

Effect of Phototherapy on Serum Ionized Calcium Level in Term Neonates with Unconjugated Hyperbilirubinemia

Ikhlās Ali Ahmed* FICMS, Saba Shallal Farhan* MBChB, Sawsan Abdulwahab Hommadi* DCH, Mahdi Mohammed Murad** CABP

ABSTRACT

Background: Phototherapy has a major role in treatment of jaundice in neonates particularly during first week of life and it may lead to many complications including neonatal hypocalcaemia.

Objective: To evaluate the effect of phototherapy on serum ionized calcium level in newborns with unconjugated hyperbilirubinemia.

Methods: This is a cross-sectional study that conducted in neonatal care unit of Central Child Teaching hospital from 1st of June 2017 to 1st of June 2018 where patients collected randomly. Inclusion criteria included: term neonates with unconjugated hyperbilirubinemia >15 mg/dl who required phototherapy for treatment of jaundice, with appropriate weight (>2.5kg), during 3-7 days of life on breast, formula or mixed feeding. Exclusion criteria included any neonate with any medical condition that interfered with serum calcium level (e.g. sepsis, infant of diabetic mother, respiratory distress, etc.) and hypocalcaemia before phototherapy. Serum ionized calcium and total serum bilirubin is measured at time of start of phototherapy and after 24-72 hours from phototherapy and the results were compared.

Results: The total number of neonates collected within the period of study was 147, from those only 100 fulfilled our inclusion criteria. The total serum bilirubin level among study patients before phototherapy was ranging from (15-18) mg/dl with a mean of 16.28 (± 0.97) mg/dl, whereas it was measured among them after phototherapy from (10-14) mg/dl with a mean of 12.02 (± 1.12) mg/dl. There was statistically highly significant decrease of the total serum bilirubin level after phototherapy, as compared with that before phototherapy in the study patients ($P=0.001$). With respect to the calcium level, ionized serum calcium level before phototherapy was ranging from (1.12-1.33) mmol/L with a mean of 1.225 (± 0.049) mmol/L, whereas the ionized serum calcium level after phototherapy was ranging from (0.65-1.29) mmol/L with a mean of 1.038 (± 0.183) mmol/L. There was highly statistically significant decrease of the serum calcium levels after phototherapy, as compared with serum calcium levels before phototherapy in the study patients ($P=0.001$). After phototherapy, neonates with hypocalcaemia represented 47 cases (47%) and those with normal calcium represented 53 cases (53%).

Conclusion: Hypocalcaemia is a significant complication of phototherapy in full term neonates.

Keywords: Neonatal jaundice, Total serum bilirubin, Ionized serum calcium.

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Neonatal Jaundice (NJ), defined as an abnormally high concentration of bilirubin more than 85 mmol/l (5 mg/dL) in the circulating blood⁽¹⁾. It affects about 60% of term and 80% of preterm infants⁽²⁾, usually occurs during first days of life.

In most of cases, it is benign and no intervention is required, approximately 5-10% of them have clinically significant hyperbilirubinemia in whom the use of phototherapy becomes mandatory⁽³⁾. Jaundice clinically appears as yellowness of skin due to deposition of bilirubin in skin and mucosal membranes and it reflects normal physiological phenomenon in most newborns unconjugated hyper-

*Central Child Teaching Hospital, Baghdad, Iraq.

**Dept. of Pediatrics, Medical College, Al-Mustansiriyah University, Baghdad, Iraq.

bilirubinemia⁽⁴⁾. Neonatal jaundice is mainly due to immaturity in bilirubin metabolism resulting in imbalance between bilirubin production and elimination due to increase red blood cell (RBC) volume per kilogram, decreased RBC life span, increased enterohepatic circulation, defective uptake of bilirubin and immaturity of liver. In spite of basic physiology is the same in preterm and term newborns but preterm newborns at higher risk make proper monitoring and treatment is essential⁽⁵⁾.

As phototherapy was one of the options for management of jaundice, so hypocalcaemia is one of the less known complications but potential adverse effect of phototherapy. Neonatal hypocalcaemia is defined as total serum calcium concentration of < 7 mg/dl or serum ionized calcium decrease less than 1.2 mmol (4.8mg/dl in full term infant and less than 1 mmol (4mg/dl) in preterm infant⁽⁶⁾, usually manifested indifferent ways.

The current study aims to evaluate the effect of phototherapy on serum ionized calcium level in newborns with unconjugated hyperbilirubinemia and to evaluate and interprets it is clinical significance.

Methods

This is a prospective cross-sectional study that was conducted at the neonatal care unit of Central Child Teaching Hospital in Baghdad from the 1st of June 2017 till the 1st of June 2018 were patients collected randomly during this period.

A total of 147 neonates with jaundice only 100 neonates (54 male and 46 female) met our criteria those with unconjugated jaundice requiring phototherapy for at least 24 hours and had a normal serum calcium level before initiation of phototherapy and 47 cases excluded from our study.

The inclusion criteria were: Full term neonates (gestational age 37-41 weeks) with unconjugated jaundice. Hyperbilirubinemia after 48 hours of birth till seventh day. Body weight > 2.5 kg. Bilirubin

level above 15mg/dl. Newborns received breast, artificial, mixed feeding.

Whereas exclusion criteria were: Jaundice appears in first 24 hours of life. Neonatal hypocalcaemia. Preterm babies. Neonates receiving sodium bicarbonate. Neonatal sepsis diagnosed clinically or by laboratory investigations. Perinatal asphyxia. Infant of diabetic mother. Neonates with renal failure. Neonates with respiratory distress syndrome. Any neonates with congenital malformations. Cephalohematoma. Any neonates suspected to have inborn error of metabolism.

After taking consents from parents of selected neonates, history was taken from parents of all neonates and complete physical examination of the newborns was conducted. Laboratory investigations were applied to all neonates which included, blood group and Rh for the neonate and mother, complete blood count and blood film, reticulocytes count, ionized serum calcium (ISC) level and total serum bilirubin (TSB) before and after exposure to phototherapy, direct and indirect bilirubin level, C-reactive protein and blood culture.

Ionized calcium normal value as follows: At 48 hours of age and thereafter: 4.8-4.92 mg/dl (1.12 – 1.23 mmol/L).

According to our laboratory reference (1.12- 1.31mmol/l) based on kit used during study⁽⁶⁾.

Results

Regarding gender, the highest proportion of study patients was male (54%) with male to female ratio of 1.17:1. Study patient's gestational age (GA) ranging from (37-42 weeks), with a mean of 37.96 (± 0.99) week and the highest proportion of study patients delivered between 37 and 39 weeks (54%). Considering mode of delivery, 54% of the patients were delivered by Cesarean section (C/S) and 46% by normal vaginal delivery (NVD). The weights of neonates were ranging from 2-4 kg, the mean was 3.18 (± 0.565) kg. Table 1 shows the chronological age of studied

patients which was ranging from 3 to 7 days with a mean of 4.65 (± 1.31) days. The highest proportion of study patients was found in age group (4-5) days 46% and 68% of them were on breast feeding, the duration of phototherapy was ranging from (1-3) days, with mean of 1.89 (± 0.51) day and the highest proportion of study patients needed phototherapy for two days 74% and no one need phototherapy more than 3 days.

The mean of TSB among study patients before phototherapy was 16.28 (± 0.97) mg/dl, and after phototherapy was 12.02 (± 1.12) mg/dl. There was highly statistically significant decrease after phototherapy, ($P=0.001$).

With respect to the SIC level, the mean before phototherapy was 1.225 (± 0.049) mmol/L, and after phototherapy was 1.038 (± 0.183) mmol/L. There was highly statistically significant decrease after phototherapy, ($P=0.001$).

After exposure to conventional phototherapy, neonates who developed hypocalcaemia represented 47 cases (47%) and those with normal calcium represented 53 cases (53%), (Table 2).

We noticed that there was no significant association ($P \geq 0.05$) between serum calcium level and others factors such as age, gender, mode of delivery, duration of phototherapy and type of feeding, (Table 3).

Table 1: Distribution of study patients by general characteristics.

Variable	No. (n=100)	Percentage (%)
Age (Days)		
3	24	24.0
4 - 5	46	46.0
6 - 7	30	30.0
Duration of phototherapy		
One day	18	18.0
Two days	74	74.0
Three days	8	8.0
Type of feeding		
Breast	68	68.0
Bottle	12	12.0
Mixed	20	20.0

Table 2: Mean of TSB and serum calcium before and after phototherapy.

Variable	Before phototherapy		After phototherapy		P-value
	Mean	SD	Mean	SD	
TSB (mg/dl)	16.28	± 0.97	12.02	± 1.12	0.001
Serum ionized calcium (mmol/L)	1.225	± 0.049	1.038	± 0.183	0.001

Table 3: Association between serum calcium level and certain factors.

Variable	Serum Calcium level		Total (%) n=100	P- value
	Hypocalcaemia (%) n= 47	Normal (%) n= 53		
Age group(days)				
< 4	13 (54.2)	11 (45.8)	24 (24.0)	0.577
4 - 5	22 (47.8)	24 (52.2)	46 (46.0)	
≥ 6	12 (40.0)	18 (60.0)	30 (30.0)	
Gender				
Male	23 (42.6)	31 (57.4)	54 (54.0)	0.338
Female	24 (52.2)	22 (47.8)	46 (46.0)	
Mode of delivery				
C/S	22 (40.7)	32 (59.3)	54 (54.0)	0.174
NVD	25 (54.3)	21 (45.7)	46 (46.0)	
Duration of phototherapy (Days)				
One day	5 (27.8)	13 (72.2)	18 (18.0)	0.071
Two days	36 (48.6)	38 (51.4)	74 (74.0)	
Three days	6 (75.0)	2 (25.0)	8 (8.0)	
Type of Feeding				
Bottle	7 (58.3)	5 (41.7)	12 (12.0)	0.702
Breast	31 (45.6)	37 (54.4)	68 (68.0)	
Mixed	9 (45)	11 (55)	20 (20.0)	

Discussion

Hypocalcaemia is one of the less known complications but potential adverse effect of phototherapy⁽⁹⁾. Only the serum ionized calcium has been found be physiologically active and when the serum ionized calcium level drops below normal, nervous system progressively becomes very sensitive to such change and produce various of clinical signs and symptoms. It is essential for many biochemical processes, including blood coagulation, neuromuscular excitability, cellular enzymatic, cell membrane function and many of the cellular enzymatic activities in the body⁽⁷⁾. In this study, we analyzed 100 full term neonates with unconjugated jaundice and needed phototherapy.

The current study found that mean chronological age was 4.65 (± 1.31) days. The highest proportion of study patients was found in age group (4-5) days 46%. Approximate result was found by Karamifar et al, observed that mean of chronological age was 5.69 (± 2.6) days⁽⁸⁾ but higher mean

was found by Taheri et al, the mean SD for chronological age 6 (± 3) days and can be explained by age limitation in our study⁽⁹⁾.

Regarding gender of our included neonates, the highest proportion of study patients were males 54% with male to female ratio of 1.17:1. Similarly in Rozario et al⁽¹⁰⁾ males constituted highest proportion 59% can be explained by gender preference. In concern to mode of delivery, our study found that 46% of included neonates were the product of normal vaginal delivery and 54% were the product of C/S.

In contrast to these results obtained, the included neonates were predominately the product of vaginal delivery in Rozario et al⁽¹⁰⁾ and Manoj et al⁽¹¹⁾, while Bahbah et al and Tehrani et al^(12,13) showed similar results to ours which can be explained by variation in obstetrical approach indications.

The current study shows that the mean of TSB among study patients before phototherapy was 16.28 (± 0.97) mg/dl,

which dropped after receiving phototherapy to 12.02 (± 1.12) mg/dl. Similar results were found by Bahbah et al, mean TSB 15.48 (± 2.10) mg/dl before phototherapy and after phototherapy 12.41 (± 1.12) mg/dl and Tehrani et al also observed mean TSB before phototherapy 17.59 (± 2.24) mg/dl which decreased 13.76 (± 2.51) mg/dl after photo-therapy^(12,13). Regarding duration of phototherapy, our study shows that highest proportion of study patients required phototherapy for 2 days 74%, similar results were found in Rozario et al⁽¹⁰⁾ and Tehrani et al⁽¹³⁾. Regarding serum ionized calcium level, the mean level before phototherapy was 1.225 (± 0.049) mmol/L, dropped after phototherapy to 1.038 (± 0.183) mmol/L. There was highly statistically significant decrease of the serum ionized calcium after phototherapy, as compared with serum ionized calcium before phototherapy in the current study patients ($P=0.001$), similar results found by Tehrani et al and Prabhakar et al^(13,14) that can be explained by sampling procedure used.

In present study, there was no significant association between reduction in serum ionized calcium following phototherapy regarding age, gender, mode of delivery, type of feeding and duration of phototherapy, similar results was found by Rozario et al⁽¹⁰⁾, Karamifar et al⁽⁸⁾ and Mashal et al⁽¹⁵⁾. Regarding hypocalcemia, our study shows that 47% of included neonates were hypocalcemia, while Bahbah et al and Prabhakar et al^(12,14) showed lower results, that could be attributed to variation in phototherapy duration.

In conclusion: Neonates who exposed to phototherapy are at higher risk of developing hypocalcaemia as complication of phototherapy.

Recommendations: Serum calcium level should be monitored in neonates who exposed to phototherapy for the risk of developing symptomatic hypocalcaemia. We recommended that in future, to evaluate

the beneficial outcome of prophylactic calcium administration to neonates who need phototherapy, in reduction of symptomatic hypocalcaemia.

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