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Electrolyte Changes Following Phototherapy in Neonatal unconjugated Hyperbilirubinaemia

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Abstract

Background: Neonatal hyperbilirubinemia is a prevalent concern in the early stages of life, often necessitating phototherapy. This study aimed to assess the electrolyte changes following phototherapy in neonates admitted to pediatric department In Benha university hospital. **Methods:** This study was carried out in the NICU of Benha University Hospital and involved the participation of 61 healthy newborns diagnosed with unconjugated hyperbilirubinemia requiring phototherapy. The research included a comprehensive evaluation, comprising detailed maternal, obstetric, and neonatal histories, meticulous clinical examinations, and a diverse range of investigations. These investigations involved complete blood counts, determination of blood group, profiling of bilirubin levels, and the quantification of electrolyte concentrations (sodium, potassium, chloride, calcium, and magnesium). Blood samples were collected both before and after the phototherapy sessions. **Results:** This study involved a cohort of 61 cases, with 32 being male (52.5%) and 29 female (47.5%). Their ages had a mean ± SD of 5.77 ± 1.94. 41 cases had a Normal Birth weight. The mode of delivery revealed that 44.3% of cases were delivered through Normal Vaginal Delivery (NVD), while 55.7% were delivered through Cesarean Section (CS). Examining gestational age, the majority (62.3%) fell within the 36–39-week range, 26.2% had a gestational age of ≥40 weeks, and the Mean ± SD gestational age was 38.0 ± 1.84 weeks. Of the cases, 68.9% underwent conventional phototherapy, while 31.1% were treated with LED. Significant differences were observed between pre- and post-treatment Total Bilirubin levels ($p<0.001$). **Conclusions:** Our study revealed a significant reduction in total bilirubin levels following phototherapy, along with notable changes in calcium, sodium, and magnesium levels. Serum electrolyte levels were not correlated with mode of delivery or birth weight. Additionally, hypocalcemia after phototherapy was more prevalent in preterm neonates (<36 weeks) compared to term neonates (≥36 weeks).

Keywords: Neonatal Hyperbilirubinemia; Phototherapy; Electrolyte Levels; Calcium; Sodium; Magnesium; Preterm Neonates.

1. Introduction

Neonatal hyperbilirubinemia, characterized by an elevated level of bilirubin in the blood, is a common physiological phenomenon in newborns. Unconjugated hyperbilirubinemia, arising from the breakdown of red blood cells and the immaturity of the neonatal liver's bilirubin conjugation processes, can lead to jaundice, posing potential risks to the developing infant [1].

Phototherapy, a widely utilized therapeutic approach, has been proven effective in reducing serum bilirubin levels and preventing the complications associated with hyperbilirubinemia. However, while the impact of phototherapy on bilirubin metabolism has been extensively investigated, its potential influence on electrolyte homeostasis in neonates remains an area that warrants closer examination [2, 3].

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 [4]. Emerging evidence suggests that phototherapy, despite its 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 [2, 5].

To date, research exploring the potential impact of phototherapy on electrolyte balance in neonates has been limited. Most studies have primarily focused on bilirubin reduction and clinical outcomes, with less attention directed towards electrolyte shifts. Therefore, this study aims to assess the electrolyte changes following phototherapy in neonates admitted to pediatric department In Benha university hospital.

2. Methods

This prospective study was conducted in the Neonatal Intensive Care Unit (NICU) of Benha University Hospital from February

2019 to April 2020. The study included 61 healthy newborns of both genders with indirect hyperbilirubinemia requiring phototherapy.

Inclusion Criteria were healthy neonates of both sexes, appropriate for gestational age (AGA), neonates with unconjugated hyperbilirubinemia requiring phototherapy, typically lasting from 48 to 96 hours.

Exclusion criteria encompassed neonates with conjugated hyperbilirubinemia, babies undergoing exchange transfusion, infants with jaundice persisting beyond 14 days, neonates exhibiting other clinical signs or undergoing additional medical interventions, and those with associated comorbidities including birth asphyxia, sepsis, renal failure, or neonates born to mothers taking anticonvulsant drugs.

Ethical Considerations: Parents or surrogates were provided with a clear explanation of the study's purpose and nature before enrollment, and informed consent was obtained. The study protocol was presented to the Scientific Ethics Committee of the Pediatrics Department, Faculty of Medicine, Benha University, which approved the study design.

All neonates enrolled in the study underwent a comprehensive series of assessments to gather essential data:

A] Detailed Maternal, Obstetric, and Neonatal History:

Maternal information was collected, encompassing gravidity, parity, maternal illness, and medications. The obstetric history included details about the mode of delivery and premature rupture of membranes lasting more than 18 hours. Neonatal data encompassed gestational age, birth weight, onset of jaundice, day of presentation, and feeding method (breast milk, formula, or a combination). Additionally, any family history of neonatal jaundice was documented.

B] Thorough Clinical Examination:

General Examination: The neonates underwent a meticulous examination, including the estimation of gestational age using the Ballard score. Measurements were taken for weight, length, and head circumference. Vital signs such as respiratory rate (RR), heart rate (HR), blood pressure (BP), and temperature were carefully assessed. Signs indicating severe illness, such as decreased perfusion and lethargy, were identified. Neonatal reflexes, including Moro, grasping, and suckling, were evaluated. The BIND score, which indicates bilirubin-induced neurological disorders, was calculated. **Systemic Examination:** A comprehensive systemic examination was conducted, covering chest, cardiac, abdominal, and neurological evaluations.

C] Investigations: An array of essential investigations was undertaken to procure pivotal information, encompassing a complete blood count, determination of blood group, profiling of bilirubin levels, and meticulous measurement of electrolyte levels, including sodium (Na), potassium (K), chloride (Cl), calcium (Ca), and magnesium (Mg).

Sample Collection and Storage:

Venous blood samples were collected from neonates and analyzed for total bilirubin, direct bilirubin, electrolytes, and blood group. Total and direct bilirubin were measured using the Diazo method; electrolytes (Na, K, Cl, Mg) were analyzed using an Erba EM 200 autoanalyzer machine, and calcium was measured using the Arsenazo method. Newborn blood groups were determined using the antisera method. Samples were collected at 0 hours (pre-phototherapy) and at phototherapy discontinuation or 2 days post-phototherapy, with the first sample serving as a control for comparison.

Phototherapy:

Neonates received phototherapy using various systems, including fluorescent tubes, light-emitting diodes (LED), and intensive phototherapy. Routine measures such as blindfolding the eyes and covering genitalia were employed during phototherapy, which was administered continuously except for infant feeding, weighing, and physical examinations.

Statistical analysis:

The data underwent coding and analysis utilizing SPSS version 25, encompassing diverse statistical techniques. Quantitative data were summarized through mean, standard deviation, median, minimum, and maximum for normally distributed variables, and frequency/percentage for categorical data. Comparisons between groups employed the unpaired t-test for normally distributed quantitative variables, while non-normally distributed quantitative variables were assessed via the non-parametric Mann-Whitney test. Spearman correlation coefficients were employed to scrutinize correlations among quantitative variables. Significance was established at $p < 0.05$. IBM SPSS version 20.0 facilitated data analysis for qualitative and quantitative data, encompassing descriptive measures and tests for normality. Tests such as the paired t-test, Student t-test, F-test (ANOVA), and Chi-square test were utilized for various comparisons. Corrections like Fisher's Exact or Monte Carlo were employed as needed. McNemar and Marginal Homogeneity Test addressed specific significance analyses between stages.

3. Results

This study encompassed 61 cases. Of these, 32 were males (52.5%), and 29 were females (47.5%). Their ages spanned from 2.0 to 11.0 years, with a mean ± SD of 5.77 ± 1.94. Among them, 48 cases fell within the 5–9-year age range (78.7%), 10 cases were <5 years old (16.4%), and 3 cases were females aged 10-11 years (4.9%). Notably, 41 cases had a Normal Birth weight. The mode of delivery revealed that 44.3% of cases were delivered through Normal Vaginal Delivery (NVD), while 55.7% were delivered through Cesarean Section (CS). Examining gestational age, the majority (62.3%) of cases fell within the 36–39-week range, 26.2% had a gestational age of ≥40 weeks, and the Mean ± SD gestational age was found to be 38.0 ± 1.84 weeks. 68.9% used a conventional mode of phototherapy, and 31.1% were treated by LED.

There was a highly statistically significant difference between pre and post according to Total Bilirubin where p<0.001. **Table 1**

Table (1) Comparison between pre and post according to total bilirubin n= 61)

Total Bilirubin	Pre	Post	t	p
Min. – Max.	13.30 – 22.0mg	8.0 – 15.80mg		
Mean ± SD.	17.20 ± 1.87mg	11.91 ± 1.64mg	15.089*	<0.001*
Median IQR)	17.30 16.0 – 18.40)mg	12.20 10.80 – 13.0)mg		

t: Paired t-test, p: p value for comparing between pre and post, *: Statistically significant at p ≤ 0.05.

A statistically significant difference was observed between the pre- and post-treatment levels of Calcium and Sodium. Additionally, the mean serum magnesium level was 2.25 mg/dL before phototherapy and demonstrated a significant decrease to 2.03 mg/dL after the treatment (p=0.01). However, no statistically significant difference was noted in the pre- and post-treatment levels of Potassium and Chloride. **Table 2**

Table (2) Comparison between pre and post according to serum electrolytes (n=61).

Serum electrolytes	Pre		Post		Test of sig.	p
	No.	%	No.	%		
Calcium						
<7	61	100.0	6	9.8	McN	0.031*
7-11	0	0.0	55	90.2		
Min. – Max.	7.0 – 11.50		6.10 – 11.50			
Mean ± SD.	9.22 ± 0.99		8.60 ± 1.21		t=3.210*	0.002*
Median IQR)	9.20 8.50 – 9.20)		8.80 7.70 – 8.80)			
Sodium						
<135	5	8.2	16	26.2		
135-145	56	91.8	44	72.1	MH	0.033*
>145	0	0.0	1	1.6		
Min. – Max.	131.0 – 144.70		129.20 – 148.10			
Mean ± SD.	138.93 ± 2.77		137.52 ± 3.63		t=2.176*	0.033*
Median IQR)	139.10 (137.30 – 141.0)		137.60 (134.70– 139.30)			
Potassium						
<3.5	2	3.3	1	1.6		
3.5-5.5	57	93.4	58	95.1	MH	0.705
>5.5	2	3.3	2	3.3		
Min. – Max.	3.10 – 6.20		3.40 – 5.90			
Mean ± SD.	4.59 ± 0.54		4.65 ± 0.55		t=0.595	0.554
Median IQR)	4.60 4.30 – 4.60)		4.70 4.30 – 4.70)			
Chloride						
<95	4	6.6	3	4.9		
95-105	48	78.7	48	78.7	MH	0.695
>105	9	14.8	10	16.4		
Min. – Max.	94.30 – 108.30		93.70 – 110.0			
Mean ± SD.	101.44 ± 3.29		101.27 ± 3.53		t=0.265	0.792
Median IQR)	101.60 99.40 – 101.60)		101.30 98.70 – 103.70)			

Total magnesium level mg/dl)				
Min. – Max.	1.84 – 3.79	1.44 – 2.78		
Mean ± SD.	2.76 ± 0.61	2.09 ± 0.37	t=7.357*	<0.001*
Median IQR)	2.68 2.27–3.34)	2.12 1.75–2.34)		

t: Paired t-test, McN: McNemar test, MH: Marginal Homogeneity Test, p: p value for comparing between pre and post, *: Statistically significant at p ≤ 0.05.

4. Discussion

Neonatal hyperbilirubinemia, a prevalent condition within the first week of life, commonly raises parental concern and represents a primary cause for neonatal hospital readmissions [6]. Jaundice, characterized by a yellowish skin hue due to unconjugated bilirubin accumulation, typically manifests when bilirubin levels surpass 7 mg/dL. Among neonates, jaundice emerges in 60% of term and 80% of preterm cases during the first week of life, with only a small fraction of term neonates (6.1%) reaching bilirubin levels >12.9 mg/dL and a mere 3% exceeding 15 mg/dL [7, 8]. Root causes include heightened fetal red cell breakdown, immature liver bilirubin processing, and elevated enterohepatic circulation, with preterm neonates being more susceptible. Phototherapy, exchange transfusion, and pharmacological interventions stand as treatment options for neonatal hyperbilirubinemia, with phototherapy as the primary strategy, effectively reducing bilirubin levels and related complications. While phototherapy introduces side effects such as hyperthermia, feed intolerance, and electrolyte imbalances, they are generally manageable and not severe [9, 10].

Limited research exists concerning phototherapy's impact on electrolytes, with most studies indicating an association between phototherapy and hypocalcemia, particularly pronounced in preterm neonates (90%) compared to term neonates (75%). Some studies have also suggested a heightened risk of hyponatremia and hypomagnesemia following phototherapy [11, 12]. The primary aim of this study was to evaluate electrolyte changes subsequent to phototherapy in neonates.

This prospective comparative study, conducted at Benha University Hospital, enrolled 61 neonates with unconjugated hyperbilirubinemia, undergoing phototherapy lasting between 48 and 96 hours. The study's duration spanned 6 to 12 months. Demographically, the study encompassed 61 cases, with 32 males (52.5%) and 29 females (47.5%), aged between 2.0 and 11.0 days (mean ± SD: 5.77 ± 1.94). Among them, 48 (78.7%) were aged 5-9 days, 10 (16.4%) were <5 days, and 3 (4.9%) were 10-11 days old. Notably, 41 cases had a normal birth weight. Regarding mode of delivery, 44.3% were born through Normal Vaginal Delivery, while 55.7% were delivered via Cesarean section. Comparison of pre- and post-phototherapy total bilirubin levels revealed a highly significant difference (p<0.001).

Our findings are consistent with related research. A study by Bezboruah and Kumar Majumder [13], which observed neonates receiving phototherapy in NICU, reported a significant decline in total bilirubin levels post-treatment. Similarly, Frargy et al. [14] noted a substantial difference in total bilirubin levels before and after phototherapy in neonates with hyperbilirubinemia (p<0.001).

Regarding serum calcium, our study identified a statistically significant difference between pre- and post-phototherapy levels. This finding aligns with Reddy et al. [15], who reported a significant decrease in mean serum calcium levels following phototherapy in term neonates (p<0.001), and with Bezboruah and Kumar Majumder [13] who observed a similar decrease (p<0.0001). Hyponatremia, characterized by serum sodium levels <135 mEq/L, was supported by Gözetici et al. [16], who found a statistically significant decrease in calcium levels following phototherapy (p<0.001).

Our study also noted a significant decline in serum sodium levels post-phototherapy, consistent with Reddy et al. [15], Bezboruah and Kumar Majumder [13], and Gözetici et al. [16]. However, no significant differences were observed in pre- and post-phototherapy potassium and chloride levels. Similar findings were reported by Reddy et al. [15] and Purohit et al. [17] concerning potassium and chloride changes. Gözetici et al. [16] also found non-significant differences in potassium levels.

Regarding serum magnesium, our study revealed a statistically significant decrease following phototherapy. This aligns with findings by Bezboruah and Kumar Majumder [13] and Frargy et al. [13], demonstrating a substantial decline in total and ionized magnesium levels after phototherapy (p<0.0001). Contrarily, our study found no significant correlations between mode of delivery, birth weight, gestational age, or duration of phototherapy with serum electrolyte levels.

5. Conclusion

Our study revealed a significant reduction in total bilirubin levels following phototherapy, with a statistically significant difference between pre- and post-phototherapy calcium levels. Moreover, there were statistically significant differences in sodium and magnesium levels before and after phototherapy. However, no statistically significant differences were observed in pre- and post-phototherapy potassium and chloride levels. The study found no discernible correlation between serum electrolyte levels and mode of delivery, nor between serum electrolyte levels and birth weight. Regarding the relationship between gestational age and serum electrolytes, it was observed that the incidence of hypocalcemia following phototherapy was more pronounced in preterm neonates (<36 weeks) compared to term neonates (≥36 weeks).

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