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Serum zinc changes in term neonates with hyperbilirubinemia after phototherapy.

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Abstract

Background: Neonatal jaundice occurs due to the elevated levels of unconjugated bilirubin and may induce neurological sequelae, such as encephalopathy. Phototherapy remains the main primary management in neonatal jaundice; one of its effects is elevated in zinc level.

Objectives: Assess serum zinc level in full term neonates who had hyperbilirubinemia and treated by phototherapy before and after phototherapy and study it's relation to selected neonatal, maternal and labour factors.

Methods: A prospective study has been carried out in Basrah maternity and children hospital, 2nd neonatal care unit to assess serum zinc on 60 term neonates appropriate for gestational age with unconjugated hyperbilirubinemia treated by phototherapy. Neonatal, maternal data were collected, serum zinc was assessed before and after phototherapy, (normal range: 50 µg/dL-150 µg/dL), elevated in serum zinc was studied in relation to selected variables.

Results: It was found that total serum bilirubin was lower after phototherapy and serum zinc was elevated. The result is statistically significant. Elevated serum zinc was found in 33.3% of cases. It was more in in extensive phototherapy than double or single. P value<0.05. Also, more with prolonged period of phototherapy but the result was statistically not significant. It was not related to other neonatal or maternal characters.

Conclusion: Serum zinc is elevated after phototherapy in neonates with hyperbilirubinemia, increase level is more with use of extensive phototherapy and increase level of total serum bilirubin.

Keywords: Phototherapy, Elevated zinc level, Hyperbilirubinemia, Neonates.

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Introduction

Jaundice is a common and in most cases, benign problem in neonates, it is observed during the 1st week after birth in approximately 60% of term infants and 80% of preterm infants. Neonatal jaundice occurs due to the elevated levels of unconjugated bilirubin and may induce neurological sequelae, such as encephalopathy. Hyperbilirubinemia is considered when the total serum bilirubin raises more than 95th percentile for age in early neonatal period [1].

Phototherapy remains the main primary management (prevention and treatment) in neonatal jaundice but has many adverse effects like feeding intolerance, hyperthermia, skin rashes, loose stool, retinal changes, bronze baby syndrome, dehydration and redistribution of blood flow, genotoxicity and changes in micronutrients and minerals levels like calcium, magnesium and zinc which is essential component of many metalloenzymes involved in virtually all aspects of metabolism. Zinc is an integral component of nearly 300 enzymes in different species of all phyla. It might affect the process of bilirubin binding proteins or excretion as it plays both the structural and enzymatic roles in many proteins [2].

Zinc levels was significantly lower in jaundice patients (compared with the healthy newborn. Zinc, as it affects bilirubin binding proteins and excretion, it prevents the lipid depolarization of the cell membranes and hypozincemia may modulate the erythrocyte membrane. It may result in deficient synthesis of assorted enzymes that play a role in the bilirubin metabolism [3].

It was reported that phototherapy increases the serum zinc levels in neonates with hyperbilirubinemia. Zinc salts can reduce phototherapy duration by precipitating unconjugated bilirubin in the intestine, bilirubin and zinc can form a complex in physiologic pH so bilirubin reduction by phototherapy may increase serum zinc levels [4].

New therapeutic methods appear to be necessary to decrease elevated serum bilirubin and preventing bilirubin neurotoxicity is *via* reducing the unconjugated bilirubin level by inhibition of enterohepatic circulation. Zinc salts have a potential to inhibit enterohepatic circulation of bilirubin probably by precipitating unconjugated bilirubin in the intestine. Accordingly, some clinical trials have evaluated the effects of zinc supplementation on hyperbilirubinemic neonates undergoing phototherapy.

This study was done to assess serum zinc level in full term neonates who had hyperbilirubinemia and treated by phototherapy before and after phototherapy and study it`s relation to selected neonatal, maternal and labour factors.

Materials and Methods

A prospective study has been carried out in Basrah maternity and children hospital, 2nd neonatal care unit from 1st of June till end of December 2017 to assess serum zinc on 60 term neonates appropriate for gestational age and on exclusive breast feeding; 28 were males and 32 were females; their ages ≤ 14 days with unconjugated hyperbilirubinemia treated by phototherapy. Informed consent was obtained from the parents [5].

Exclusion criteria

Neonates who had neonatal asphyxia, respiratory distress, sepsis or premature neonates, small for gestational age, infant of diabetic mother, those who had exchange transfusion, congenital malformations, had been formula fed were excluded.

Data collection

A special questionnaire was designed for the purpose of the study to assess neonatal data which include name, gender, date of birth, age, gestational age, weight, date of admission to hospital, type and duration of phototherapy, type of feeding, family history of neonatal jaundice or hemolytic anemia. Full neonatal examinations were done including general, systemic examination, growth measures were recorded. Maternal data included name, age, parity, blood group, last menstrual period, chronic maternal diseases (hemolytic anemia, hypertension, diabetes mellitus), complications of pregnancy: Antepartum hemorrhage, fever, anemia urinary tract infections and prolonged rupture of membrane. Labour and delivery data include place of delivery: Hospital or at home, mode of delivery: Vaginal or caesarean [6].

Methods

Neonates with jaundice who were admitted to second neonatal care unit are kept on single, double or extensive phototherapy unit using of fluorescent blue light lamps which supplies spectral irradiance of ≥ 5 mw/cm^2/nm with wave-length (420-470) nm/cm^2. Naked neonates were placed while covering eyes and genitalia at a distance of 30 cm from phototherapy unit. The position of the neonate was changed from time to time [7].

- To asses serum zinc levels venous blood samples were drawn from the neonates at arrival and 48 hours after phototherapy into plain tubes, were either analyzed within 2 h or centrifuged and the separated plasma was stored at -20°C in a refrigerator for further analysis by using the atomic absorption spectrometry method (Ziest Chem Diagnostics kit, (normal range: 50-150 µg/dL)).
- Total Serum Bilirubin (TSB) was assessed by (BIL READ) Bilirubin meter using special standardized solution put in capillary tube, both direct and indirect bilirubin estimated by spectrophotometer.
- Other investigations done included complete blood count using hematological analyzer morphology, blood group and Rh typing, others according to need.

Statistical analysis

Collected data were fed into SPSS version 20.0 for tabulation and analysis. Frequency and percentages were used to display categorical data while mean and standard deviation were used to summarize continuous or scale variables with normal distribution and accompanied by median when they were nonparametric. To test normality of variables, Komogorov and Shapiro's tests were the principal approach. Significance level was set to be 0.05 and values below this cut-off were considered statistically significant. To compare mean, t-test was used or its analogue (Mann Whitney's test) if the variables under analysis were non-parametric [8].

Results

The current study was done on 60 neonates admitted to neonatal care unit with hyperbilirubinemia and needed phototherapy, 28 (46.7%) of them were male, 32 (53.3%) were female, their mean age was 6.08 ± 1.700 days, weight 3114.17 ± 397.139 gm, gestational age 38.27 ± 0.756 weeks, born to mothers of mean age 29.43 ± 5.391, 43 (71.7%) of them were delivered vaginally, 17 (28.3%) by CS, 13 (21.7%) were delivered at home, 47 (78.3%) at hospital. After phototherapy serum bilirubin was significantly reduced, this was accompanied by significant elevation of serum zinc in 20 (33.3%) of cases. This elevation was related to type of phototherapy, use of extensive phototherapy was associated with more cases of elevated serum zinc and the result was statistically significant. Nearly 70% of cases of elevated serum zinc needed 3 and 4-days period of phototherapy while normal level zinc group need 2 days duration in 60% of cases but the result was stastically not significant, p value>0.05. This elevation was not related to other neonatal characters like age, sex, gestational age and weight. Maternal characters like age, parity, maternal complications and pregnancy complications were found not related to zinc level changes. Also type and place of delivery were not related to zinc level (Tables 1-3) [9].

Variable	Mean	± SD	No.	%
Neonatal characters				
Gestational age (weeks)	38.27	0.756		

Weight (gm)	3114	396.139		
Age (days)	6.08	1.7		
Gender				
Male			28	46.7
Female			32	53.3
Maternal characters				
Age	29.43	5.391		
Parity	2.6	1.102		
Delivery type				
Vaginal			43	71.7
C.S			17	28.3
Place				
Home			13	21.7
Hospital			47	78.3

Table 1. Selected neonatal and maternal characters.

Variable	Before phototherapy Mean ± SD	48 hours after phototherapy Mean ± SD	P-value for paired t-test
T.S.B mmol/l	309.25 ± 47.22	196.43 ± 23.97	0.002
S Zn µg/dl	84.05 ± 22.77	133.61 ± 52.70	<0.001

Table 2. Serum zinc and bilirubin level in neonates before phototherapy and 48 hours after.

Variables	No (%)	Serum zinc		Mean ± SD
		Lower value	Upper value	
Normozincemic group, (50-150 µg/dl)	40 (66.67%)	92.541	108.909	100.725 ± 25.589
Elevated S Zn group (>150 µg/dl)	20 (33.33%)	189.468	209.332	199.40 ± 21.22

Table 3. Frequency of cases of increase in S Zn after phototherapy, (normal range: 50-150 µg/dl).

Discussion

Permanent neuronal injury in neonates can result from deposition of indirect bilirubin in the neuron membrane. Prevention of bilirubin encephalopathy and its chronic result is important aim of detecting and treating neonatal hyperbilirubinemia. There are several treatment modalities for neonatal hyperbilirubinemia. Phototherapy is the most common method. One of the important phototherapy effects after reducing the bilirubin level is: That it can cause an increase in the serum zinc level.

This study was done on 60 full term hyperbilirubinemic neonates receiving phototherapy, it was found that zinc level was increased after phototherapy in 33.3% of neonates, the result was statistically significant. This is similar to other study done at Tehran.

This occurs because Zn salts inhibit the enterohepatic cycling of unconjugated bilirubin. Zinc salts have a scope l to inhibit enterohepatic circulation of bilirubin probably by precipitating unconjugated bilirubin in the intestine. The chemical structure of bilirubin has the potential to chelate metal ions, such as zinc. As a result, bilirubin reduction by phototherapy may cause an increase in serum zinc levels [10]. As phototherapy has many adverse effects and because zinc inhibits enterohepatic circulation, many studies were done to assess zinc as medication to reduce hyperbilirubinemia.

It was noticed from the current study that all neonates with elevated zinc level received double or extensive phototherapy while most neonates who had normal zinc level need single phototherapy. The result was stastically significant.

Most of elevated zinc level group need longer period of phototherapy but statistically not significant result. As double and extensive phototherapy, prolonged period of exposure to phototherapy are used for moderate to severe hyperbilirubinemia so increase zinc level after phototherapy is related to level of bilirubin, more elevation in zinc level was observed among neonates who were admitted with higher level of bilirubin. This result is similar to study done at Tehran. This is explained by reduction in serum bilirubin due to phototherapy can lead to increase in serum zinc because bilirubin is chelating agent to zinc.

Conclusion

In this study there was no relation between increase in zinc level and some neonatal characters like (gestational age, post-natal age, gender and weight). Selected maternal factors like: Age, parity, maternal disease or complication during pregnancy were found not related to elevated zinc level. Also type and place of delivery were not related to zinc level. The results were stastically not significant (value>0.05).

So, phototherapy as treatment of neonatal hyperbilirubinemia can be associated with elevated level of serum zinc. Measurement of serum zinc is recommended for hyperbilirubinemic neonates before and after phototherapy. Further study is needed to assess zinc effect as medical therapy for hyperbilirubinemia as none of the potential consequences of zinc excess been reported in neonates. Zinc excess is not of major clinical concern, produces no direct toxicity problems. Much of this zinc passes through the gastrointestinal tract and is excreted in the feces.

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