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Effect of Phototherapy on Serum Electrolytes and Alkaline Phosphatase During Management of Neonatal Hyperbilirubinemia

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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.

Aim of Study: The aim of the study was to evaluate the electrolyte changes in neonates receiving phototherapy with find out the high risk neonates for electrolyte changes and to compare the effect on electrolytes in preterm and term neonates receiving phototherapy.

Subjects and Methods: This was a clinical trial, the study was conducted in special care baby unit at Al-Wahda Teaching Hospital, Derna, Libya over a period of six months from August 1 st 2021 to February 2022. Sixty newborns 34 Male, 26 Female were enrolled in the study.

Results: There was a significant decrease in total bilirubin, sodium, calcium, and magnesium levels after phototherapy. However, there is a slight change in potassium, chloride, phosphorous, and ALP but without statistically significant difference.

Conclusion: Serum electrolytes significantly decreased during phototherapy. This study shows that neonates exposed to phototherapy are at a risk of developing electrolyte imbalances and consequently their complications. Hence, close monitoring of such babies are needed to prevent imbalances and their untoward consequences.

Key Words: *Electrolytes – Jaundice – Phototherapy – Neonatal hyperbilirubinemia.*

Introduction

NEONATAL hyperbilirubinemia (NH) is the most common clinical problem noted during the early neonatal period. NH occurs as a consequence of unconjugated bilirubin (UCB) accumulation due to ineffective erythropoiesis, deficient liver enzymes, excess production of bilirubin, deficient conjugation and immature bilirubin excretory pathway with increased enterohepatic circulation. It manifests as yellowish discoloration of sclera and skin and is clinically evident when total serum bilirubin (TSB) level is >5mg/dL or more than 86 micromole/L [1].

Inability to recognize and treat pathological hyperbilirubinemia may lead to kernicterus with its possible neurodevelopmental disability, so an assessment of the risk of development of hyperbilirubinemia and prompt treatment is crucial. However, pathological hyperbilirubinemia that requires treatment may occur in some healthy neonates without any apparent cause, and some of them may develop kernicterus [2].

NH is usually managed by phototherapy (PT) in which on exposure to blue-green light (wavelength = 460-490nm), bilirubin molecule gets converted to soluble, non-toxic isomers that can be readily eliminated by kidneys through urine and via the gastrointestinal tract through faeces. Phototherapy is well tolerated and non-invasive modality of bilirubin reduction. Also, its sensible usage has reduced the need for Double volume exchange transfusion (DVET) in neonates which is indicated in indicated in emergency situation [3].

Availability of simple, economical, noninvasive, and reliable markers allowing physicians to recognize which of the neonates discharged early are at a higher risk for development of significant hyperbilirubinemia has become necessary in these situations so as to initiate treatment as early as possible and thus reduce the risk of bilirubin-induced brain damage. This ideal marker also can help physicians in early discharge of the neonates and selectively follow-up of the high-risk ones [4].

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Different methods have been used to assess the risk of hemolysis and hyperbilirubinemia in the neonates. Measurement of bilirubin level and alpha-fetoprotein in cord blood has been used as a marker for detecting this risk. Moreover, alkaline phosphatase (ALP) level after birth was used for the first time by Nalbantoglu et al., [5] for this purpose.

Although, some studies have reported changes in levels of calcium, magnesium, sodium, potassium & chloride but most of them are from developed countries and there is paucity of data from the developing world who have their own limitation of resources in terms of funds, sophisticated tools, trained personnel's and lack of awareness among parents. Therefore, in this study we intend to evaluate the electrolyte changes in neonates receiving phototherapy with find out the high risk neonates for electrolyte changes and to compare the effect on electrolytes in preterm and term neonates receiving phototherapy.

Subjects and Methods

The study was conducted in Special Care Baby Unit at Al-Wahda Teaching Hospital, Derna, Libya over a period of six months from August 2021 to February 2022 sixty Newborns 34 Male 26 Female were enrolled in the study.

This prospective study including 60 healthy neonates of both genders who were appropriate for gestational age presenting with indirect NH requiring phototherapy according to American Academy of Paediatrics recommendations Ullah et al., [6] was carried out over 6 months in in special care baby unit at Al-Wahda Teaching Hospital, Derna, Libya.

The included neonates had no other associated complaints and/or 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.

Ethical considerations: The study protocol ethics was approved by the committee of special care baby unit at Al-Wahda Teaching Hospital, Derna, Libya. An informed consent was taken from the parents before enrollment.

Data collection: 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 maternal and neonatal blood groups, Coombs test, and total and direct serum bilirubin. Serum electrolytes (Na, K, Ca, Magnesium, Chloride, Phosphorous and ALP) were measured on admission and then after 24 and 48h of phototherapy.

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

Table (1): Basic patient characteristics.

Variable	Mean ±SD	Median (Range)
Age (days)	4.51±4.46	3 (0.1 -23)
	N	%
Sex:		
Male	34	56.7
Female	26	43.3
GA:		
Preterm	20	33.3
Term	39	65
Post-term	1	1.7

This table shows that mean age was 4.51 ±4.46 days and 56.7% of the patients were males while 65% of patients were term, 33.3% were preterm.

Table (2): Blood group distribution among neonates and mothers.

Blood group	Neonate		Mother	
	N	%	N	%
A^+	16	26.7	14	23.3
A^-	2	3.3	4	6.7
B^+	17	28.3	9	15
B^-	3	5	3	5
AB^+	5	8.3	3	5
AB^-	1	1.7	1	1.7
O^+	15	25	20	33.3
O^-	1	1.7	6	10

This table shows that the most common blood group among neonates is B^+ while O^+ was the most common blood group among mothers.

Table (3): Clinical characteristics before and after phototherapy.

Variable	Pre-phototherapy	Post-phototherapy	*p*
Total bilirubin	16.98±3.81	11.0±2.69	<0.001
Sodium	139.89±4.27	138.76±3.48	.004
Potassium	5.06±0.650	4.97±0.640	.422
Calcium	9.07±0.922	8.55±0.802	<0.001
Magnesium	2.22±0.432	2.09±0.3 80	<0.001
Chloride	108.04±3.52	107.66±2.94	.365
Phosphorous	5.66±0.852	5.59±0.767	.460
ALP	483.98±152.3	471.28±159.4	.224

This table shows that there is a significant decrease in total bilirubin, sodium, calcium, and magnesium levels after phototherapy. However, there is a slight change in potassium, chloride, phosphorous, and ALP but without statistically significant difference.

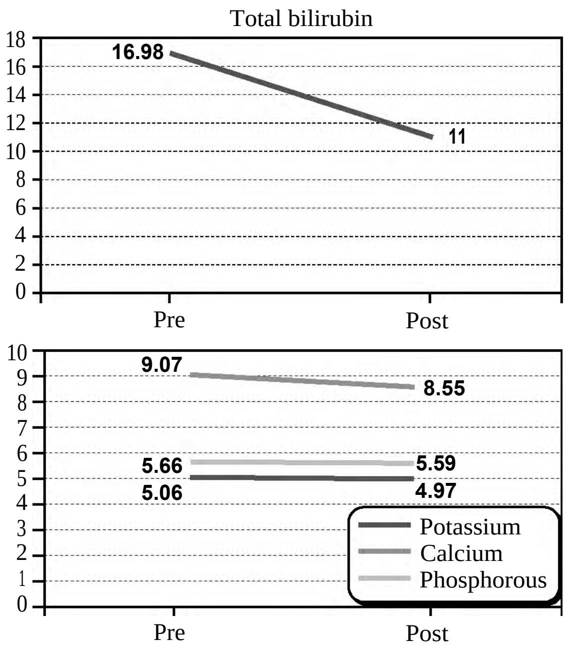

Fig. (1)

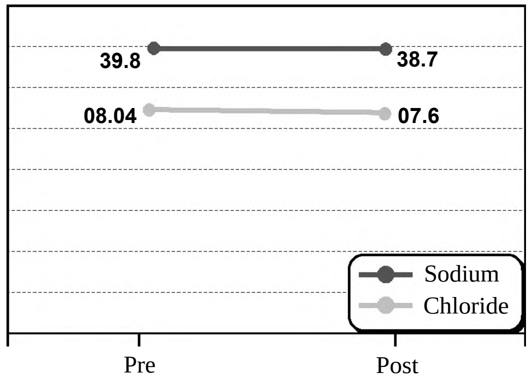

Fig. (2)

Discussion

Neonatal hyperbilirubinemia is an unusual physical finding observed by clinicians during the initial week of life noted in around 60-80% live births. Healthy term infants are frequently discharged from the hospital relatively earlier after delivery for medical, social, and economic reasons. According to a study, neonates with a post-delivery hospital stay of less than 72 hours had a much higher risk of readmission than newborns with a stay of more than 72 hours. Early discharge of healthy term newborns is generating concern due to reports of bilirubin-induced brain damage leading in complications such as kernicterus. The importance of early diagnosis of hyperbilirubinemia in prematurely discharged newborns cannot be overstated **[7]**.

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 wave length, the irradiance and the surface area of the body exposed, and the distance between the infant and the light source **[8,9]**.

Phototherapy has become the most commonly utilized therapeutic method. This is the most current treatment of choice for reducing the severity of newborn unconjugated hyperbilirubinemia. Phototherapy, like any other treatment, has adverse effects. Unlike other side effects, there are currently just a few studies that depict the negative impact of phototherapy on serum electrolytes. A few recent researches have focused on the occurrence of hypocalcaemia as a result of phototherapy **[1]**. The goal of this research was toevaluate the electrolyte changes in neonates receiving phototherapy with find out the high risk neonates for electrolyte changes and to compare the effect on electrolytes in preterm and term neonates receiving phototherapy.

In the current study, we found that the mean age was 4.51 ±4.46 days and 56.7% of the patients were males while 65% of patients were term, 33.3% were preterm.

The demographics of this study group had many similarities with other studies involving jaundiced neonates as regards gestational age in Iskander et al., [10], male predominance as in each of Alnujaidi et al., [11]; Goyal et al., [12], and weight as in Sunil Kumar et al., [13] and Purohit A, Verma SK [14].

A study of Ahmad pour-Kacho et al., [15] reported that a total of 105 cases were followed-up. Three cases were lost to the study. The remaining 102 cases consisted of 50 (49%) males and 52 (51%) females. Ninety eight (96%) infants were born by cesarean section and 4 (4%) by vaginal delivery. Apgar scores were normal (9-10) at birth in all cases. The mean gestational age was 38.7 weeks and the mean birth weight 3649.59 grams.

Vlad et al., [16] reported thatin neonates receiving phototherapy, gestational age at delivery ranged from 37 to 41 weeks with a mean of 39.1 weeks (SD ± 1.33 weeks) and a median of 39 weeks.

Hyperbilirubinemia in a neonate is one of the most common problems that may occur in 60-70% of term and 80% of preterm babies. It is known to be associated with significant morbidity like neonatal bilirubin encephalopathy and even death. Clinically, and almost exclusively ABO incompatibility occur in 'A' and 'B' blood group babies of O '+ve' mothers. These babies are reported to be at high risk of severe hyperbilirubinemia (serum bilirubin level more than 16mg/dl) [17].

Furthermore, in the present study,the most common blood group among neonates is B + while O+ was the most common blood group among mothers.

In comparison with the study of Kalakheti et al., [18] in which a total of 37 (18.5%) babies had developed hyperbilirubinemia and among them 14 (38%) were from group of babies having 'O' Positive blood group and 23 (62%) were from group of babies having other than 'O' Positive blood group. There was 2.6 times higher chance of having hyperbilirubinemia in the babies with ABO incompatibility than 'O' Positive babies after adjusting other significant variables.

In the current study, we found that there was a significant decrease in total bilirubin, sodium, calcium, and magnesium levels after phototherapy. However, there is a slight change in potassium, chloride, phosphorous, and ALP but without statistically significant difference.

The study of Tosson et al., [19] reported that 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 48h. The comparison between types was conducted all through the first 48h 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 this study and in the studies by Bezboruah and Majumder [20], Jena et al. [7], and Rangaswamy et al. [21].

Some studies of Xiong et al., [22]; Bezboruah and Majumder, [20] also documented a significant decrease in serum Ca. All these studies evaluated the electrolytes level prior and after 48h or at discontinuation of phototherapy. This came in accordance with our work. However, we could also demonstrate and document the continuous decline over the 48h and showed that it increased with the duration of phototherapy.

A study by Suneja et al., [23] 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), although they also documented a decline in urea and BG which was insignificant in their study (p=0.0751 and p=0.74, respectively).

Moreover, Sharma et al., [1] reported that before PT, the mean serum sodium was 141.3 ±2.69 mmol/L and after PT, the mean serum sodium was 140.5±2.70mmol/L. Serum sodium level was found to decreased significantly after PT (p=0.0001) in the study. This decline was proposed to be as a result of diarrhea causing reduced gastrointestinal absorption of sodium and also generous frequent feeding ensured in our institution.

Similar results were recorded by Jena et al., [7] and Suneja et al., [23] the mean serum potassium was 4.43±0.52 mEq/L before PT and was 4.23±0.48 mEq/L after PT. The decline in serum potassium level was found to be statistically significant after PT (p=0.0001). However, this decline was marginal with levels close to near normal range in all the cases.

The results are in accordance with Krishna and Soans, [24] study (statistically significant). In this studyKrishna and Soans, [24] notable decline in the serum calcium was appreciated following completion of phototherapy with 53 neonates (46.08%) showing hypocalcemia in contrast to no neonate at the time of start of study. However, none exhibited any clinical evidence of hypocalcemia with only trivial deflection of levels hovering around the lower limit of normal range in majority of the cases.

According to Sethi et al., in [25], following PT, 75% of term newborns had hypocalcemia. After PT, 66.6 percent of term newborns had a substantial decrease in calcium levels, according to Yadavet al., [26]. After 48 hours of PT, 56 percent of infants had lower blood calcium levels; PT inhibits melatonin production by the pineal gland. As a result, corticosterone's impact on bone calcium is reduced. Because melatonin levels drop during PT, the level of corticosterone in the blood also drops. As a result, reduced corticosterone reduces bone resorption, resulting in hypocalcemia. Hypocalcemia was produced by a decrease in parathormone production in jaundiced newborns treated with PT [1].

Conclusions:

This study documented that phototherapy significantly affects the serum electrolytes. Hence, continuous follow-up and efforts to shorten/ minimize the duration should be considered a high-priority during management of neonatal hyperbilirubinemia.Even though the exact mechanism for this decline could not be understood clearly, further large sample studies are needed to elucidate the same. We must not forget that these imbalances might have an adverse effect on the neonates and must remain keen eyed. Although, we do not recommend measurement of serum electrolytes routinely; we suggest one to remain vigilant regarding the same.

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تأثير العلاج الضوئى على إلكترؤيتات الدم والفوسفاتاز القلوى أثناء علاج فرط بيلير وبين الدم عند الأطفال حديثى الولادة

\الخلفية: فرط بيلير وبين الدم عند الأطفال حديثى الولادة (NH) هو من بين الأمراض الوليدية الشائعة. العلاج الضوئى هو التدخل العلاجى الأكثر استخداماً. أنظمة وأنواع توصيل مختلفة متوفرة حالياً.

\الهدف و\الأهدا\ف: كان الهدف من الدراسة هو تقييم التغيرات التى تحدث للإلكتروليتات فى الأطفال حديثى الولادة الذين يتلقون العلاج الضوئى مع معرفة الأطفال حديثى الولادة المعرضين لخطر التغيرات التى تحدث للإلكتروليت ومقارنة التأثير على الإلكتروليتات عند الخدج والأطفال حديثى الولادة الذين يتلقون العلاج الضوئى.

\الموضوعات و\الطرق: كانت هذه تجربة سريرية، أجريت الدراسة فى وحدة رعاية الأطفال الخاصة بمستشفى الوحدة التعليمى ـ درنة ـ ليبيا على مدى ستة أشهر (١ أغسطس ٢٠٢١ إلى فبراير ٢٠٢٢). تم تسجيل ستين من الأطفال حديثى الولادة (٣٤ ذكر، ٢٦ أنثى) فى الدراسة.

\النتائج: كان هناك انخفاض ملحوظ فى مستويات البيليروبين الكلى والصوديوم والكالسيوم والمغنيسيوم بعد العلاج الضوئى. ومع ذلك، هناك تغيير طفيف فى البوتاسيوم، والكلوريد، والفوسفور، والفوسفاتيز القلوى ولكن بدون فرق معتد به إحصائياً.

\الاستنتاج: انخفاض إلكتروليتات الدم بشكل ملحوظ أثناء العلاج الضوئى. تظهر هذه الدراسة أن حديثى الولادة الذين يتلقون العلاج الضوئى معرضون لخطر الإصابة باضطراب وخلل فى توازن الالكتروليتات وبالتالى مضاعفاتهم. وبالتالى، هناك حاجة إلى مراقبة هؤلاء الأطفال عن كثب لمنع الاختلالات وعواقبها غير المرغوبة.