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Effects Of Phototherapy On Serum Calcium Level In Neonates With Hyperbilirubinemia

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Abstract

Objective: To study the frequency of hypocalcemia in neonates receiving phototherapy with indirect hyperbilirubinemia
Materials and Methods: Descriptive case series study was conducted from September 5, 2018, to March 5, 2019, in the NICU of the Paediatric Department Benazir Bhutto Hospital, Rawalpindi.
Approval was sought from the hospital's ethical committee. Neonates fulfilling inclusion criteria were enrolled in the study after obtaining informed consent from the parents. Before giving phototherapy, serum calcium levels were checked. Phototherapy was given for 48 hours. Serum calcium levels were reassessed after 48 hours of phototherapy. Data was entered on a structured proforma and statistical analysis of data was performed.
Results: Out of 150 patients enrolled in the study 83(55.33%) were male and 67(44.67%) were female. The mean age of patients was 52.52 hours with minimum and maximum ages of 26 hours and 80 hours. The mean Indirect serum bilirubin level was 15.59 ± 2.36. A total of 50(33.33%) cases had hypocalcemia after 48 hours of phototherapy, all of these neonates had normal calcium levels before phototherapy. When hypocalcemia was stratified for gestational age, birth weight and serum bilirubin levels at baseline, there was no significant difference in the frequency of hypocalcemia concerning these effect modifiers.
Conclusion: It is concluded that the frequency of hypocalcemia is higher in neonates with indirect hyperbilirubinemia after receiving phototherapy. One needs to be vigilant in dealing with neonates in this context, while serial measurements of calcium levels and monitoring for complications of hypocalcemia should be included in every institution's policy.
Keywords: Hypocalcaemia, Term neonates, Jaundice, Phototherapy.

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1. Introduction

Neonatal jaundice is a common condition in the neonatal period. About 60% of term and 80% of preterm infants develop jaundice in their first week of life.[1] In most cases it is physiological and self-limiting and does not require any treatment[2].
Although transient, the condition accounts for up to 75% of hospital admissions in the first week after birth.3 Approximately 5-10% of them have clinically significant hyperbilirubinemia for whom the use of phototherapy becomes mandatory.[4]
Phototherapy is a non-invasive, effective, and conveniently available modality in the degradation of unconjugated bilirubin. The blue light used in clinical practice is most effective in the breakdown of bilirubin.5 However, the use of phototherapy may be associated with undesired effects like skin rash, thrombocytopenia, bronze baby syndrome, hyperthermia, dehydration, riboflavin deficiency, and deoxyribonucleic acid (DNA) damage.[6] Based on animal studies, it has been proposed that phototherapy may decrease melatonin secretion leading to decrease glucocorticoid secretion and an increase in bone calcium uptake, which results in hypocalcemia.[7] To prevent deposition of unconjugated bilirubin on the outer neuronal membranes, intracellular magnesium moves out from the neurons, erythrocytes, and cardiocytes and gets deposited on the outer membrane causing increased plasma magnesium that itself leads to neuronal and cardiac damage. As phototherapy reduces bilirubin levels, the movement of magnesium from intracellular to extracellular space stops leading to a decrease in the plasma-ionized magnesium and serum magnesium. Hence, the increase in the level of corticosterone leads to hypocalcemia and hypomagnesemia[7].
Ionized calcium is maintained within a normal range for many physiological processes in the body including cell membrane function and integrity, blood coagulation, neuromuscular function, and certain enzymatic activities. Hypocalcemia can cause certain complications in neonates like lethargy, apnea, jitteriness, seizures, vomiting, and abdominal

distension.[8] According to one study, 46/100 neonates (46%) developed hypocalcemia after phototherapy.[5] Another study showed that 28/123 neonates (22.76%) developed hypocalcemia after phototherapy.[4] This study was conducted to study the effect of phototherapy on serum calcium levels in neonates with indirect hyperbilirubinemia because post-phototherapy serum calcium levels are not routinely done in our population resulting in limited data availability. It will have implications for early diagnosis and prompt treatment of hypocalcemia because of its potential complications.

2. Materials & Methods

Study design: Descriptive longitudinal study

Setting: Department of Paediatrics,

Duration of study: Six months [September 5, 2018, till Mar 5, 2019]

Sample size: sample size was calculated by a standard WHO calculator. Confidence interval 95%

Anticipated population proportion 46%[4] Absolute precision 0.8

Sample size 150

Sample technique: Non-probability consecutive sampling

Sample selection:

Inclusion criteria:

1. Term neonates
2. Any Gender
3. Birth weight >2.5 kg
4. Jaundice appearing after 24 hours of life
5. Indirect hyperbilirubinemia (as per operational definition)
6. Normal serum calcium levels before phototherapy

Exclusion criteria:

1. Comorbids (birth asphyxia, Infant of diabetic mother, sepsis)
2. Maternal risk factors (hyperparathyroidism, diabetes, use of anticonvulsants)

Data collection procedure:

Approval was sought from the hospital's ethical committee. Neonates fulfilling inclusion criteria were enrolled in the study after obtaining informed consent from the parents. Before giving phototherapy, serum calcium levels were checked. Phototherapy was given for 48 hours. All neonates were on oral feed along with 20 percent added IV fluid to account for phototherapy losses. Serum calcium levels were assessed after 48 hours of phototherapy. Reports were sent to the hospital lab and reviewed by the pathologist. Collected data was recorded on a structured proforma and statistical analysis of data was performed

Data analysis:

The collected data was entered and analyzed with SPSS-20 software. Mean+ standard deviation was calculated for quantitative data like age, weight, serum calcium, levels, and serum indirect bilirubin levels. Frequency and percentage were calculated for qualitative data like gender and hypocalcemia. Data was stratified for age, weight, and serum bilirubin levels at baseline to deal with the effect modified post-stratification. Chi-square was applied for qualitative data. p-value ≤ 0.05 was considered significant

3. Results

Out of 150 patients enrolled in the study 83(55.33%) were male and 67(44.67%) were female. The mean age of patients was 52.52 hours with minimum and maximum ages of 26 hours and 80 hours. The mean gestational age was 39.08 ± 1.39 weeks. The mean indirect serum bilirubin level was 15.59 ± 2.36. The mean birth weight was 3059.64 ± 260.27g.0ut of 150 neonates, all of whom had normal serum calcium levels before phototherapy, and 50 (33.33 %) had hypocalcemia after 48h phototherapy as shown in Figure1.

When hypocalcemia was stratified for age groups, gender, gestational age, birth weight, and serum bilirubin levels at baseline, there was no significant difference in the frequency of hypocalcemia concerning these effect modifiers.

5. Discussion

Approximately 5-10% of the neonates have clinically significant jaundice in whom the use of phototherapy becomes mandatory[11] Infants under phototherapy have long been proposed to be at risk of developing hypocalcemia, especially preterm new-borns[12] The overall prevalence of hypocalcemia in neonates receiving phototherapy was suggested to be 8.7% in full-term newborns.[9]

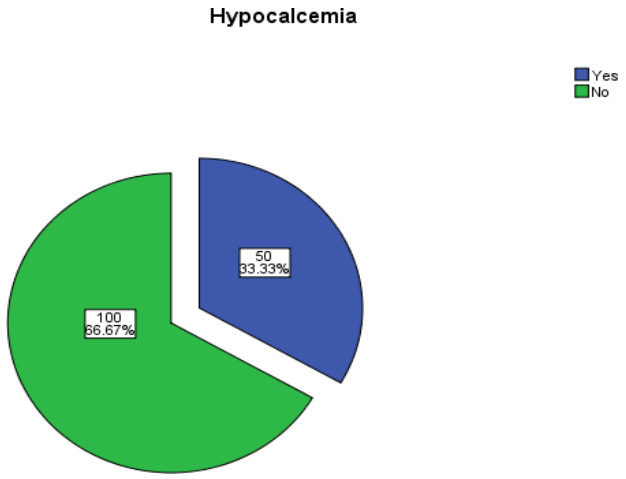

Figure-1 Frequency distribution of hypocalcemia

In the current study, the mean age of patients was 52.52 hours with minimum and maximum ages of 26 hours and 80 hours. The mean gestational age was 39.08 ± 1.39 weeks. In another local study, the mean age of the neonates was 8.35±6.74 days which is higher than the current study. The mean gestational age at the time of birth was 39.08±1.37 weeks which was similar to the current study.4 Frequency of hypocalcemia in term jaundiced neonates receiving phototherapy was observed in 22.76% (28/123) which was lower than the current study i.e., 33% 50/150. 4 In another study done by Gupta et al. in India showed the almost same frequency of hypocalcemia in term neonates (31% term new-borns) after 48 h of phototherapy[11]. Similarly, different studies show some variation in results. A study by Bahbah et al done in 2014 in Egypt reported that 26% of term neonates who received phototherapy for jaundice developed hypocalcemia after 48 hours of phototherapy.[13]

Gheshmi AN., et al. reported a decrease in the serum calcium concentration in 54% of full-term neonates after phototherapy13. Gheshmi et al. conducted a cross-sectional study on 100 full-term neonates to determine the prevalence of hypocalcemia after phototherapy in two groups, i.e., 1) those who were more than three days old and 2) those who were less than three days old, the prevalence was not significantly different in the two age groups (P = 0.217) which were similar to our study.[14] Phototherapy can lead to decreased total and ionized calcium levels in neonates, especially in preterm neonates. This effect might be attributable to increased urinary calcium excretion. In addition, light can inhibit pineal secretion of melatonin and consequently leading to hypocalcemia, hypomagnesemia with no significant effect on Vit D levels. Fortunately, only a few hypocalcemic neonates present clinically, and in almost all hypocalcemic neonates serum levels of calcium return to normal 24 h after ending phototherapy.[15] Hypocalcaemia in neonates present with tetanus, spasms of the larynx, dysfunction of myocardia and apnoea .14 myoclonic seizure, jerking, chills, tachycardia, heart failure, and decreased contractility of the heart.[17] Hypocalcaemia is a common cause of seizures in neonates.16 Neonates should have serial monitoring for serum calcium levels who receive phototherapy for > 48 hrs for early identification and treatment

Table-1 Comparison of hypocalcemia concerning age groups (hours)

		Hypocalcaemia		Total
		Yes	No	
Age groups (hours)	**26-36**	8(16.0%)	23(23.0%)	31(20.7%)
	>36	42(84.0%)	77(77.0%)	119(79.3%)
Total		50(100.0%)	100(100.0%)	150(100.0%)

Chi-square test = 0.996 p-value = 0.318

Table -2: Comparison of hypocalcemia concerning gender

		Hypocalcaemia		Total
		Yes	No	
Gender	**Male**	33(66%)	50(50%)	83(55.3%)
	Female	17(34%)	50(50%)	67(44.7%)
Total		50(100.0%)	100(100.0%)	150(100.0%)

Chi-square test = 0.014 p-value = 0.906

Table-3 Hypocalcaemia concerning gestational age (weeks)

		Hypocalcaemia		Total
		Yes	**No**	
Gestational age (week)	**37-39**	30(60%)	59(59%)	89(59.3%)
	40-41	20(40%)	41(41%)	61(40.7%)
Total		50(100.0%)	100(100.0%)	150(100.0%)

Table-4 Hypocalcaemia concerning birth weight

		Hypocalcaemia		Total
		Yes	**No**	
Birth Weight	**2600-3000**	26(52%)	39(39%)	65(43.3%)
	3001-4000	24(48%)	61(61%)	85(56.7%)
Total		50(100.0%)	100(100.0%)	150(100.0%)

Chi-square test = 2.294 p-value = 0.130

Table-5 Hypocalcaemia concerning Baseline Indirect hyperbilirubinemia

		Hypocalcaemia		Total
		Yes	**No**	
Baseline Indirect hyperbilirubinemia	**12-15**	17(34%)	43(43%)	60(40%)
	15.1-20	33(66%)	57(57%)	90(60%)
Total		50(100.0%)	100(100.0%)	150(100.0%)

5. Conclusion

It is concluded that the frequency of hypocalcemia is higher in neonates receiving phototherapy for indirect hyperbilirubinemia. Serial monitoring for hypocalcemia and its complications should be considered an institutional policy.

CONFLICTS OF INTEREST- None

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Potential competing interests: None to report

Contributions:

Q.J - Conception of study

Q.J, U.A, U.J - Experimentation/Study conduction

S.A, N.U.A - Analysis/Interpretation/Discussion

Q.J, S.A, A.A - Manuscript Writing

N.U.A, U.A, A.A - Critical Review

U.J - Facilitation and Material analysis

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