serum bilirubin was 14.53 mg/dl ± 2.91 mg/dl and 10.29 mg/dl ± 2.13 mg/dl respectively whereas serum calcium level before and after initiating phototherapy was 9.23 ± 1.11 mg/dl and 8.37 ± 0.69 mg/dl respectively. Hypocalcemia was found in 22.5% of jaundiced neonates receiving phototherapy.

Conclusions: Phototherapy which is the mainstay of treating hyperbilirubinemia in neonates decreases serum calcium level in jaundiced neonates.

Keywords: hyperbilirubinemia, phototherapy, hypocalcemia

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INTRODUCTION

Jaundice or hyperbilirubinemia is one of the most common clinical conditions that require evaluation, assessment and management in neonates. It is defined as yellowish discoloration of the sclera and body due to high bilirubin in blood. Bilirubin pigment gets deposited in different tissues and the baby looks icteric. In adults, normal serum bilirubin is less than 1 mg/dl, but they appear icteric when serum bilirubin level is more than 2 mg/dl. Newborns appear icteric when serum bilirubin level is more than 7 mg/dl.[1] 60% of all term newborns and most premature newborns approximately 80% develop clinical jaundice[2] , but only 5 to 10% of them require treatment.[3] Hospital record of KAHS of 075/076 B.S showed that out of 178 cases admitted in Special Newborn Care Unit(SNCU), 21 cases of neonatal jaundice were admitted.

Although bilirubin plays a role as an antioxidant, elevation of indirect (unconjugated) bilirubin is potentially neurotoxic. Elevation of bilirubin in neonates can lead to kernicterus, acute and chronic bilirubin encephalopathy with focal neurological deficit (e.g. sensory neural hearing loss), neurobehavioral problems and intelligence quotient deficits.[4,5] So, bilirubin has to be removed either by increasing its excretion via phototherapy or mechanically by exchange transfusion.[6] Phototherapy is one of the most widely used treatment options for neonatal jaundice. It has proven effective in controlling bilirubin levels and preventing the need for exchange transfusion. If phototherapy fails to decrease the level of bilirubin, exchange transfusion remains the primary treatment modality.[7]

Phototherapy, though considered as a safe method, may cause various complications that includes tanning of skin and skin rash, insensible water loss resulting in dehydration, hyperthermia, retinal damage, watery diarrhea, DNA strand breaks, bronze baby syndrome and hypocalcemia.[8] Hypocalcemia is one of the lesser-known side effects, but is a significant complication induced by phototherapy.[9]

Melatonin helps in stimulating corticosterone secretion, later eventually minimizing calcium absorption. Phototherapy inhibits pineal gland by transcranial illumination, which causes the decreased level of melatonin resulting hypocalcemia.[10]

For treating hyperbilirubinemia, phototherapy is most frequently used in our hospital, but no study has been done, till date, in our setting regarding effect of phototherapy in serum calcium level of jaundiced neonates. Thus, this study aims to see the effect of phototherapy on serum calcium level on jaundiced neonates that may help us to predict the occurrence of hypocalcemia, and intervention at earliest may be started which will prevent hypocalcemia.

MATERIAL AND METHODS

A cross sectional study was done at the Neonatal Intensive Care Unit and Special Newborn Care Unit of Karnali Academy of Health Sciences (KAHS), Jumla from May 2020 to April 2021. Institutional ethical clearance was taken from the Institutional Review Committee (IRC) of KAHS before starting the study (Ref: 076/077/32). The sample size was calculated by using prevalence formula, $n = Z_{\alpha}^2 PQ / d^2$ where $Z_{\alpha} = 1.96$, P= 11.79% and d= 10%.

So, a total of 40 cases fulfilling the inclusion criteria (jaundiced neonates requiring phototherapy) and exclusion criteria (neonates with jaundice requiring exchange transfusion, birth asphyxia, culture proven sepsis, parents not giving consent) presenting to SNCU and NICU in KAHS were seen after taking informed written consent. History taking and clinical examination were done before sending laboratory investigation. They were then recorded in proforma.

Various tests that included hemoglobin level, blood group, Rhesus typing, total serum bilirubin, direct bilirubin, serum albumin and serum total calcium were done. A conventional phototherapy equipment of Phoenix Company, containing four blue light fluorescent lamps was adjusted at a distance of 35 cm from the neonates under standard

protocol with eyes and genitals completely covered. Total serum bilirubin level and total calcium level were measured before and after stoppage of phototherapy. Total serum calcium of <8 mg/dl was considered as hypocalcemia in present study. Neonates were also clinically assessed for features of hypocalcemia.

Data were presented as tables, bar-diagrams and analyzed by using SPSS 16. Continuous variables that were used in this study like age, total duration of phototherapy and gestational age at time of birth were calculated in terms of mean, median and standard deviations. After tabulating all data, they were then analyzed statistically so as to find out hypocalcemia being one of the complications following phototherapy. By the use of chi squared test, variables like age, sex, gestational age at the time of birth, duration of jaundice and phototherapy used were controlled through stratification and p-value <0.05 was considered statistically significant for this study.

RESULTS

Among total 40 babies, 30 (75%) were male and 10 (25%) were female with Male: Female ratio of 3:1 as shown in Table 1.

Table 1: Distribution of sample size according to gender

Sex	Frequency (n=40)	Percentage
Male	30	75%
Female	10	25%

The mean age of the neonates was calculated as 4.12 ± 1.09 days with the youngest being 1 day old and the oldest 6 days from the study whereas the mean gestational age of the study population at which the baby was born was 38.55 ± 2.34 weeks. Similarly, the mean gestational age for males and females were 38.50 ± 2.27 weeks and 38.70 ± 2.67 weeks respectively.

The mean and median weight of the neonates in the study was found to be 2620 ± 634.96 grams and 2600 grams respectively, with the minimum and maximum weight of neonate being 1400 grams and 3800 grams respectively.

The mean and median age at which jaundice was noticed in the neonates was 4.13 ± 1.4 days and 4 days respectively. Similarly, mean and median age for the hospital consultation was done was 1.23 ± 0.62 days and 1 day respectively.

In our study, 25 neonates (62.5%) had birth weight between 2.5 to 4 kg, 15 neonates (37.5%) were below 2.5 kg and no neonate had birth weight of 4 kg or more.

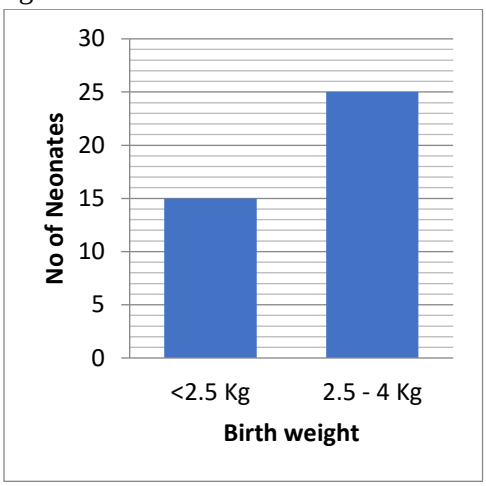

Figure 1: Distribution of sample size according to birth weight

Out of the total cases, 29 (72.5%) neonates had Spontaneous Vaginal Delivery (SVD), 9 (22.5%) neonates were delivered by Lower Segment Cesarean Section (LSCS) and 2 (5.0%) cases were delivered by forceps (Assisted delivery). (Figure 2)

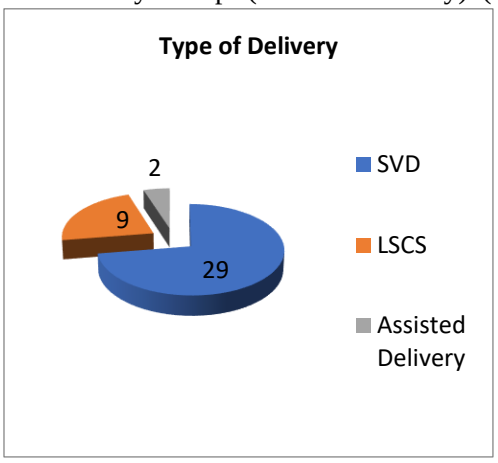

Figure 2: Distribution of sample size according to type of delivery

The study population was divided into three groups according to gestational age. Among the neonates, 34 (85.0%) were above 37 weeks of gestational age, 5 (12.5%) were from 34-37 weeks and 2

(2.5%) were less than 34 weeks as shown in table 2

Table 2: Distribution of sample size according to gestational age

Gestational age (in weeks)	Frequency	Percentage
<34 weeks	1	2.5 %
34-37 weeks	5	12.5%
> 37 weeks	34	85.0%

The level of Total serum bilirubin (TSB) and serum calcium before and after phototherapy in whole study population as well as males and females has been calculated (Table 3).

The mean TSB level before starting phototherapy was 14.53 mg/dl with S.D of 2.91 mg/dl, and that after phototherapy was 10.29 mg/dl with SD of 2.13 mg/dl. This decrease in TSB after phototherapy is statistically significant with p-value <0.05.

Table 3: Table showing the mean parameters of TSB and Serum Calcium before and after phototherapy

Variables	TSB Mean ± SD (mg/dl)		Serum Calcium Mean ± SD (mg/dl)	
	Before Phototherapy (n=40)	After Phototherapy (n=40)	Before Phototherapy (n=40)	After Phototherapy (n=40)
Neonates	14.53 ± 2.91	10.29 ± 2.13	9.23 ± 1.11	8.37 ± 0.69
Males	14.38 ± 2.84	10.15 ± 2.16	9.06 ± 1.04	8.27 ± 0.65
Females	14.98 ± 3.22	10.69 ± 2.08	9.76 ± 1.21	8.68 ± 0.74

Table 4: Comparison between TSB and serum calcium measures before and after phototherapy treatment among cases (n=40)

Variables	Before Phototherapy (n=40)	After Phototherapy (n=40)	Paired-t test	p- value
TSB (mg/dl)	14.53 ± 2.91	10.29 ± 2.13	12.73	0.001
Serum calcium (mg/dl)	9.23 ± 1.11	8.37 ± 0.69	5.89	0.001

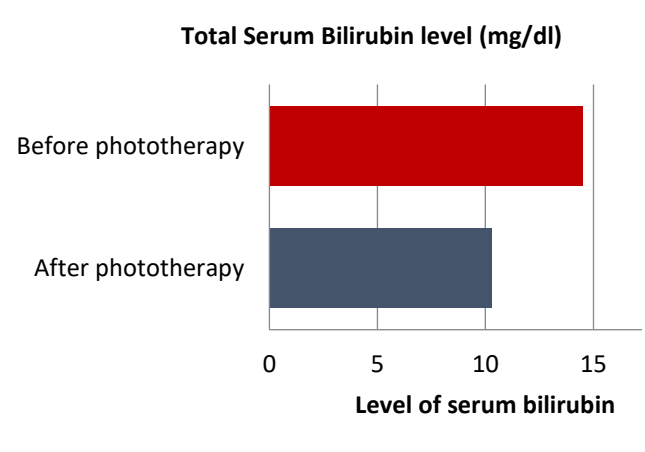

Figure 3: TSB level before and after phototherapy

The mean serum total calcium before starting and after the stoppage of phototherapy was 9.23 ± 1.11mg/dl and 8.37 ± 0.69mg/dl respectively. Decreased serum calcium level after the stoppage of phototherapy is statistically significant, with p-value <0.05 in 1 degree of freedom with critical value of 1.96. (Table 4)

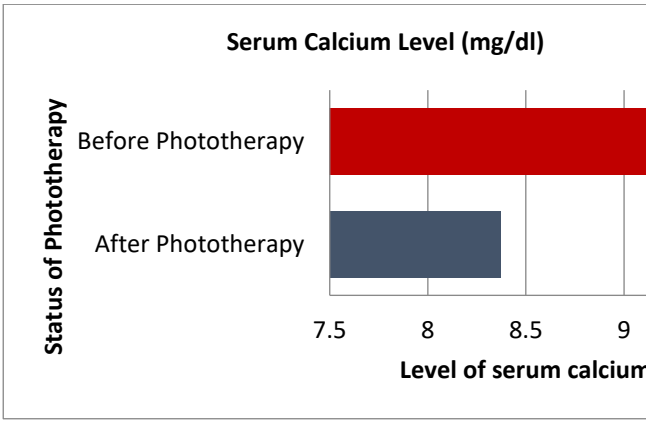

Figure 4: Serum Calcium level before and after phototherapy

Serum calcium levels after phototherapy was >8mg/dl in 31 (77.5%) neonates and hypocalcemia i.e. serum calcium levels < 8mg/dl in 9 (22.5%) neonates as illustrated in Figure 5.

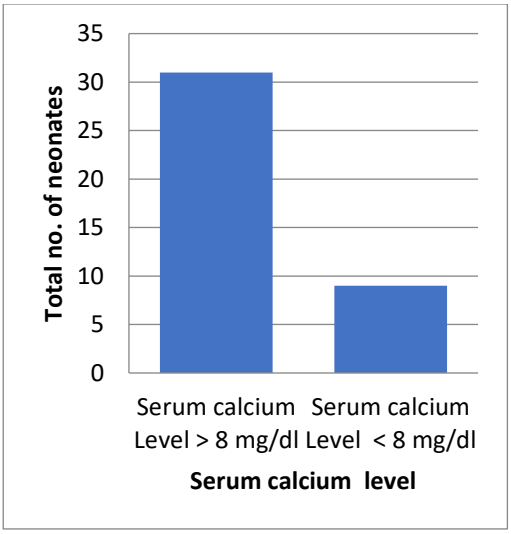

Figure 5: Incidence of hypocalcemia in neonates after phototherapy

DISCUSSION

Neonatal jaundice or hyperbilirubinemia is a common manifestation among newborns that most frequently is seen in the first week of life which may be a common indication for hospital admission.[11] Phototherapy has emerged as most widely and safe tool for treating hyperbilirubinemia in newborns. Romagnoli et al. first described the effect of phototherapy on serum calcium level.[12]

Our study included 75% males and 25% of females. It was similar to the study done by Goyal et al.[13] in India where 61 % were male and 39% were female. The study included more males than female. This may be due to the reason that the study being done at the rural part where boys are preferred over girls in any terms whether it is education or in health. The mean age of the neonates was 4.12 ± 1.09 days that was similar to the study done by Shahriarpanah et al.[14] in Iran where the mean age was 5.52 ±2.45 days.

In this study, there was a significant decrease in serum calcium levels after phototherapy. Total serum calcium decreased in 92.5% of the cases after phototherapy in our study. In our study, hypocalcemia was observed in 22.5 % of neonates after phototherapy. It was similar to the study done by Goyal et al.[13] where 35 % of neonates had hypocalcemia after phototherapy and Bahbah et al.[15] in which post phototherapy 26 % neonates had hypocalcemia. Shrivastav et al.[16] and Abdulrahman[17] also observed hypocalcemic effect of phototherapy in 30.0% and 31% of term neonates respectively. But it was contrary to the study done by Tehrani et al.[18] where only 7.5% neonates developed hypocalcemia after receiving phototherapy and the study done by Sethi et al.[6], where they observed hypocalcemia in 75% of term neonates after phototherapy. In our study, symptomatic hypocalcemia was observed in 2.5% of neonates which were similar to study performed by Goyal et al.[13] who observed 2.86% symptomatic hypocalcemic neonates. Yadav et al.[19] also observed similar percentage of symptomatic hypocalcemic neonates in their study. It may be because most of the sample population of our study was term neonates and hypocalcemia are more common in preterm neonates than term neonates.[13, 15]

In our study, 50% of preterm and 18% term neonates had hypocalcemia. Study conducted by Jain et al.[20] in India also showed occurrence of hypocalcemia in 55% of preterm and 30% of terms after phototherapy. Comparable results were shown by another study in India done by Gupta et al.[21] where 57% of preterm and 31% of the term neonates developed hypocalcemia after phototherapy. Study done by Yadav et al.[19] reported that phototherapy caused hypocalcemia in

80% of preterm and 66% of term neonates. Bahbah et al.[15] also found hypocalcemia after exposure to phototherapy, with a higher percentage among the preterm neonates, as compared with term neonates. So, most of the studies have shown the occurrence of hypocalcemia being more in preterm neonates than the term neonates. The reason for a higher incidence of hypocalcemia in preterm infants is still unknown.[15] Our study also suggested a significant effect of phototherapy on the calcium on neonates with jaundice, receiving phototherapy.

Serum calcium was calculated at the onset and after 48 hrs of phototherapy in many studies performed to find out the prevalence of hypocalcemia after phototherapy.[22, 23] However, in our study we measured the serum calcium level only after stoppage of the phototherapy irrespective of its duration. The mean duration of phototherapy was found to be 39.2 ± 3.45 hours in our study. This was similar to the study done by Khan et al.[24] where it was 1.74±0.98 days (41.76 ± 23.52 hours). Our study showed no significant relationship between level of calcium decreased after phototherapy and the duration of phototherapy. This was similar to the study done by Khan et al.[24] where they found that level of calcium decreased after phototherapy was not statistically significant with the duration of phototherapy.

CONCLUSION

Phototherapy significantly decreases the level of serum calcium. So, along with serum bilirubin level, it is important to monitor serum calcium level in neonates before and after phototherapy. Also, we can recommend calcium supplementation for neonates who are receiving phototherapy as prophylactic treatment.

Limitation: Since this study was conducted in a small sample of population in a limited time period, it may not represent the whole neonatal population of Nepal.

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