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Corelation of Hypocalcaemia with Use of Phototherapy in Neonates with Hyperbilirubinemia: A Prospective Observational Study

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Abstract

To evaluate the effect of phototherapy on serum calcium level in neonates with hyperbilirubinemia To determine hypocalcaemia in neonates with unconjugated hyperbilirubinemia receiving phototherapy. Prospective Observational Study conducted in neonatal intensive care unit, Government Medical College Miraj for 4 months from January 2024 to April 2024. Term neonates with unconjugated hyperbilirubinemia having total serum bilirubin within phototherapy range were included in the study. Before starting phototherapy, serum calcium level was documented. Serum calcium level was repeated after completion of phototherapy. Pre and post phototherapy serum calcium levels were compared In study group, 90 neonates who received phototherapy, 53.3% were male and 46.7% were female. Mean serum calcium level of neonates before and after provision of phototherapy was 8.473 mg/dl±0.75 and 7.958 mg/dl±0.70 respectively, which is statistically significant (<0.001). Hypocalcaemia is an important complication in neonates with unconjugated hyperbilirubinemia after continuous phototherapy. hypocalcaemia has clinical impact and adds to morbidity, and if left untreated, can lead to mortality.

INTRODUCTION

Hyperbilirubinemia is one of the most frequent and benign problem in neonates. During first week of life, around 80% of preterm neonates and 60% of full-term neonates have hyperbilirubinemia. Severe unconjugated hyperbilirubinemia, if not treated timely, can lead to permanent brain damage in the newborn^[1]. Hyperbilirubinemia can be managed either by phototherapy, exchange transfusion or pharmacological agents^[2]. Phototherapy is the most effective therapy for management of neonatal hyperbilirubinemia which lowers serum bilirubin level by converting bilirubin through structural photo isomerization and photo-oxidation into non-toxic form that is excreted out of the body^[3]. Complications of phototherapy are dehydration, diarrhoea, skin rash, hyperthermia, retinal degeneration, DNA damage to lymphocytes, patent ductus arteriosus (PDA) and bronze baby syndrome^[4] lesser-known side effect, but a potential complication of phototherapy is hypercalcemia. Melatonin concentration is reduced in newborns with phototherapy which in turn leads to hypercalcemia^[5]. The association between phototherapy and hypercalcemia was first reported by Shafiq MB *et al.* in preterm infants^[6]. The pathophysiology and the underlying mechanism by which phototherapy causes Hypocalcemia was suggested by Hayat and Hunter and reported that phototherapy inhibit the secretion of melatonin by pineal gland and this results in blockage of the effect of cortisol on bone calcium^[7]. Study by Husain *et al.* suggested that neonates receiving phototherapy have reduced level of parathyroid hormone which leads to hypocalcemia^[8]. While Hooman in a study reported that urinary excretion of calcium was significantly higher in patients exposed to phototherapy^[9]. Complications of hypocalcemia in newborns include apnoea, convulsion, muscle cramp, tremor and tetanus. The relation of hypocalcemia with phototherapy is an important aspect to be considered due to the potential complications of hypocalcemia. This study aimed to cater the burden of hypocalcemia in term neonates treated with phototherapy so as to highlight this aspect, that can further emphasize in modifying local strategies and research priorities.

MATERIALS AND METHODS

This observational study was carried out at neonatal intensive care unit, Government Medical College Miraj for 4 months from January 2024 to April 2024. Clearance from institutional ethical review committee was taken before the initiation of the study. Informed consent was taken from their parents/guardians. A total of 90 neonates were included in the study, the sample size was taken duration based. They were hemodynamically stable term neonates with unconjugated hyperbilirubinemia

requiring phototherapy and had a normal calcium level before initiating phototherapy. Neonates hemodynamically unstable with jaundice requiring exchange transfusion, birth asphyxia, sepsis, respiratory distress and infants of diabetic mother were excluded from the study. All the information including socio-demographics and serum calcium levels (pre and post phototherapy) were recorded on a pro-forma. Hypocalcemia was defined as a total serum calcium level of less than 8 mg/dL in a term neonate^[10]. A sample of 3ml venous blood was sent to the laboratory for serum calcium level before starting conventional phototherapy and after completion of phototherapy. All the information including gestational age, gender, weight, age, mode of delivery and serum calcium levels (pre and post phototherapy) were recorded on pro-forma. SPSS version 22 was used to analyse data. Quantitative variables like age and serum calcium were described in terms of mean±standard deviation. Frequency and percentages were used to describe categorical variables like gender and hypocalcemia. Hypocalcemia was stratified by age and gender to see effect modifiers. Post stratified chisquare test was applied in which p value <0.05 was considered as significance value.

RESULTS AND DISCUSSIONS

(Table 1) summarizes the distribution of participants by sex, showing that among the 90 individuals, 42 (46.7%) are female and 48 (53.3%) are male. This breakdown provides a clear overview of the gender composition within the sample population.

(Table 2) summarizes Frequency of hypocalcemia in neonates with respect to gender after phototherapy was 26 (24%), out of which 15 were male patients and 11 were female patients.

The (Table 3) presents statistical data comparing serum calcium level before and after phototherapy. The mean serum calcium level of neonate before and after phototherapy were 8.47mg/dl±0.75 and 7.95mg/dl±0.70 respectively. The p-value was <0.001 which is highly significant indicating a strong association between these variables.

Neonatal jaundice is a frequent cause of morbidity in newborns worldwide and the most frequent cause of hospitalization and readmission in the initial week of life^[11]. Phototherapy is the most effective treatment for management of neonatal hyperbilirubinemia which lowers serum bilirubin level by converting bilirubin into non-toxic excretable form. In our study, the frequency hypocalcemia was 24% in neonates with unconjugated hyperbilirubinemia after completion of phototherapy. In study conducted in Karachi by M^[12] the frequency of hypocalcemia in term jaundiced neonates receiving phototherapy was 22.76% similar to our study. Shrivastva^[13] in a study observed that the frequency of hypocalcemia was 30% in term neonates while

Table 1: Distribution of participants by sex, showing that among the 90 individuals

Sex	Frequency	Percentage
Female	42	46.7%
Male	48	53.3%
Total	90	100%

Table 2: Frequency of hypocalcemia in neonates

Hypocalcemia	Frequency			Percentage
	Male	Female	Total	
Yes	15	11	26	24%
No	33	31	64	76%
Total	48	42	90	100%

Table 3: Statistical data comparing serum calcium level before and after phototherapy

Variables	Mean	SD	SEM	paired t test	p value	Significance
Sr Calcium Before phototherapy	8.473	.7532	.0794	15.92	<0.001	Highly Significant
Sr Calcium After Phototherapy	7.958	.7023	.0740			

Table 4: Frequency of Hypocalcemia

Studies	Frequency of Hypocalcemia
Karachi by M <i>et al.</i>	22.76%
Shrivastva <i>et al.</i>	30%
Haq <i>et al.</i>	75%
Our Study	24%

Table 5: Studies

Studies	M:F
Khan <i>et al.</i>	1.67:1
Alizadeh TP	1.08:1
Our Study	1.36:1

Table 6: Mean Calcium Level

Studies	Mean Calcium Level	
	Before Phototherapy	After Phototherapy
Khan M <i>et al.</i>	8.73±0.68	7.47±0.8
Bahbah <i>et al.</i>	9.36±0.29	8.58±0.76
Our Study	8.47±0.75	7.95±0.70

Haq^[14] reported hypocalcemia to be present in 75% of the neonates exposed to phototherapy.

In a study by Kha^[12] there were 62.6% males and 37.4% females. Also, in a study by Alizadeh TP there were 49% female neonates and 51% were males. 15 Observation in our study is similar to the above studies where number of male neonates is higher than that of females

In our study, the mean calcium level before and after phototherapy was 8.47mg/dl±0.75 and 7.95mg/dl ±0.70 respectively. Mean calcium level before and after phototherapy in the local study conducted by Khan M^[12] was 8.73±0.68 mg/dl and 7.47±0.8 mg/dl which is comparable with our study. Similarly, mean calcium level before and after phototherapy in the study conducted by Bahbah^[2] was 9.36±0.29 mg/dl and 8.58±0.76 mg/dl which is also comparable with our study. This study is conducted on small group of subjects so further studies on larger scale should be conducted so that results can be extrapolated to larger population. Further studies are required to elaborate this aspect and to find out ways to avoid hypocalcemia after phototherapy either by using calcium supplements or refining application of phototherapy. Hence, results of this study will be useful for practitioners to devise meaningful early interventions

to avoid complications of hypocalcemia in neonates receiving phototherapy at neonatal intensive care units.

CONCLUSION

Hypocalcaemia is an important complication in neonates with unconjugated hyperbilirubinemia after continuous phototherapy. hypocalcaemia has clinical impact and adds to morbidity. Therefore, it should be timely diagnosed by monitoring serum calcium level in neonates receiving phototherapy and appropriately treat with calcium supplementation. Our study will help pediatricians to plan prompt interventions to avoid complications of hypocalcemia in neonates receiving phototherapy.

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