Effect of Phototherapy on Serum Electrolyte Levels

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Abstract

Objective: This study aimed to investigate the effect of phototherapy on serum electrolyte levels in neonates admitted to neonatal intensive care unit with the diagnosis of neonatal hyperbilirubinemia.

Methods: Demographic profiles, laboratory findings, and electrolyte levels before phototherapy and 48-72 hours after phototherapy of 260 patients hospitalized with neonatal hyperbilirubinemia between June 2016 and June 2018 were compared in this retrospective study.

Results: The mean sodium level significantly decreased from 140.5 mg/dL to 139.1 mg/dL after phototherapy. The decrease in potassium level was not statistically significant. The mean calcium level significantly decreased from 9.98 mg/dL to 9.55 mg/dL. The mean chloride level before phototherapy significantly decreased from 106.4 mmol/L to 105.9 mmol/L after phototherapy.

Conclusion: The level of serum electrolytes in newborns may change with phototherapy. Serum sodium, chloride, and calcium levels may decrease after phototherapy. For prevention of possible adverse effects, the changes in electrolyte levels should be considered in the clinical course of newborns receiving phototherapy and appropriate fluid-electrolyte treatments should be given.

Keywords: Electrolyte, hyperbilirubinemia, jaundice, newborn, phototherapy

Fototerapinin Serum Elektrolit Düzeyleri Üzerine Etkisinin Araştırılması

Öz

Amaç: Sarılık tanısıyla yenidoğan yoğun bakıma yatırılmış yenidoğanlarda fototerapinin serum elektrolit düzeyleri üzerine etkisinin araştırılması amaçlanmıştır.

Yöntemler: Haziran 2016 ve Haziran 2018 tarihleri arasında sarılık tanısıyla hastaneye yatırılan 260 hastanın, fototerapi öncesinde ve 48-72 saat sonrasında bakılan kan tetkiklerindeki elektrolit düzeyleri retrospektif olarak karşılaştırılmıştır.

Bulgular: Fototerapi öncesinde sodyum değeri fototerapi sonrasında ortalama 140,5 mmol/L'den 139,1 mmol/L'ye düşmüştür (p<0,001). Fototerapi öncesinde potasyum değeri fototerapi sonrasında ortalama 4,94 mmol/L'den 4,87 mmol/L'ye düşmüş fakat p değeri 0,054 olarak bulunarak istatistiksel olarak anlamlı görülmemiştir. Ortalama kalsiyum değeri 9,98 mg/dL'den 9,55 mg/dL'ye düşmüş ve bu fark istatistiksel olarak anlamlı bulunmuştur (p<0,001). Fototerapi öncesinde klor değeri ortalamasının 106,4 mmol/l'den fototerapi sonrasında 105,9 mmol/l'ye düştüğü görülmüş ve bu fark istatistiksel olarak anlamlı bulunmuştur (p=0,004).

Sonuç: Sarılık tanısıyla yatırılıp fototerapi verilen yenidoğanlardaki serum elektrolitlerinin düzeyi fototerapi ile değişebilmektedir. Sodyum, klor ve kalsiyum düzeyi fototerapi sonrasında düşmektedir. Fototerapi alan yenidoğanların klinik izlemi, elektrolit düzeylerindeki bu değişimler göz önüne alınarak yapılmalı, olası yan etkiler ve sıvı-elektrolit tedavileri gözden geçirilmelidir.

Anahtar Kelimeler: Elektrolit, fototerapi, hiperbilirubinemi, sarılık, yenidoğan

Jaundice is the visible symptom of hyperbilirubinemia [1]. Indirect hyperbilirubinemia develops in 60% of term babies and 80% of preterm babies in the first week of life; therefore, neonatal jaundice is the one of the most common causes of hospitalization in the first 2 weeks of life [2-4]. Untreated severe hyperbilirubinemia is an important health problem, as it may cause acute bilirubin encephalopathy, kernicterus, cerebral palsy, and mental retardation [5].

In the treatment of hyperbilirubinemia, the aim is to reduce the high bilirubin levels. Phototherapy has been used worldwide as the main therapy for this purpose [6]. Phototherapy provides rapid oxidative reactions and allows the formation of urine-inducible mutant bilirubin isomers by intermolecular rearrangement [7, 8].

The most common side effects associated with phototherapy include bronze baby syndrome, skin rash, dehydration, diarrhea, hemolysis, skin burns, retinal damage, and lactose intolerance [2]. Less common side effects that are more prominent in premature cas-

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es include hypocalcemia; PDA nonclosure; riboflavin deficiency; a decrease in levels of luteinizing hormone, follicle-stimulating hormone, and growth hormone; gonadal damage; the suppression of immune system; and a decrease in cardiac pulse [9-18].

Reddy et al. [19] reported the incidence of phototherapy-associated hypocalcemia and hyponatremia as 13.1% and 6%, respectively, in 252 infants. However, they found no significant change in serum potassium and chloride levels. Shilpa et al. [20] reported a significant decline in serum sodium, potassium, calcium, and chloride levels after phototherapy in 119 neonates.

The aim of this study was to investigate the effect of phototherapy on electrolyte levels in hospitalized infants with jaundice in the neonatal intensive care unit (NICU).

Material and Methods

This study was conducted on 260 eligible neonates admitted to Okmeydani Training and Research Hospital NICU between June 2016 and June 2018 after obtaining ethical approval from the institutional ethical committee (approval number: 1059, Date: 12.12.2018).

Term infants with early neonatal hyperbilirubinemia who were hospitalized were included in the study. The exclusion criteria were as follows: preterm infants (< 37 weeks of gestation),.postnatal age of <5 and >10 days, prolonged jaundice, the presence of dehydration, additional disease other than jaundice such as sepsis, asphyxia, respiratory distress, administration intravenous fluid support, or an additional treatment other than phototherapy.

This was a retrospective study and all demographic and clinical data were obtained from an electronic database. The levels of electrolytes were checked at 0 hour (the first sample during the admission to NICU) and at 48-72 hours after the cessation of phototherapy (at the first routine follow-up after discharge). A comparative study was carried out between these two groups of samples to determine changes in the levels of electrolytes.

A gel-reagent biochemistry tube was used for sampling. Following coagulation, the serum was centrifuged at 4000 g for 8 minutes to obtain serum. Sodium, potassium, and chloride tests were carried out using ion-selective electrodes by direct Ion Selective Electrode (ISE) method. Calcium reacts with 5-nitro-5′-methyl-1,2-bis(o-aminophenoxy)ethane-N,N,N′,N′-tetraacetic acid (NM-BAPTA) under alkaline conditions to form a complex. This complex reacts with Ethylenediaminetetraacetic acid (EDTA) in the second step. The change in the absorbance of the alkaline pH Ca ++ NM-BAPTA + EDTA complex is directly proportional to the calcium concentration, and this ratio was measured photometrically. All the measurements were performed in Okmeydani Training and Research Hospital Biochemistry Laboratory.

Statistical analyses

Quantitative data of groups were analyzed with *t*-tests and qualitative data were compared with chi-square test by using Statistical Package for Social Sciences 22.0 (IBM SPSS Corp., Armonk, NY, USA) software. A value of $p<0.05$ was considered statistically significant.

Results

A total of 260 infants were enrolled in the study, and 138 (53%) were female. No statistically significant difference was observed in terms of gender.

The mean gestational age was 38.5±0.94 weeks, and the mean maternal age was 28.7±6.08 years. From the study population, 147 (56.5%) infants had a history of vaginal birth.

The mean age at the admission was 136.77±30.65 hours. The mean birth weight was 3189±379 g and the mean weight at the admission was 3064±389 g. The mean weight loss percent after birth was found to be 4.2±1.79%. The mean duration of phototherapy was 27.7±8.7 hours. The most common blood group was A Rh (+) in newborns, and 72 (27%) infants had positive Coombs test.

The mean total serum bilirubin levels at the admission and during discharge were 18.4 mg/dL and 10.5 mg/dL, respectively. The difference was statistically significant ($p<0.001$). None of the cases required advanced therapies such as intravenous immunoglobulin (IVIG) and blood exchange.

After phototherapy, the mean sodium level decreased from 140.5 mmol/L to 139.1 mmol/L, which was statistically significant ($p<0.001$). Although the mean potassium level decreased from 4.94 mmol/L to 4.87 mmol/L, this difference was not significant ($p=0.054$). The mean calcium level decreased from 9.98 mg/dL to 9.55 mg/dL, and the difference was statistically significant ($p<0.001$). The mean chloride level decreased from 106.4 mmol/L to 105.9 mmol/L, and the difference was statistically significant ($p=0.004$) (Table 1).

Patients were divided into two groups. Patients with reduced sodium, calcium, and chloride levels after phototherapy were included in group 1, whereas infants with no change in electrolyte levels were included in group 2. The two groups were compared for various parameters such as gender, type of delivery, gestational week, weight loss, direct Coombs test, and duration of phototherapy. The effect of phototherapy on electrolyte levels did not change with these parameters because there was no statistically significant difference between the two groups (Table 2).

Table 1. Comparison of electrolyte levels before and after phototherapy

	Before PT[a]	After PT[a]	p
Sodium (mmol/L)	140.5±3.16 (133-149)	139.1±2.78 (132-145)	<0.001
Potassium (mmol/L)	4.94±0.53 (3.5-6.4)	4.87±0.56 (3.5-6.6)	0.054
Calcium (mg/dL)	9.98±0.80 (7.4-12.1)	9.55±0.63 (8.0-11.0)	<0.001
Chloride (mmol/L)	106.4±2.94 (96.2-115.8)	105.9±2.74 (97.4-113.8)	0.004

[a]Values are given as mean±standard deviation (minimal-maximal).
PT: phototherapy.

Discussion

To date, few studies are available that show the adverse effects of phototherapy on serum electrolytes. In this study, we aimed to investigate the electrolyte changes in 260 healthy neonates who received phototherapy in NICU. We found that serum sodium, calcium, and chloride levels decreased significantly after phototherapy in infants. Although serum potassium levels also decreased after phototherapy, the difference was not statistically significant.

A significant decrease in serum sodium levels was reported in two previous studies [19, 20]. Our results are in accordance with these studies. As the newborns with pathological weight loss were not included, the decrease in sodium levels may be attributed to phototherapy rather than an existing hypernatremic dehy-

Table 2. Relation of various parameters with the effect of phototherapy on electrolytes

Electrolyte	Parameter	Group 1	Group 2	p
	Delivery (Vaginal/cesarean)	64/94	39/43	0.65
	Gender (Female/male)	86/72	44/38	0.18
	Gestational week[a]	38.1±0.9 (38-41)	38.4±0.9 (38-41)	0.63
Sodium	Age at admission (hours)[a]	139.9±35 (120-240)	145.2±31.8 (120-240)	0.27
	Weight loss (%)[a]	3.9±2.6 (0.28-7.37)	3.6±2.8 (0.3-7.13)	0.35
	Direct Coombs (+/-)	38/120	26/56	0.29
	Duration of phototherapy[a]	28.4±9.3 (24-48)	27.2±8.2 (24-48)	0.33
	Delivery (Vaginal/cesarean)	52/25	48/24	0.53
	Gender (Female/male)	48/29	36/36	0.14
	Gestational week[a]	38.5±0.9 (38-41)	38.5±1 (38-41)	0.78
Calcium	Age at admission (hours)[a]	140.4±34.8 (120-240)	135.6±27.9 (120-240)	0.36
	Weight loss (%)[a]	3.8±2.5 (0.3-7.25)	3.6±2.5 (0.18-7.4)	0.51
	Direct Coombs (+/-)	22/55	20/52	0.13
	Duration of phototherapy[a]	26.4±7.3 (24-48)	29±9.8 (24-48)	0.08
	Delivery (Vaginal/cesarean)	58/21	23/12	0.57
	Gender (Female/male)	42/37	22/13	0.59
	Gestational week[a]	38.6±0.9 (38-41)	38.5±1 (38-41)	0.65
Chloride	Age at admission (hours)[a]	130.9±22.8 (120-240)	142.7±33 (120-240)	0.06
	Weight loss (%)[a]	3.7±2.3 (0.4-7.42)	3.37±2.4 (0.36-7.2)	0.17
	Direct Coombs (+/-)	19/60	10/25	0.32
	Duration of phototherapy[a]	27.3±8.3 (24-48)	25.3±5.6 (24-48)	0.20

[a]Values are given as mean±standard deviation (minimal-maximal).

dration. However, the mechanism has not been clearly explained. The decrease in serum sodium levels after phototherapy was suggested to be associated with the reduced intestinal absorption because of diarrhea [21]. However, no diarrhea occurred during and after phototherapy in our study population.

Although Shilpa et al. [20] found a statistically significant decrease in potassium levels from 6.09 meq/L to 5.28 meq/L after phototherapy, Reddy et al. [19] found no significant difference in serum potassium levels. Although serum potassium levels showed a decrease in our study, the difference was not statistically significant and was in agreement with the previous study.

Many studies reported that phototherapy causes hypocalcemia [22, 23]. It was also shown that fluorescent light reduced serum calcium and serum melatonin concentrations, and light-related hypocalcemia was explained by the inhibition of the pineal gland by transcranial illumination. The hypocalcemic effect of light was suggested to be associated with the acute increase in corticosterone-mediated bone calcium uptake due to decreased melatonin [22]. In addition, compared with term infants, preterm babies were reported to have a higher risk for phototherapy-related hypocalcemia, and calcium supplements were recommended for preterm babies during phototherapy [24]. Similarly, a significant decrease in serum calcium levels was found in our study.

There are few studies in the literature that investigated the effect of phototherapy on chloride levels. Curtis et al. [21] reported decreased serum chloride levels due to impaired intestinal chloride absorption during phototherapy. Similar to this finding, we established a significant decrease in serum chloride levels after phototherapy.

In our study, we found that several factors including gestational age, maternal age, type of delivery, gender, age at admission, birth weight, weight at admission, weight loss, direct Coombs positivity, and duration of phototherapy had no significant effect on postphototherapy electrolyte levels, as our study population revealed "healthy" term infants with jaundice. This may also be associated with the low duration of phototherapy in our study.

Our results suggest that phototherapy may lead to a significant decrease in serum sodium, calcium, and chloride levels in term infants with neonatal jaundice. Although the exact mechanism is not well established, it must be kept in mind that an electrolyte imbalance may develop after phototherapy. To elucidate the exact effects and possible mechanisms of phototherapy on serum electrolyte levels in neonates, further prospective studies including larger number of infants are required.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Okmeydani Training and Research Hospital (Date: 12.12.2018, Approval number: 1059)

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