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Impact of phototherapy type and duration on serum electrolytes and blood glucose in neonatal hyperbilirubinemia: a prospective single-center cohort study



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Abstract

Background: Neonatal hyperbilirubinemia (NH) is among the common neonatal morbidities. Phototherapy is its most used therapeutic intervention. Different delivering systems and types are currently available. This study aimed to detect and compare the effects of the different phototherapy types on serum electrolytes and blood glucose and to study the effect of phototherapy duration on them.

Results: Five hundred healthy newborns with indirect NH were treated by different phototherapy types (conventional, light emitting diode LED, intensive) according to severity and availability. Serum sodium (Na), potassium (K), calcium (Ca), blood urea nitrogen (BUN), creatinine (Cr), and blood glucose (Glu) were measured repeatedly over 48 h of phototherapy. In this prospective cohort study, 273 (54.6%) neonates were exposed to conventional phototherapy, 145 (29.0%) to LED, and 82 (16.4%) to intensive phototherapy. A highly significant negative correlation was found between phototherapy duration and serum levels of Na, K, Ca, BUN, and Cr (p < 0.001). There was a positive correlation between phototherapy duration and blood glucose level (p = 0.005). Each type of phototherapy individually significantly affected the Na, K, Bun, Cr, and Ca levels after 48 h. Comparing the effects of the 3 different phototherapy types together, no significant differences apart from a decline in potassium level at 48 h (p = 0.043) were recorded.

Conclusions: Serum electrolytes significantly decreased during phototherapy. These changes were affected by the phototherapy duration. The type of phototherapy had only some effect on serum potassium.

Keywords: Blood glucose, Exposure time, Indirect hyperbilirubinemia, Newborns, Phototherapy type, Serum electrolytes

Background

Neonatal hyperbilirubinemia (NH) is the commonest clinical problem occurring during the first week of life, as more than two thirds of newborns develop clinical jaundice [1, 2] that can be treated by phototherapy, exchange transfusion, or by pharmacologic agents. Phototherapy

is the most common intervention in therapy used as it is relatively safe and non-invasive [3, 4]. The conventionally used light sources in phototherapy are fluorescent tubes and halogen spotlights. However, they cannot be placed close to the infant as they produce considerable amount of heat. Due to this limitation, light-emitting diodes (LEDs) have been used as alternatives as they produce low heat rendering them safe to be placed very close to the infant [5, 6]. Intensive phototherapy can also shorten the total phototherapy time and period of hospital stay [7, 8].

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Phototherapy may produce a transient rash, transit green stools, lethargy, or abdominal distension [9]. Sometimes, there is an increase skin and muscle blood flow, insensible water loss, skin temperature, heart, and respiratory rates. So, neonates undergoing phototherapy are at a higher risk of electrolyte changes. The aim of the present study was to detect and compare the effects of various types of phototherapy (conventional, LED and intensive) and its duration on serum electrolytes (sodium, potassium, calcium, blood urea nitrogen, creatinine) and blood glucose in healthy neonates with NH.

Methods

This prospective study including 500 healthy neonates of both genders who were appropriate for gestational age presenting with indirect NH requiring phototherapy according to American Academy of Paediatrics recommendations [10] was carried out over 11 months in the neonatal intensive care units of Cairo University hospitals. The included neonates had no other associated complaints or/and co-morbidities and were not receiving any intravenous medications. Neonates receiving intravenous fluids, having undergone exchange transfusion or suffering of any co-morbidities (e.g. birth asphyxia, septicemia, acute renal failure and others) as well as infants of mothers suffering from diabetes mellitus or other diseases affecting their blood counts and chemistry were excluded from the study. The study protocol ethics was approved by the committee of the Department of Pediatrics, Faculty of Medicine, Cairo University, and the tenets of the Helsinki declaration were followed. An informed consent was taken from the parents before enrollment.

Neonates included in the study were subjected to detailed history taking and documentation of maternal data (e.g. gravidity, parity, maternal illnesses, medications, premature rupture of membranes) and neonatal data (e.g. mode of delivery, gestational age, weight, time of onset of jaundice, feeding method, age at admission). Family history of NH in previous siblings or hemolytic anemias was recorded as well. Thorough clinical examination of newborns at admission was performed (e.g. body measurements, vital signs, general activity and different systems affection). Investigations documented at admission included complete blood counts, reticulocytic count, blood culture, C-reactive protein, maternal and neonatal blood groups, Coombs test, and total and direct serum bilirubin. Serum electrolytes (Na, K, Ca) and kidney functions (BUN, Cr) were measured on admission and then after 24 and 48 h of phototherapy. Blood glucose (BG) level was measured at admission and then every 6h for the first 48h using a glucometer. The neonates were subjected to the different phototherapy delivering systems: fluorescent tubes (conventional), light-emitting diodes (LED), and intensive phototherapy (Bilisphere 360, Novos Medical System, Turkey). The eyes were routinely blindfolded and the genitalia covered. Phototherapy's application was continuous. Only for the feeding, weighing, and physical examination of newborns was it interrupted.

Statistical methods

Data was analyzed using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Quantitative data was expressed as mean, standard deviation, and median, while categorical data was presented as frequency and percentage. Comparisons between groups were done using unpaired t-test for the normally distributed quantitative variables. Non-parametric Mann-Whitney test was utilized for the non-normally distributed variables. Correlations between quantitative variables were conducted using Spearman correlation coefficient. p-values ≤ 0.05 were considered as statistically significant.

Results

This single-center study included 500 neonates (273 males and 227 females). Their mean gestational age was 37.74 ± 1.46 weeks and their mean weight 2.84 ± 1.24 kg. They had a mean head circumference of 33.53 ± 2.0 cm and a mean length of 47.87 ± 3.32 cm. Only about 30% of neonates were delivered vaginally. The mean age of onset of jaundice was 2.96 ± 1.28 days. On admission, the mean age of newborns was 5.01 ± 2.89 days, the mean total bilirubin level was 18.34 ± 5.23 mg/dl, and the mean direct serum bilirubin level was 0.8 ± 0.87 mg/dl.

Regarding phototherapy in the current study, 273 (54.6%) babies were started on conventional phototherapy, 145 (29.0%) on LED, while 82 (16.4%) required intensive phototherapy. Only 64 newborns showed some neurological affection. On admission, the mean hemoglobin (Hb) was $15.23 \pm 2.44 \,\mathrm{g/dL}$, the mean platelet count was $277.45 \pm 86.90 (10^3/\text{mm}^3)$, the mean total leucocytic count 9.94 \pm 2.67 (10³/mm³), and the mean reticulocytic count was 6.90 \pm 2.44%. Coombs test was positive in 125 neonates (25.0%). A highly significant negative correlation was found between phototherapy duration and serum levels of Na, K, Ca, BUN, and creatinine (p < 0.001), while there was a positive correlation between phototherapy duration and blood glucose level (p = 0.005) (Table 1). Each type of phototherapy individually significantly affected the Na, K, Bun, Cr, and Ca levels after 48 h. However, when comparing the effects of the different phototherapy types together, there were no significant differences as regards their effects apart from the potassium level at 48 h of phototherapy (p = 0.043) (Table 2).

Table 1 Correlation between phototherapy duration and levels of serum electrolytes, kidney functions, and blood glucose

Parameter	Time (hours)	Time (hours)			
	r (correlation coefficient)	<i>p</i> -value*			
Na	- 0.269	< 0.001			
K	– 0.236	< 0.001			
Ca	– 0.452	< 0.001			
BUN	- 0.446	< 0.001			
Creatinine	– 0.189	< 0.001			
Glucose	0.041	0.005			

Abbreviations: BUN blood urea nitrogen, Ca calcium, K potassium, Na sodium p-value ≤ 0.05 is considered significant

Discussion

Phototherapy has been accepted as the most widely used treatment for neonatal jaundice, and there are various phototherapy delivering methods. The phototherapy efficiency relies on the light source's peak wavelength, the irradiance and the surface area of the body exposed, and the distance between the infant and the light source [11, 12].

The demographics of this study group had many similarities with other studies involving jaundiced neonates

as regards gestational age [13], male predominance [14–16], and weight [13, 15, 17].

As for the laboratory data, the mean Hb in this study was 15.23 ± 2.44 g/dl, and the mean total serum bilirubin level at admission was 18.34 ± 5.23 mg/dl. This bilirubin level is very similar to the levels in the studies by Bezboruah and Majumder (2019) and Purohit et al. (2020) (18.13 \pm 2.414 mg/dl and 17.7 \pm 3 mg/dl, respectively) [17, 18].

This study demonstrated that the phototherapy type was not of significant effect on the changes of serum electrolytes, BUN, creatinine, and blood glucose apart from some effect of serum potassium at 48 h. The comparison between types was conducted all through the first 48 h of therapy. But the duration of phototherapy however proved to affect them and that is in accordance with the results of other studies. Significant decline in the levels of mean serum Na and K after 48h of phototherapy (p<0.001) was noted in the current study and in the studies by Bezboruah and Majumder (2019), Jena et al. (2019), and Rangaswamy et al. (2019) [18-20]. Some studies also documented a significant decrease in serum Ca [3, 16, 18, 19]. All these studies evaluated the electrolytes level prior and after 48 h or at discontinuation of phototherapy. This came in accordance with our work. However, we could also demonstrate and document the continuous decline

Table 2 Study parameters and the different types of phototherapy at 0, 24, and 48 h

	Duration of phototherapy	Phototherapy type			<i>p</i> -value [*]
		Conventional	LED	Intensive	
Na (mmol/L)	0 h	143.31 ± 5.25	142.21 ± 4.87	142.85 ± 4.53	0.102
	24 h	140.37 ± 3.68	140.00 ± 3.18	140.12 ± 3.12	0.566
	48 h	139.87 ± 3.41	139.46 ± 3.15	139.59 ± 3.50	0.473
K (mmol/L)	0 h	4.99 ± 0.57	4.97 ± 0.56	4.99 ± 0.74	0.962
	24 h	4.70 ± 0.55	4.78 ± 0.48	4.60 ± 0.64	0.064
	48 h	4.61 ± 0.51	4.69 ± 0.51	4.52 ± 0.53	0.043
Ca (mg/dl)	0 h	10.35 ± 0.91	10.39 ± 0.90	10.38 ± 0.88	0.902
	24 h	9.41 ± 0.84	9.38 ± 0.84	9.31 ± 0.89	0.645
	48 h	9.15 ± 0.83	9.12 ± 0.96	9.00 ± 0.94	0.433
BUN (mg/dl)	0 h	18.05 ± 9.31	18.82 ± 9.07	19.74 ± 9.91	0.329
	24 h	10.93 ± 6.17	10.90 ± 6.45	11.98 ± 6.87	0.387
	48 h	9.12 ± 4.44	9.54 ± 5.54	9.32 ± 5.30	0.708
Creatinine (mg/dl)	0 h	0.69 ± 0.52	0.68 ± 0.26	0.72 ± 0.27	0.719
	24 h	0.60 ± 0.43	0.63 ± 0.56	0.61 ± 0.21	0.802
	48 h	0.59 ± 0.46	0.54 ± 0.16	0.57 ± 0.18	0.496
Glucose (mg/dl)	0 h	102.02 ± 22.28	104.16 ± 21.26	103.30 ± 26.56	0.646
	24 h	104.94 ± 16.71	104.64 ± 16.80	105.82 ± 14.99	0.872
	48 h	104.18 ± 13.36	104.06 ± 14.17	103.15 ± 12.20	0.827

Data is presented as mean $\pm\,\mathrm{SD}$

 $\textit{Abbreviations: BUN} \ \text{blood urea nitrogen, } \textit{Ca} \ \text{calcium, } \textit{h} \ \text{hours, K potassium, LED light emitting diode, Na} \ \text{sodium}$

^{*}p-value ≤ 0.05 is considered significant

over the 48 h and showed that it increased with the duration of phototherapy.

A study by Suneja et al. (2018) including 119 patients evaluated various biochemical parameters in the serum of newborn children having NH, before and after discontinuing phototherapy at 48–96h. They reported significant decrease in serum Na, K, chloride, and Ca levels (p < 0.001) as well as Cr (p= 0.0029) [21], although they also documented a decline in urea and BG which was insignificant in their study (p = 0.0751 and p = 0.74, respectively). However, in our work, there was a significant difference as regards BUN before and after phototherapy over the whole study period (p<0.001).

Conclusions

This study documented that the duration of phototherapy rather than its type significantly affects the serum electrolytes and blood glucose levels. Hence, continuous follow-up and efforts to shorten/minimize the duration should be considered a high-priority during management of neonatal hyperbilirubinemia.

Abbreviations

BUN: Blood urea nitrogen; Ca: Calcium; Cr: Creatinine; Glu: Glucose; Hb: Hemoglobin; K: Potassium; LED: Light emitting diode; Na: Sodium; NH: Neonatal hyperbilirubinemia.

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Not applicable

Authors' contributions

AMST, AAA, and NM conceptualized and designed the study. They supervised the collection and analysis of data. RY collected the data and carried out the initial analysis. AMST. AAA, and NM conducted formal data analyses. All authors contributed to the initial draft and revised and approved the final manuscript as submitted.

Fundina

No funding was received for conducting this study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol ethics was approved by the committee of the Department of Pediatrics, Faculty of Medicine, Cairo University, and the tenets of the Helsinki declaration were adhered to. Informed consent was obtained from parents.

Consent for publication

Not applicable

Competing interests

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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