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To Study Phototherapy Induced Hypocalcemia In Term Neonates Having Hyperbilirubinemia

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Abstract:
Background*: In the first week of life Jaundice is a common morbidity encountered in newborns. It is the most common clinical feature in neonates. Phototherapy is the main stay of treatment for jaundice in new born. The present study is aimed to evaluate phototherapy induced hypocalcaemia in term neonates having hyperbilirubinemia.This study aims to study the effect of phototherapy in causing hypocalcaemia in term neonates having hyperbilirubinemia.*
Materials and Methods*: Total 100 term neonates having hyperbilirubinemia were taken, to study phototherapy induced hypocalcaemia and its clinical significance. A Chi-square test was applied to study phototherapy induced hypocalcaemia in term neonates having hyperbilirubinemia. P-value less than 0.05 has been considered significant..*
Results*: It revealed that the mean Total serum bilirubin levels at starting time of phototherapy was 15.29±3.39 mg/dl, at 24 hours of phototherapy was 14.92±3.14 mg/dl and at 48 hours of phototherapy was 12.02±2.39 mg/dl and the mean difference was statistically significant (p<0.05). It revealed that the mean serum ionized calcium levels at the time of starting phototherapy was 1.25±0.05 mmol/L, at 24 hours of phototherapy was 0.98±0.14 mmol/L and at 48 hours of phototherapy was 0.88±0.14 mmol/L and the mean difference was statistically significant (p<0.05).*
Conclusion: *All the term neonates with hyperbilirubinemia who require phototherapy should be closely monitored for this reduction in serum ionized calcium levels and should be managed accordingly if required to avoid the symptoms of hypocalcaemia.*
Key Word*: Neonatal Jaundice; Hyperbilirubinemia; Serum calcium; Phototherapy; Hypocalcemia*

I. Introduction

In early neonatal period Jaundice is one of the common encounteredmorbidi.[1]Approximately 60% of healthy term neonates and 80% of preterm neonates develop clinically visible jaundice in the first week of life. In most of jaundice cases requires no treatment. Hyperbilirubinemia in term neonates ≥ 37 weeks gestation is defined as total serum bilirubin (TSB) >95th percentile on the hour specific Bhutani nomogram.[2]Screening for significant jaundice in the first 24 hours and after 2 weeks of life needs to be looked for so that pathological causes are diagnosed promptly and treated appropriately. Phototherapy remains the mainstay of treatment of significant unconjugated hyperbilirubinemia, and its optimal use will usually keep the level of jaundice below the threshold for a potentially hazardous exchange blood transfusion.[3]Phototherapy usually a safe treatment, a few side effects after phototherapy are skin rash, diarrhoea, dehydration, rise in body temperature, low platelet count, photo retinitis, retinal degeneration, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency, DNA damage, nasal obstruction, etc.[4]Nonetheless, no change in blood ions/metabolites has been reported except for fall in calcium levels.[5]There is hypothesis that melatonin secretion is inhibited from pineal gland post phototherapy, which blocks the effect of cortisol on bone calcium. Uncontrolled Cortisol have a direct hypocalcaemia result and more calcium is absorbed from bone.[6]Neonatal hypocalcaemia is defined as total serum calcium concentration of < 8 mg/dl or ionized calcium level < 3.0 to 4.4 mg/dl (< 1.15 to 1.35 mmol/l), depending on the method (type ofelectrode) used. There is paucity of literature on phototherapy

induced hypocalcaemia. Hence, the present study is aimed to evaluate phototherapy induced hypocalcaemia in term neonates having hyperbilirubinemia.

II. Material And Methods

This prospective observational study was carried out on patients of Department of Pediatrics at SGT Medical College, Hospital and Research Institute, Budhera, Gurugram from October 2019 to April 2021. A total 100 term neonates were taken in this study.

Study Design: Prospective Observational study

Study Location: This was a tertiary care rural hospital based study done in Department of Pediatrics, at SGT Medical College, Hospital and Research Institute, Budhera, Gurugram.

Study Duration: October 2019 to April 2021.

Sample size: 100 term neonates

Sample size calculation: The sample size was estimated on the basis of a single proportion design. We assumed that the confidence interval of 10% and confidence level of 95%. The sample size actually obtained for this study was 96 patients. We planned to include 100 patients.

Subjects & selection method: Term neonates fulfilling the inclusion criteria.

Inclusion criteria:

1. Term neonates >2.5 kgs birth weight requiring phototherapy for hyperbilirubinemia.

Exclusion criteria:

1. Term neonates having hypocalcaemia before the start of phototherapy
2. Icterus within the first 24 hours of life
3. Icterus more than 14 days of life
4. Requirement of exchange transfusion
5. Birth asphyxia
6. Sepsis.

Procedure methodology

After approval of the ethical committee, informed consent was obtained from the parents of the selected neonates. Serum ionized calcium was checked before the start of phototherapy & 24/48/72 hours after exposure to phototherapy as per requirement of duration of phototherapy in the term neonates.5 ml blood sample was taken at the start of phototherapy & at 24/48/72 hours after exposure to phototherapy. Phototherapy was given using LEDs (Light Emitting Diodes) at a distance of 30-40 cms from the neonate. Laboratory investigations were done for total serum bilirubin (conjugated & unconjugated) and serum ionized calcium before the start of phototherapy and 24/48/72 hours after phototherapy as per requirement of duration of phototherapy in the term neonates.

Statistical analysis

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). A Chi-square test was applied to study phototherapy induced hypocalcaemia in term neonates having hyperbilirubinemia. P-value less than 0.05 have been considered significant.

III. Result

In our study shows no significant difference in distribution of weight, gender, mode of delivery (table 1). In this study the majority (47%) of the neonates had B+ blood group, around 10% of the neonates had O+ blood group, about 20% of the neonates had A+ blood group (table 2).The mean comparison of the total serum bilirubin levels (mg/dl) among neonates between at starting time, 24 hrs and 48 hrs of Phototherapy was shown in table 3. Repeated measures of ANOVA were computed to find the significant mean difference. On comparison of serum bilirubin level after phototherapy, the mean difference was a statically significant (p<0.05). The mean comparison of the serum ionized calcium levels (mg/dl) at starting time, 24 hrs and 48 hrs among neonates with hyperbilirubinemia on phototherapy, revealed the mean difference was a statically significant (p<0.05). It revealed that there was a gradual decline in serum ionic calcium levels as the duration of phototherapy was increased among neonates having hyperbilirubinemia, which resulted in hypocalcaemia among neonates.

Table 1: Distribution based on gender, bodyweight and mode of delivery

Background variables	**Frequency**	**Percentage**
Gender		
Male	62	62.0
Female	38	38.0
BODYWEIGHT		
<3kg	59	59.0
>3 kg	41	41.0
Mode of Delivery		
LSCS	33	33.0
NVD	67	67.0

Table 2: Distribution based on blood group in mothers and new-borns

Newborn Blood group			**Mother blood group**	
	Frequency	**Percentage**	**Frequency**	**Percentage**
A+	20	20.0	17	17
A-ve			2	2
B+	47	47.0	35	35
B-	3	3.0	2	2
AB+	8	8.0	9	9
AB-ve			2	2
O+	19	19.0	31	31
O-	3	3.0	2	2

Table 3: Comparison of mean Total serum bilirubin levels (mg/dl) among neonates with hyperbilirubinemia at different time points (at starting time, 24 Hrs and 48 Hrs) Phototherapy)**.**

Serum bilirubin levels (mg/dl)	**Mean**	**SD**	**F value**	***p* value**
At Starting time	15.29	3.39	14.35	0.001 (S)
24 Hrs	14.92	3.14		
48 Hrs	12.02	2.39		

Table 4: Comparison of mean serum ionized calcium levels (mg/dl) among neonates with hyperbilirubinemia at different time points (at starting time, 24 hrs and 48 hrs.

Serum Ionized Calcium levels (mg/dl)	**Mean**	**SD**	**F value**	***p* value**
At Starting time	1.25	0.05	198.04	0.001 (S)
24 Hrs	0.98	0.14		
48 Hrs	0.88	0.14		

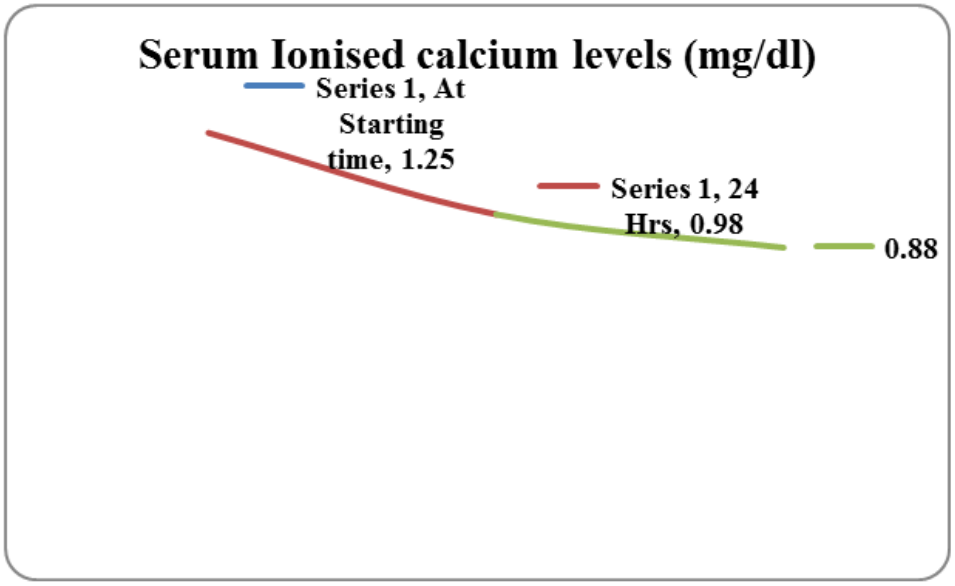

Figure 1: Serum ionized calcium levels among neonates at starting time, 24 hrs and 48 hrs of phototherapy.

IV. Discussion

In our study, a total of 100 term neonates with hyperbilirubinemia (according to Kramer's staging/Bhutani's[7] nomogram/NICE guidelines' chart) were included, excluding all the neonates falling under the exclusion criteria. In our study, 62% of the neonates were males and 38% of the neonates were females with a ratio of males: females being 1.6:1, with the ratio in other studies being 0.6 in Prabhakar et al[8]and 1 in case of Taheri et al[9]. Here in this study, we had included term neonates with hyperbilirubinemia weighing 2.8±0.2 kgs, which was similar to other studies like in Taheri et al[9]. It was 3.1 ± 0.4 kgsand in Jain et al[10] it was 2.8 ± 0.2 kgs. In our study, we found that the mean serum ionized calcium levels 'at the time of starting phototherapy' was 1.24±0.06 mmol/L and 'after 24 hours of exposure to phototherapy' was 0.96±0.14 mmol/L. In contrast to our study, the incidence of hypocalcaemia in term neonates was more in other studies like 7% (10) in Taheri et al[9] and 66.7% (16) in Prabhakar et al [8]. Even in studies with both preterm and term study groups, the incidence of hypocalcaemia was more in both the groups like in Karamifar[11] et al 8.7% and 22.6%, in term and preterm respectively, 66.6% and 80 % in term and preterm inYadav et al[12] respectively. In our study, the hypocalcaemia cut off lab value is <1.15 mmol/L in all the term neonates.The mean comparison of the serum ionized calcium levels (mmol/L) among neonates with hyperbilirubinemia'at the time of starting phototherapy' and 'after 24 hours of exposure to phototherapy' revealed that the ionized calcium levels 'at the time of starting phototherapy' was 1.24±0.06 mmol/L and 'after 24 hours of exposure to phototherapy' was 0.96±0.14 mmol/L& the mean difference was statistically significant ($p<0.05$). This was similar to other studies like Eghbalian et al[13], where the mean serum calcium was 9.85±1.23 mg/dl and 9.09 ± 0.93 mg/dl, before and after phototherapy, respectively, with significant p-value, even in studies like Karamifar et al[11] and Taheri et al [9] there was significant fall in serum calcium values with p-value being < 0.05.

LIMITATIONS: The irradiance of the phototherapy units was not checked during the study. The intensive power of phototherapy given to the neonates, such as single surface, double surface or intensive phototherapy and its effect on serum ionized calcium were not categorised.

V. Conclusion

This study concludes that neonates with hyperbilirubinemia undergoing phototherapy for 24/48/72 hours as per requirement of duration of phototherapy are at a higher risk of reduction in serum ionized calcium levels. So, all the term neonates with hyperbilirubinemia who require phototherapy should be closely monitored for this reduction in serum ionized calcium levels and should be managed accordingly if required to avoid the symptoms of hypocalcaemia.

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