

EFFECT OF PHOTOTHERAPY ON ZINC STATUS IN TERM NEONATES WITH INDIRECT HYPERBILIRUBINEMIA

By

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ABSTRACT

Background: Jaundice is the most common clinical sign in neonatal medicine. Phototherapy is the most commonly used intervention to treat and prevent severe hyperbilirubinemia. Zinc has a vital role in maintenance of cell functions, protein synthesis, and immune-functions.

Objective: To study the effect of phototherapy on zinc status in term neonates with indirect hyperbilirubinemia.

Patients and methods: This was a prospective study carried out on 50 term neonates with indirect hyperbilirubinemia in neonatal intensive care unit at Damietta Al-Azhar University Hospital during the period from February 2019 to February 2020. Total serum zinc was measured before and after phototherapy.

Results: About 26 (52%) were males and 24 (48%) were females. The mean zinc levels before and after phototherapy showed no statistically significant difference. There were no statistically significant difference in total serum bilirubin (TSB) level at admission and after 12 hrs following admission but there were statistically significant differences after 24 hrs and at discharge. However, the majority of neonates with hyperbilirubinemia were deficient in zinc level.

Conclusion: Phototherapy has no effect on serum zinc level. However, zinc supplementation encouraged in cases with neonatal jaundice as they usually have zinc deficiency.

Keywords: Neonatal jaundice; Pathological jaundice; Hyperbilirubinemia; Zinc; Phototherapy.

INTRODUCTION

Jaundice incidence reaches up to 60% of healthy term, infants and 80% of premature infants (Ives, 2012). In most of cases, jaundice is mild and transient, resulting from immature hepatic pathway of bilirubin excretion. Another cause of hyperbilirubinemia in a newborn is failure of conversion of conjugated bilirubin to stercobilin as a result of the relative

deficiency of bacteria in the gut in the first weeks of life. Hyperbilirubinemia may also be linked to increased activity of the beta-glucuronidase enzyme in the sterile gut and the mild alkalinity of the intestine (Singh, 2010).

Phototherapy is the most common intervention used in the treatment and prevention of marked hyperbilirubinemia. It reduces the total bilirubin concentration

decreasing the rate of usage of exchange transfusion. However, phototherapy might have its own side effects. It can result in neonatal hyperthermia, increased peripheral blood flow and insensible water loss. Furthermore, phototherapy increases the incidence of diarrhea, in addition to upset of maternal-infant interaction (Zhang *et al.*, 2016).

Zinc has crucial role in a lot of biological processes such as maintaining cellular architecture and functions, protein synthesis, and immune functions via its action as a co-factor for production of more than 200 enzymes (Jyotsna *et al.*, 2015). In addition, zinc is crucial for the development of the brain, respiratory and intestinal tract in pre- and postnatal life (Terrin *et al.*, 2013).

This work aimed to assess the impact of phototherapy on zinc status in term neonates with indirect hyperbilirubinemia.

PATIENTS AND METHODS

The current study was a prospective study carried out in neonatal intensive care unit at Damietta Al- Azhar University Hospital on 50 term neonates with indirect hyperbilirubinemia during the period from February 2019 to February 2020. Written consents were taken from the parents. Cases were hospitalized and received phototherapy when their total serum bilirubin level indicated phototherapy according to American Academy of

Pediatrics (AAP) guidelines (2004). Total serum zinc was measured before and after phototherapy. Exclusion criteria included infants with diabetic mother or neonates with pathological jaundice, major congenital malformations, hypoxic ischemic encephalopathy and inborn errors of metabolism or proven sepsis.

The studied newborns were subjected to full maternal and perinatal history. In addition, family history of siblings who have had jaundice was documented.

The studied newborns were examined thoroughly including general, chest, abdominal and neurological examination, any signs of zinc deficiency including periorificial and acral dermatitis, diarrhea and neurologic disturbances. Investigations were done for all the studied newborns, including complete blood count, blood group for mother and neonate at admission, reticulocyte count, Coomb's test (direct and indirect), serum total and direct bilirubin level and serum Zinc level before and after phototherapy.

Statistics:

All data were analyzed using Statistical Package for the Social Science (SPSS) version 20.0. Paired student t-test was used to compare mean and SD of 2 sets of quantitative normally distributed data, while $P < 0.05$ was considered significant.

RESULTS

About 26 (52%) of the current study were males and 24 (48%) were females. The mean GA of the studied cases in weeks was (37.76±0.77). The mean age at admission in hours, age of onset of jaundice in hours, length in cm, weight in kg at admission and at discharge were

(81.8 ± 20.15), (55.6±11.51), (50.17±0.95), (3.37 ±0.04) and (3.38 ±0.045) respectively. As regard type of feeding about 36 (72%) were breast fed, 10 (20%) were fed artificially and 4 (8%) were mixed feeders (**Table 1**).

Table (1): Neonatal data of the studied cases

Variables		All cases (N=50)
Sex	Male	26 (52%)
	Female	24 (48%)
GA (wks)		37.76±0.77
Age at admission (hrs)		81.8 ± 20.15
Age of onset of jaundice (hrs)		55.6 ± 11.51
Length (cm)		50.17±0.95
Weight at admission (Kg)		3.37 ± 0.04
Weight at discharge (Kg)		3.38 ± 0.045
Type of feeding	Breast	36 (72%)
	Artificial	10 (20%)
	Mixed	4 (8%)

The mean maternal age in years was (25.7 ± 4.03), 50% of which were multipara and 50% were primipara. As regard mode of delivery, 82% of mothers

were subjected to caesarian section while only 18% delivered by normal vaginal delivery (**Table 2**).

Table (2): Maternal Data in the study

Variables		All cases (N=50)	
Maternal age (yrs)		25.7 ± 4.03	
Multiparity	Present	25	50%
	Absent	25	50%
Mode of delivery	CS	41	82%
	NVD	9	18%

Quantitative data were expressed as median (range)

The total serum bilirubin (TSB) in the studied cases. The mean ± SD of the TSB at admission, 12 hours, 24 hours and at discharge were (16.44±1.09), (14.52±1.52), (13.48±1.71) and (8.76±0.67) respectively. There were no statistically significant difference in TSB level at admission and after 12 hours

following admission (P=0.085) but there statistically significant differences after 24 hours (P=0.043) and at discharge (p < 0.001). Moreover, there were statistically significant difference in TSB level at discharge compared to bilirubin levels at 12 hours (P< 0.001) and 24 hours (P=0.049). The mean ± SD of the DSB at

admission, 12 hours, 24 hours and at discharge were (0.767 ± 0.114) , (0.764 ± 0.115) , (0.762 ± 0.126) and (0.753 ± 0.124) respectively. There were no

statistically significant differences in the mean $SD \pm$ of the DSB at all times ($P > 0.05$) (Table 3).

Table (3): Total serum bilirubin (TSB) in the studied cases

Study group (N=50) TSB	At admission	12 hours	24 hours	At discharge	Paired student t-test P-value
Mean \pm SD	16.44 \pm 1.09	14.52 \pm 1.52	13.48 \pm 1.71	8.76 \pm 0.67	P <0.001
P ₁		0.085	0.043*	< 0.001*	
P ₂			0.437	< 0.001*	
P ₃				0.049*	

In addition, zinc levels in $\mu\text{g/dl}$ before and after phototherapy in the studied cases were (121.14 ± 9.72) and (121.72 ± 10.61) respectively with insignificant difference ($P=0.051$). Before phototherapy, 10 cases

(20%) have normal zinc level, while 40 cases (80%) were deficient. At discharge, 11 cases (22%) have normal zinc level, while 39 cases (78%) were deficient (Table 4).

Table (4): Zinc levels in the studied cases

Zinc levels ($\mu\text{g/dl}$)		N=50
Mean zinc levels	Before phototherapy	121.14 \pm 9.72
	After phototherapy	121.72 \pm 10.61
	T = - 2	P = 0.051
State of before phototherapy	Normal	10 (20%)
	Deficient	40 (80%)
State of zinc at discharge	Normal	11 (22%)
	Deficient	39 (78%)

SD: standard deviation, P₁: comparison in relation to TSB at admission

F for ANOVA test, P₂: comparison in relation to TSB at 12 hours

P₃: comparison in relation to TSB at 24 hours

Categorical data expressed as Number (%), Quantitative data are expressed as mean \pm SD.

T= paired samples t-test, P: probability

The mean age of onset of phototherapy (hours) was (87.43 ± 24.35) and the mean duration of phototherapy (hours) is (59.96 ± 3.78) . Source of phototherapy is single in all cases (100%). The main side effect of phototherapy is rash, which present

only in two cases (4%). As regards, previous siblings having jaundice, eight cases (16%) needed phototherapy and no one need exchange transfusion (0%) (Table 5).

Table (5): Phototherapy parameters in the study groups

Variable		All cases (N=50)
Age of onset of phototherapy (in hrs)		87.43 ± 24.35
Duration of phototherapy (hrs)		59.96± 3.78
Number of phototherapy units used	Single	50 (100%)
	More than one	0 (0%)
Side effects of phototherapy	Rash	2 (4%)
	Other	0 (0%)
Previous siblings jaundice (8 siblings)	Need phototherapy	8 (16%)
	Need exchange transfusion	0 (0%)

DISCUSSION

Phototherapy is an effective therapeutic modality of treatment for neonatal pathological. Zinc salts can decrease the duration of phototherapy duration via the precipitation of unconjugated bilirubin in the intestine. One cohort study revealed that zinc and bilirubin levels are inversely correlated in neonates with marked hyperbilirubinemia. Additionally, phototherapy caused a marked elevation in the rates of neonates with potentially toxic zinc levels (zinc > 200 µgm/dl) among neonates with marked hyperbilirubinemia, while no significant change was reported amongst those with mild to moderate cases (*Mosayebi et al., 2016*).

Another study measured zinc levels before and after phototherapy in neonates with unconjugated hyperbilirubinemia that hemoglobin level at admission was within normal range (*Boskabadi et al., 2015*). The current study revealed that the mean zinc levels before and after phototherapy

showed no statistically significant difference. In the same line in another study, it has been shown that intensive phototherapy had no effect on zinc level, while exchange transfusion changed the level to be comparable with that of normal healthy neonates (*El-Mazary et al., 2017*).

Similarly, a number of studies revealed that there was not any zinc toxicity after phototherapy for hyperbilirubinemia cases in zinc supplemented neonates (*Rana et al., 2011; Kumar et al., 2014 and Maamouri et al., 2014*). Another Iranian study revealed that there were no correlation between the level of serum bilirubin and zinc in neonates with jaundice. In addition, there was no relationship between serum level of direct bilirubin and zinc (*Boskabadi et al., 2015*).

The current study revealed that there was gradual decrease in bilirubin level as the mean difference of the TSB at admission was (16.58± 1.31) and at

discharge was (8.76 ± 0.67) with highly statistically significant difference, however; there was no statistically significant differences in the mean value of the DSB on admission and at discharge ($P=0.179$). This is agreed to some extent with a recent study in 2019 that revealed that bilirubin level was (16.46 ± 1.47) in the first day (at admission) and (10.08 ± 1.07) at the third day (*Sardari et al., 2019*).

The current study revealed that most neonates with hyperbilirubinemia were deficient in zinc (80%), while only 20 % have normal zinc level. In agreement, *El-Mazary et al. (2017)* revealed that neonates with indirect hyperbilirubinemia had lower serum zinc levels than healthy neonates which were not related to their maternal serum levels. Moreover, another study revealed that the level of serum zinc in the neonates with indirect hyperbilirubinemia was lower than in those without jaundice (*Boskabadi et al., 2015*).

As regards the duration of phototherapy, the current study came in agreement with *Sardari et al., (2019)* that revealed that the mean duration of phototherapy in their study was 48 hours. Regarding the side effects of phototherapy, the current study revealed that the most common complication was skin rash, which developed in about 4% of cases only. This was in agreement with the same study in 2019 that stated the most common complication was skin rash however; the incidence in their study was higher, as it occurred in about 15% of their studied neonates.

CONCLUSION

Phototherapy has no impact on serum zinc level. Most of cases with neonatal jaundice have lower than normal serum zinc levels.

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تأثير العلاج الضوئي على مستوى الزنك في مصل حديثي الولادة مكتملي العمر الرحيمي المصابين باليرقان غير المباشر محمود علي أحمد عبد المجيد ، محمد محمد المزاحي، محمد إبراهيم السنودي، مجدي ذكي الغنام

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خلفية البحث: يعد مرض الصفراء أهم الأعراض الأكثر شيوعاً في طب حديثي الولادة. يعد العلاج الضوئي هو التدخل الأكثر شيوعاً لعلاج ارتفاع نسبة البيليروبين بالدم والوقاية منه. إن لعنصر الزنك دور حيوي في الحفاظ على وظائف الخلية، وتخليق البروتين، والوظائف المناعية.

الهدف من البحث: دراسة تأثير العلاج بالضوء على حالة الزنك في حديثي الولادة المصابين بفرط بيليروبين الدم غير المباشر.

المرضى والطرق: أجريت الدراسة على خمسين طفلاً من حديثي الولادة المصابين بفرط بيليروبين الدم الغير المباشر في وحدة العناية المركزة لحديثي الولادة في مستشفى دمياط الأزهر الجامعي في الفترة من فبراير 2019 إلى فبراير 2020. وشملت معايير الاستبعاد الرضع مع أم مصابة بالسكري أو الصقراء نتيجة لمرض معين، والتشوهات الخلقية، ونقص الأكسوجين، وأمراض التمثيل الغذائي وتم قياس إجمالي الزنك في الدم قبل وبعد العلاج بالضوء.

نتائج البحث: أجريت الدراسة الحالية على خمسين طفلاً من حديثي الولادة المصابين بفرط بيليروبين الدم غير المباشر. حوالي 26 (52%) من الذكور و24 (48%) من الإناث. لم يظهر متوسط مستويات الزنك قبل وبعد العلاج الضوئي أي فرق ذو دلالة إحصائية ولم تكن هناك

فروق ذات دلالة إحصائية في مستوى البيليروبين الكلي في الدم عند الحجز بالمستشفى وبعد 12 ساعة بعد الحجز ولكن هناك فروق ذات دلالة إحصائية بعد 24 ساعة وعند الخروج. ومع ذلك، فإن غالبية الولدان المصابين بفرط بيليروبين الدم كان لديهم نقص في مستوى الزنك.

الإستنتاج: قد لا يكون للعلاج الضوئي تأثير على مستوى الزنك في الدم. ومع ذلك ترجح الدراسة إستخدام مكملات الزنك لعلاج حالات الصفراء في حديثي الولادة نظرا لوجود نقص في معدلات الزنك لديهم.