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IMPACT OF PHOTOTHERAPY ON ELECTROLYTE BALANCE IN TERM NEONATES WITH HYPERBILIRUBINEMIA - A PROSPECTIVE OBSERVATIONAL STUDY

Vasant Dhawas[1], Snehal Korde[1], Girish Nanoti[2]

[1]Assistant Professor, Department of Paediatrics, NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur, Maharashtra, India
[2]Professor and Head, Department of Paediatrics, NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur, Maharashtra, India

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Corresponding Author:
Dr. Snehal Korde,
Email: snehaldalal87@gmail.com

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ABSTRACT

Background: Neonatal hyperbilirubinemia is a common condition in early infancy, frequently requiring phototherapy as a treatment. This study aimed to evaluate electrolyte changes at 0 and 48 hours after the initiation of phototherapy, or upon its discontinuation, in term neonates. **Materials and Method:** A total of 90 term neonates with unconjugated hyperbilirubinemia normal electrolyte level at start of phototherapy were included in the study. Blood samples were taken at the start and end of phototherapy to measure serum calcium, sodium, and potassium. **Results:** A statistically significant association was observed between birth weight and serum calcium levels (p=0.049), while no significant associations were found between birth weight and serum sodium (p=0.079) or potassium levels (p=0.213). Phototherapy led to a significant decrease in mean serum calcium, sodium, and potassium levels, with hypocalcemia observed as statistically significant (p<0.001) in all neonates, irrespective of birth weight. Low-birth-weight neonates were particularly susceptible to electrolyte imbalances due to factors like renal immaturity and fluid loss. These findings suggest that phototherapy may exacerbate dyselectrolytemia. **Conclusion:** Given the impact of phototherapy on electrolyte levels, it is recommended to monitor serum calcium, sodium, and potassium at least once every 24 hours during treatment, particularly for low-birth-weight neonates. In normal birth-weight infants, calcium monitoring is essential, with sodium and potassium checks based on clinical judgment.

INTRODUCTION

Neonatal hyperbilirubinemia, the most common physical finding in the first seven days of life, is marked by elevated bilirubin levels and occurs in over two-thirds of newborns. This condition causes yellowish discoloration of the skin and sclera, affecting almost 60% of term and 80% of preterm infants.[1] Serum bilirubin levels exceed 12.9 mg/dL in 6.1% of healthy term newborns, and about 3% have levels above 15 mg/dL. Indirect hyperbilirubinemia is a typical physiological condition in most neonates. Physiological hyperbilirubinemia typically shows serum bilirubin levels of 1–3 mg/dL at birth, rising to a peak of 5–6 mg/dL by days 2–4 and gradually decreasing by day 7.[2] However, pathological neonatal hyperbilirubinemia is characterized by the appearance of jaundice within the first 24 hours of life, a rapid increase in total serum or transcutaneous bilirubin levels exceeding 0.2 mg/dL per hour, and the presence of associated signs like vomiting, lethargy, poor feeding, excessive weight loss, apnea, tachypnea, or temperature instability, indicating that the condition may require further medical evaluation and intervention.[2]

Phototherapy, a widely utilized treatment, has been proven effective in reducing serum bilirubin levels and preventing the complications associated with hyperbilirubinemia. But phototherapy have some side effects like hyperthermia, feed intolerance, loose stools, skin rashes, bronze baby syndrome, retinal changes, dehydration, genotoxicity, and electrolyte changes.[2] While its impact on bilirubin metabolism is well-studied, its effect on neonatal electrolyte balance remains less explored.[3,4] Electrolytes are essential ions in the body that play pivotal roles in maintaining cellular function, fluid balance, and overall physiological stability. The interplay between bilirubin metabolism and electrolyte regulation is complex and not yet fully elucidated.[5] Emerging evidence suggests that phototherapy, despite its

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benefits in reducing bilirubin concentrations, could potentially influence electrolyte levels in neonates. Understanding the intricate relationship between phototherapy and electrolyte changes is crucial for providing comprehensive care to neonates with unconjugated hyperbilirubinemia.[3-7]

Research on the impact of phototherapy on neonatal electrolyte balance is limited, with most studies focusing on bilirubin reduction and clinical outcomes, with less attention directed towards electrolyte shifts. Therefore, this study aims to evaluate electrolyte changes (sodium, potassium, calcium) at 0 and 48 hours after the initiation of phototherapy, or upon its discontinuation, in term neonates.

MATERIALS AND METHODS

This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) of tertiary care hospital during a period from 1st September 2019 to 31st October 2021, after taking informed consent from parents and approval from the institutional ethics committee (No. NKPSIMS & RC and LMH /IEC/25/2019 Dated 15/10/2019). A total of 90 term neonates with unconjugated hyperbilirubinemia normal electrolyte level at start of phototherapy were included in the study. This was a hospital-based study where the participants were selected by convenience sampling method with all term neonates having neonatal hyperbilirubinemia and receiving phototherapy. Neonates having sepsis, conjugated hyperbilirubinemia, perinatal asphyxia, infants of diabetic mothers and preterm neonates were excluded from the study. Also, those neonates on diuretics, who were hemodynamically unstable and neonates who develop sepsis during phototherapy were withdraw from the study.

2ml of venous blood samples were collected with due antiseptic method from the neonates without any stasis of blood and sent for total bilirubin, indirect bilirubin, and in same sample serum electrolytes (sodium, potassium, calcium) were run. Total and direct bilirubin was measured by Diazotization method on Dimension RXL (SEIMENS) machine. Calcium by O-cresopthaline complexone method also by Dimension RXL (SEIMENS) machine. Sodium and potassium by Ion selective Electrode method. Total and indirect serum bilirubin, serum sodium, potassium, and calcium were checked at 0 hours, and at 48 hours of phototherapy or at discontinuation of phototherapy whichever was earlier recorded. Comparative study was done between these two groups to evaluate the changes in electrolytes. Hyponatremia is considered when the level of sodium in serum falls below 135 mEq/L 8. Hypokalemia is considered when the level of potassium in serum falls below 3.5 mEq/L 9. Hypocalcemia is considered when the level of serum calcium falls below 7 mg/dl in term neonates 10.

Statistical analysis: Data was entered in excel sheet and analyzed in statistical software R version 4.1.2. Data analysis includes both descriptive and inferential statistics. The mean, standard deviation, frequency and percentages were used to summarize quantitative and qualitative variables. Inferential statistics include both point estimates (%) and interval estimates (95% confidence intervals) for frequency and proportions. Chi-square test was used to compare the difference in proportions in subgroups by various patient characteristics. A p-value < 0.05 was considered statistically significant for all comparisons.

RESULTS

Among 90 study participants, 47 (52.20%) were females and 43 (47.80%) were males. We found that out of the total 47 female study participants, 16 (34.00%) were low birth weight and 31 (66.00%) were having normal birth weight. Out of the total 43 male study participants, 11 (25.60%) were low birth weight while 32 (74.40%) had normal birth weight.

Among 90 neonates, 47 (52.22%) required phototherapy for more than 24 hours, and 43 (47.78%) for less than 24 hours. Of those required >24 hours, 11 (25.6%) were low birth weight, and 32 (74.4%) had normal birth weight. For those requiring <24 hours, 16 (34.0%) were low birth weight, and 31 (66.0%) had normal birth weight. No significant association was found between birth weight and phototherapy duration (p=0.519), [Table 1].

A statistically significant association between birth weight and serum calcium levels was observed (p=0.049). However, no statistically significant association was found between birth weight and serum sodium levels (p=0.079) or serum potassium levels (p=0.213), [Table 2].

There was no statistically significant association was found between the duration of phototherapy and serum calcium levels (p=0.270), serum sodium levels (p=0.999), or serum potassium levels (p=0.243) as shown in [Table 3].

There was a significant decrease in the mean levels of serum calcium (difference=0.65; p-value<0.001), sodium (difference=2.09; p-value<0.001) and potassium (difference=0.30; p-value<0.001) post-phototherapy as compared to pre-phototherapy. phototherapy caused hypocalcemia but did not cause hyponatremia and hypokalemia. [Table 4].

Table 1: Distribution of birth weight of the study participants according to their duration of phototherapy

Birth Weight	<24 hrs	Phototherapy >24 hrs	Total
LBW (<2.5 kg)	11(25.6%)	16(34%)	27(30%)
Normal (> 2.5 kg)	32(74.4%)	31(66%)	63(70%)
Total	43(100%)	47(100%)	90(100%)
	X2=0.416 .df=1	φ=0.092 · p=0.519	

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Table 2: Distribution of birth weight of neonates according to their electrolyte's levels (calcium, sodium, potassium).

Birth weight	Calcium (mg/dl)		Sodium (mEq/L)		Potassium (mEq/L)	
	< 7	7-11	<135	135-145	<3.5	3.5-5.5
LBW (<2.5 Kg)	05 (62.5%)	22 (26.8%)	03 (75%)	24 (27.9%)	02 (66.7%)	25 (28.7%)
Normal (>2.5 kg)	03 (37.5%)	60 (73.2%)	01 (25%)	62 (72.1%)	01 (33.3%)	62 (71.3%)
Total	08 (100%)	82 (100%)	04 (100%)	86 (100%)	03 (100%)	87 (100%)
P value	0.049 (Significant)		0.079 (Insignificant)		0.213 (Insignificant)	

Table 3: Distribution of study participants according to the duration of phototherapy received and their electrolyte's levels (calcium, sodium, potassium)

Electrolyte's levels		Phototherapy		Total (n=90)
		<24 hours (n=43)	>24 hours (n=47)	
Calcium (mg/dl)	< 7	02 (4.7%)	06 (12.8%)	08 (8.9%)
	7-11	41 (95.3%)	41 (87.2%)	82 (91.1%)
	P value	p=0.270 (Insignificant)		
Sodium (mEq/L)	<135	02 (4.7%)	02 (4.3%)	04 (4.4%)
	135-145	41 (95.3%)	45 (95.7%)	86 (95.6%)
	P value	p=0.999 (Insignificant)		
Potassium (mEq/L)	<3.5	00 (0.0%)	03 (6.4%)	03 (3.3%)
	3.5-5.5	43 (100.0%)	44 (93.6%)	87 (96.7%)
		p=0.243 (Insignificant)		

Table 4: Distribution of study participants received phototherapy and, calcium, sodium, and potassium levels

Electrolytes	Pre- Phototherapy	Post-Phototherapy	Difference	t value	p-value
Calcium	9.12	8.47	0.65	5.180	<0.001
Sodium	141.07	138.98	2.09	5.403	<0.001
Potassium	4.82	4.52	0.30	4.068	<0.001

DISCUSSION

Neonatal hyperbilirubinemia affects both term and preterm neonates within their first few weeks of life.[11,12] Treatment of choice for unconjugated hyperbilirubinemia is phototherapy. Phototherapy is proved to decrease the serum bilirubin level significantly but the fact that it can affect the electrolytes level is not studied in detail. In the present study, term neonates delivered between 37 and 42 weeks of gestational age who met the inclusion criteria were included to see for electrolyte changes which was like studies by Eghbalian et al., Taheri PA et al., and Rozario CI et al.[13-15] The mean birth weight of neonates in current study was 2.71±0.391 kg which is comparable with the previous studies done by Reddy et al., and Kumar S. et al.[16,17]

In the present study, the frequency of hypocalcemia was 9%, with a higher occurrence in low birth weight (LBW) neonates (18.51%) compared to normal-weight neonates (4.76%), aligning with findings by Reddy et al who found the incidence of hypocalcemia being 13.1%.[16] Notably, post-phototherapy, we observed a statistically significant decline in mean serum calcium levels (p<0.001). However, this decline did not result in symptomatic hypocalcemia. Similar findings have been reported by Rozario CI et al, Reddy et al, and Suneja et al, who also noted a reduction in serum calcium following phototherapy without inducing hypocalcemia.[15-20] These findings underscore the importance of monitoring calcium levels during phototherapy, especially in LBW neonates, to prevent potential complications of electrolyte imbalances.

We found that 11.11% of neonates developed hyponatremia following phototherapy, with only 1.51% of normal-weight neonates affected, which aligns with findings from studies by Reddy, and Kumar S.[16.17] This suggests that LBW neonates are at more risk for developing hyponatremia. According to Curtis MD et al, neonates undergoing phototherapy experience significantly impaired absorption of water, sodium, potassium, and chloride 19. Our results indicated mean serum sodium levels of 141.07±2.795 mmol/dL before phototherapy and 138.98±4.751 mmol/dL afterward, reflecting a decline consistent with the observations of Reddy et al., (139.02±3.12 and 138.16±3.36), Kumar S. et al (139.01±3.119 and 138.15±3.35), as well as Suneja et al, (159.38 ± 22.7 and 148.80 ± 10.9).[16-18] These findings underscore the necessity for careful monitoring of sodium levels in neonates, particularly those with low birth weight, during and after phototherapy to mitigate potential risks associated with electrolyte imbalances.

In current study, our study discovered that 7.4 percent of LBW neonates and only 1.59 percent of normal neonates developed hypokalemia. This was highly significant statistically ($p < 0.001$). It is consistent with Suneja et al study they reported a decrease in serum potassium levels.[17] Although the reasons as hypothesized by Curtis MD et al., who suggested that prolonged phototherapy could lead to diarrhea, impairing the absorption of electrolytes, particularly potassium, chloride, and sodium.[19]

In this study, a significant reduction in serum potassium levels was seen, decreasing from 4.82±0.683 to 4.52±0.666, with a p-value of <0.0001. This finding underscores the notable impact of phototherapy on potassium levels in neonates. Similarly, Suneja et al also reported a significant decrease in serum potassium levels, from 6.095±1.4 to 5.28±1.08, with a p-value of 0.001.[18] These

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results collectively highlight the physiological effects of phototherapy on electrolyte balance, particularly potassium, which is critical for maintaining proper cellular function in neonates.

From current study and other research, it is evident that low birth weight neonates are at a higher risk for electrolyte imbalances after receiving phototherapy. However, as our study population was limited to a single tertiary hospital, the results may not be generalizable. Further studies with larger sample sizes and from diverse regions are necessary to provide specific recommendations for managing the care protocols of newborns receiving phototherapy.

CONCLUSION

The present study revealed a statistically significant occurrence of hypocalcemia among subjects receiving phototherapy, regardless of birth weight. Additionally, there was a notable decrease in serum sodium and potassium levels in both low birth weight and normal birth weight neonates. Low birth weight infants are particularly vulnerable to electrolyte imbalances due to decreased stores, renal immaturity, and increased fluid loss. Phototherapy contributes to these imbalances, underscoring the necessity for regular monitoring of serum sodium, potassium, and calcium levels, with assessments at least once every 24 hours.

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