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Effects of Phototherapy on Serum Electrolytes in Neonates Admitted in a Tertiary Care Center, Barabanki

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Abstract: ***Background**: Neonatal jaundice affects over 50% of full-term newborns and is even more common in late-preterm infants. Elevated serum bilirubin levels lead to hyperbilirubinemia, primarily involving unconjugated bilirubin. Phototherapy, particularly using blue light, is the primary treatment to prevent bilirubin-induced neurotoxicity. However, phototherapy's impact on serum electrolytes in neonates remains understudied. **Aim**: To estimate and compare alterations in serum electrolytes, specifically sodium, calcium, and potassium, in healthy term and late preterm neonates before and after phototherapy. **Methods**: A prospective observational study was conducted at a tertiary care center over 18 months from 12th July 2022 to 12th January 2024. The study included 100 neonates aged, requiring phototherapy for neonatal hyperbilirubinemia. Blood samples were collected before and within 24 hours of stopping phototherapy to measure serum sodium, calcium, and potassium levels using standard laboratory methods. Data were analyzed using SPSS version 21.0, with statistical significance set at p<0.05. **Results**: The median age at phototherapy initiation was 48 hours. The study included 55 males (55%) and 45 females (45%). The mean birth weight was 2850 grams, 57% were late preterm and 43% term. There was significant decrease in sodium levels post-phototherapy in late preterm neonates and females (p=0.002), significant decrease (p=<0.001) in potassium levels post-phototherapy in both genders, particularly in late preterm neonates, also there is significant decrease in calcium levels post-phototherapy across all categories. **Conclusion**: Phototherapy significantly reduces serum calcium and alters potassium levels in neonates, while sodium levels remain unaffected. These changes are more prominent in late preterm neonates in comparison to term neonates. These findings highlight the need for careful monitoring of serum electrolytes during phototherapy to manage potential imbalances effectively.*

Keywords: neonatal jaundice, phototherapy, serum electrolytes, hyperbilirubinemia, late preterm neonates

1. Introduction

Neonatal jaundice is a prevalent condition affecting over 60% of full-term newborns, with heightened severity observed in late-preterm infants. Notably, the most frequent presentation of neonatal jaundice is an elevation in unconjugated bilirubin levels. This manifestation underscores the importance of monitoring bilirubin levels in newborns to promptly identify and address potential complications associated with neonatal jaundice [1].

While various treatment approaches exist in clinical settings, blue light emerges as the predominant method of management for averting the onset of bilirubin encephalopathy (Kernicterus) resulting from the unconjugated bilirubin buildup. Elevated levels of unconjugated bilirubin have the potential to induce neurotoxicity, though physiological jaundice has protective antioxidant effects [2].

In recent years, a growing body of evidence has suggested that phototherapy can trigger various complications, encompassing gene damage, increased cancer risk. The specific mechanisms responsible for these adverse effects induced by phototherapy are not yet fully understood, underscoring the need for additional in-depth studies to unravel the underlying processes. Developing novel interventions is imperative to ensure the well-being of newborns undergoing phototherapy, considering the emerging concerns and uncertainties surrounding its potential adverse effects [3]. Although phototherapy is a safer treatment modality, it does have some adverse effects, such as dehydration fluid loss, hyperthermia, rashes on exposed areas,

loose stools, damage to the retina, bronze baby syndrome, hypocalcemia, and toxicity to genitalia.

Our study objective was to estimate alterations in serum electrolytes based on gender, gestation and mode of delivery before and after phototherapy.

2. Materials & Methods

Study Design

This prospective observational study was conducted in a tertiary care hospital in Uttar Pradesh over a period of 18 months from 12thJuly 2022 to 12thJanuary 2024. This extended duration facilitated the inclusion of a representative sample of neonates and collection of data across different seasons, potentially influencing the study outcomes. The study was conducted after obtaining ethical clearance from the Institutional ethical committee (Ethical Clearance no: MIMS/2022/EX/196) dated 12th July 2022.

Neonates (Term and late preterm) requiring phototherapy for neonatal hyperbilirubinemia whose parents or guardians gave consent for participation were included in the study. Neonates whose parents did not consent to part, with acute or chronic illness other than hyperbilirubinemia, who had received any form of electrolyte supplementation or treatment that could influence the study outcome and neonates with congenital anomalies or significant co morbidities were excluded from the study.

Sample Size: Sample size of approximately 100 neonates was calculated with a margin of error of 5.94% around the estimate at a 95% confidence level. This sample size is sufficient to provide reliable data for making inferences about the effects of phototherapy on serum electrolytes within the neonate population in our study setting

$$n = \left(\frac{Z^2 \times p \times (1-p)}{E^2}\right)$$

$$n = \left(\frac{1.96^2 \times 0.10 \times (0.90)}{0.0594^2}\right) \approx 100$$

Data Collection: Data collection involved demographic Information including age at the start of phototherapy (in hours), gender, birth weight (in grams), mode of delivery (Lower Segment Caesarean Section or Normal Vaginal Delivery), gestation (Late preterm, Term), weight-for-Gestational Age (Appropriate for Gestational Age, Small for Gestational Age, Large for Gestational Age). Laboratory values of Serum bilirubin, sodium, calcium and potassium.

Statistical Analysis: The data collected was compiled and tabulated using Microsoft excel. Categorical variables were expressed as numbers and percentages and Continuous Variables as mean ± standard deviation (SD). Differences in electrolyte levels before and after phototherapy were analyzed using the Paired t-test/Wilcoxon signed rank test, depending on the distribution of data. Associations between categorical variables were analyzed using the Chi-Square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant. Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0.

3. Results

A total of 100 term & late preterm neonates admitted to neonatal care units for LED phototherapy were assessed for electrolytes (Na^+, K^+, Ca^{+2}) in this study. Among these, 55 (55%) were males and 45 (45%) were females. Study participants had a mean birth weight of 2.63±0.33kg (Late preterm) 2.83±0.35kg (Term), mean gestational age of weeks, and 64.04±10.25 mean hours of life on admission for phototherapy. The total mean duration of phototherapy was 54.03±16.34 hours (Table *1*).

In female neonates, the mean sodium level decreased from 142.15 ± 3.65 mmol/L before phototherapy to 141.42 ± 3.69 mmol/L after phototherapy. ($p < 0.05$). In late preterm neonates, the mean sodium level decreased from 140.91 ± 5.51 mmol/L to 137.66 ± 4.54 mmol/L after phototherapy ($p < 0.05$). For infants delivered by LSCS (Lower Segment Caesarean Section), sodium levels decreased from 142.41 ± 3.73 mmol/L to 141.13 ± 4.38 mmol/L with a p-value of 0.228, indicating no significant change. For infants delivered by NVD (Normal Vaginal Delivery), sodium levels slightly increased from 142.03 ± 3.73 mmol/L to 142.27 ± 3.54 mmol/L with a p-value of 0.799, also indicating no significant change.

For female neonates, the mean potassium level decreased from 4.52 ± 0.68 mmol/L before phototherapy to 3.57 ± 0.65 mmol/L after phototherapy. In male neonates, it decreased from 4.35 ± 0.62 mmol/L to 3.50 ± 0.62 mmol/L. The p-values are <0.001 ($7.96\times10^{-7}$for females and 1.81×10^{-6} for males) indicate that the changes in potassium levels are statistically highly significant. Late preterm neonates had a mean potassium level decrease from 4.73 ± 0.71 mmol/L to 3.16 ± 0.73 mmol/L, while term neonates showed a decrease from 4.49 ± 0.62 mmol/L to 4.40 ± 0.64 mmol/L. For LSCS deliveries, the mean potassium level decreased from 5.23 ± 0.63 mmol/L to 4.59 ± 0.67 mmol/L, while NVD deliveries showed a decrease from 5.32 ± 0.68 mmol/L to 4.48 ± 0.61 mmol/L. The p-values are <0.001 (0.0003for LSCS and 5×10−6for NVD) suggest statistically significant change.

The mean calcium level in female neonates decreased from 9.30 ± 1.44 mg/dL before phototherapy to 8.62 ± 0.86 mg/dL after phototherapy. In male neonates, it decreased from 9.44 ± 1.58 mg/dL to 8.48 ± 0.86 mg/dL. The p-values (0.030 for females and 0.004 for males) suggest that these changes are statistically significant. For late preterm neonates, the mean calcium level decreased from 9.58 ± 0.79 mg/dL to 7.19 ± 1.59 mg/dL after phototherapy. Term neonates showed a decrease from 9.54 ± 0.88 mg/dL to 8.41 ± 1.49 mg/dL (Table *2*). For late pre-term infants, calcium levels significantly decreased from 9.58 ± 0.79 to 7.19 ± 1.59 with a p-value of <0.001 (6.92×10^{-10}) (Table3). For term infants, calcium levels also significantly decreased from 9.54 ± 0.88 to 8.41 ± 1.49 with a p-value of <0.001(0.0007). In neonates delivered by LSCS, the mean calcium level decreased from 10.35 ± 1.60 mg/dL to 8.52 ± 0.84 mg/dL, while NVD deliveries showed a decrease from 10.39 ± 1.45 mg/dL to 8.57 ± 0.88 mg/dL. The p-values are <0.001 ($7.52\times10^{-7}$for LSCS and $2.17\times10^{-7}$for NVD) indicate statistically significant change.

Table 1: Demographic Characteristics of Neonates

Sample size (N=100)		Before Phototherapy Mean ± SD	After Phototherapy Mean ± SD	p-value
Serum Sodium (mmol/L)	Female	142.15 ± 3.65	141.42 ± 3.69	0.002
	Male	141.42 ± 3.80	139.21 ± 4.09	0.724
	LSCS	142.41 ± 3.73	141.13 ± 4.38	0.228
	NVD	142.03 ± 3.73	142.27 ± 3.54	0.799
Serum Potassium (mmol/L)	Female	4.52 ± 0.68	3.57 ± 0.65	<0.001
	Male	4.35 ± 0.62	3.50 ± 0.62	<0.001
	LSCS	5.23 ± 0.63	4.59 ± 0.67	<0.001
	NVD	5.32 ± 0.68	4.48 ± 0.61	<0.001
Serum Calcium (mg/dl)	Female	9.30 ± 1.44	8.62 ± 0.86	0.030
	Male	9.44 ± 1.58	8.48 ± 0.86	0.004
	LSCS	10.35 ± 1.60	8.52 ± 0.84	<0.001
	NVD	10.39 ± 1.45	8.57 ± 0.88	<0.001

LSCS (lower segment caesarean section), NVD (normal vaginal delivery), SD (standard deviation), p-value (<0.05) is significant.

Table 2: Effects of Phototherapy on Serum Electrolytes in Term Neonates

	Serum Electrolytes	Before Phototherapy Mean ± SD	After Phototherapy Mean ± SD	p-value
Term	Sodium (mmol/L)	142.00 ± 3.50	141.02 ± 3.51	0.28
	Potassium (mmol/L)	4.49 ± 0.62	4.40 ± 0.64	0.582
	Calcium (mg/dl)	9.54 ± 0.88	8.41 ± 1.49	<0.001

SD (standard deviation), p-value (<0.05) is significant.

Table 3: Effects of Phototherapy on Serum Electrolytes in Late Preterm Neonates

	Serum Electrolytes	Before Phototherapy Mean ± SD	After Phototherapy Mean ± SD	p-value
Late Pre- Term	Sodium (mmol/L)	140.91 ± 5.51	137.66 ± 4.54	0.01
	Potassium (mmol/L)	4.73 ± 0.71	3.16 ± 0.73	<0.001
	Calcium (mg/dl)	9.58 ± 0.79	7.19 ± 1.59	<0.001

SD (standard deviation), p-value (<0.05) is significant.

4. Discussion

Phototherapy is a widely used treatment for neonatal jaundice, a common condition in newborns characterized by high levels of bilirubin in the blood. This treatment involves exposing the infant's skin to a specific type of light that helps break down bilirubin into substances that can be more easily excreted from the body. While phototherapy is generally considered safe and effective, there are concerns about its potential effects on various physiological parameters, including serum electrolytes, which are crucial for maintaining normal bodily functions. Therefore, understanding the impact of phototherapy on serum electrolytes is essential for ensuring the comprehensive care of these vulnerable patients.

Previous studies on this topic have yielded mixed results, with some reporting significant changes in electrolyte levels during phototherapy, while others have found no substantial effects. These discrepancies may be due to variations in study design, patient demographics, and the specifics of phototherapy protocols used.

Ultimately, the goal of investigating the effects of phototherapy on serum electrolytes in neonates is to enhance the safety and efficacy of this essential treatment [1].

In our study, we observed a statistically significant decrease in the mean sodium levels in female neonates after phototherapy, with a p-value of 0.002. In the study by Melis Akpınar et al;(2021), a total of 260 infants were enrolled in the study, and 138 (53%) were female [4].No statistically significant difference was observed in terms of gender. Comparing our study on calcium levels by gestational category with findings from Goyal M et.al; (2018) on calcium levels reveals notable similarities and implications [5]. In our study, both term and late preterm neonates exhibited a statistically significant decrease in mean calcium levels. This underscores that neonates of any gestational age are vulnerable to calcium disturbances induced by phototherapy. In contrast, the study by Baraton L et.al; (2009) provides a broader perspective on the long-term implications of electrolyte disturbances. Their findings indicate that large changes in serum sodium levels during infancy are associated with increased risks of impaired functional outcomes at 2 years of age [6].

This underscores the clinical significance of maintaining electrolyte balance during critical developmental periods, aligning with the implications of our study and emphasizing the importance of monitoring and managing electrolyte levels in neonates undergoing phototherapy. Similar studies also collectively support the need for precise monitoring and management strategies to optimize clinical outcomes in neonates undergoing phototherapy [7].

In our study, we observed a significant decrease in mean potassium levels in both female and male neonates following phototherapy. The study by Karan S et.al; (2020) also reported a significant decrease in potassium levels after phototherapy [8]. Additionally, their analysis showed that only a small proportion of newborns (2.70%) had potassium levels below 3.5 mmol/L post-phototherapy, and the difference between term and preterm newborns was not statistically significant (p=0.3602). In our study, the changes were more pronounced, with mean potassium levels dropping below 3.5 mmol/L in both female and male neonates, where as Karan S et.al;(2020) observed a more moderate reduction. However, both studies underscore the importance of monitoring potassium levels during and after phototherapy to manage potential hypokalemia effectively.

In our study, the potassium levels in late preterm neonates significantly decreased after phototherapy. Karan S et.al; also explored the impact of phototherapy on potassium levels, categorizing neonates by gestational age. The difference between the term and preterm groups was not statistically significant ($p = 0.3602$). Although their study did not show significant differences between term and preterm groups, it supports the notion that preterm neonates are more susceptible to variations in potassium levels post-phototherapy. Our study however, provides a more granular analysis by demonstrating a statistically significant decrease in potassium levels specifically in late preterm neonates, reinforcing the importance of tailored clinical approaches for different gestational categories.

Our study observed a significant decrease in mean calcium levels in both female and male neonates following phototherapy. The results indicate that phototherapy significantly impacts calcium levels in both genders. Comparing our findings with those of Javaid S et al [9], we see similar trends, their study reported a significant decrease in serum calcium levels post-phototherapy (from 8.76±0.76 mg/dl to 7.98±1.12 mg/dl, $p < 0.001$) and identified preterm neonates are particularly vulnerable to hypocalcemia after phototherapy . Similarly, the study by Goyal M et.al [5] reported significant reductions in both total and ionized serum calcium levels post-phototherapy in the study group, with a p-value of <0.001. Their findings corroborate our results, showing that phototherapy leads to a significant decrease in calcium levels. This consistent evidence across studies underscores the importance of monitoring serum calcium levels in neonates undergoing phototherapy to mitigate the risk of hypocalcemia and ensure better clinical outcomes.

In our study, the mean calcium levels in both late preterm and term neonates significantly decreased after phototherapy ($p < 0.001$). Goyal M et.al demonstrated significant reductions in both total and ionized serum calcium levels post-phototherapy, in both preterm and term neonates. The pronounced reduction in calcium levels post-phototherapy in both gestational categories highlights the impact of phototherapy on calcium homeostasis, with late preterm neonates experiencing a more substantial decline. Karan S et.al; (2020) investigated the correlation between post-phototherapy calcium levels and gestational age in neonates. Their study found that among the 74 neonates, a significant portion of preterm newborns (76.47%) had calcium levels below 7 mg/dL after 48 hours of phototherapy, compared to only 3.50% of term newborns. The study reported a statistically significant difference between the term and preterm groups ($p < 0.0001$) [8]. Both studies underscore the susceptibility of preterm neonates to hypocalcemia following phototherapy, with findings of Karan S et.al further emphasizing the higher prevalence of severe hypocalcemia in preterm infants. Our study provides detailed insights into the magnitude of this decrease, while Karan S et.al work highlights the higher incidence of severe hypocalcemia in preterm infants, reinforcing the need for close monitoring and management of calcium levels in this vulnerable population.

Our study examined the impact of phototherapy on sodium, potassium, and calcium levels in neonates, focusing on differences based on the mode of delivery. For infants delivered by LSCS (Lower Segment Caesarean Section), sodium levels decreased slightly but this change was not statistically significant (p=0.228). Similarly, for infants delivered by NVD (Normal Vaginal Delivery), sodium levels showed a minor increase indicating no significant change. In contrast, potassium and calcium levels exhibited significant reductions post-phototherapy across both modes of delivery. These findings align with the study by Amneenah M et.al; (2022) which reported significant decreases in potassium and calcium levels post-phototherapy but no significant change in sodium levels [10]. The consistency of our results with those of Amneenah M et.al; underscores the importance of closely monitoring potassium and calcium levels in neonates undergoing phototherapy, regardless of the mode of delivery. This vigilance is crucial to preventing complications from electrolyte imbalances, thereby enhancing neonatal care and outcomes.

However our study had certain limitations. Since the study was done in single study center with limited sample size, it may not be the true reflection of the general population. Preterm neonates (<34 weeks) were not included; it is seen from previous studies incidence of phototherapy induced electrolytes changes is higher in preterms. Since this study is an observational cross sectional study with convenience sampling other variables affecting Serum Electrolytes were not assessed. The impact of duration of phototherapy on Electrolytes was not assessed.

5. Conclusions

The study found significant alterations in serum electrolyte levels in neonates undergoing phototherapy for neonatal hyperbilirubinemia. Specifically significant decrease in sodium levels post-phototherapy in late preterm neonates and females. Significant decrease in potassium levels post-phototherapy in both genders, particularly in late preterm neonates. Significant decrease in calcium levels post-phototherapy across all categories.

The findings underscore the need for tailored clinical protocols to address the specific needs of different neonatal subgroups, particularly late preterm neonates who are more vulnerable to electrolyte imbalances. Further studies need to be conducted to explore the underlying mechanisms of

electrolyte alterations during phototherapy and develop more effective monitoring and management strategies.

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