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Phototherapy Induced Hypocalcemia, a Jordanian and Saudi Experience

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ABSTRACT

Background: neonatal hyperbilirubinemia is a common condition in the first few days of life [(1)] and it can be divided into: pathological and physiological and indirect (unconjugated) and direct (conjugated) hyperbilirubinemia. **Objective:** This paper aimed to evaluate the effect of different types of phototherapy on serum calcium of both preterm and full-term infants with indirect hyperbilirubinemia, in either supine or prone position. **Methods:** data were taken from 100 newborns candidate by divided them into two groups. Blue and white light phototherapy were equally used for different infants of both groups. **Results:** the results showed that 31% developed hypocalcemia, 20% preterm and 11% full term infants. 38% developed hypocalcemia, where among infants who received prophylactic phototherapy 24% developed hypocalcemia. 60% of infants who received extensive phototherapy developed hypocalcemia, where 27.7% of infants who managed with single phototherapy developed hypocalcemia. Seventeen of the infants who managed in prone position and 14 infants of those who received phototherapy in supine position developed hypocalcemia. **Conclusion:** all in all, 19 infants developed hypocalcemia under blue light and 12 received white light phototherapy. Phototherapy induced hypocalcemia in both full term and premature infants. In addition to the common practice of monitoring the total serum bilirubin and PCV in all newborns on phototherapy, it is important to monitor the total serum calcium on daily base.

Keywords: phototherapy, calcium, bilirubin, preterm, full-term infant.

INTRODUCTION

Neonatal hyperbilirubinemia is a common condition in the first few days of life [(1)] and it can be divided into: pathological and physiological and indirect (unconjugated) and direct (conjugated) hyperbilirubinemia. Phototherapy proved to be a safe and effective way of treatment in cases of indirect hyperbilirubinemia even it can lead to some complications such as eye trauma, skin rash, dehydration due to rise in temperature and increase evaporation, loose stool, chills, damage to DNA and bronze baby syndrome [(1-4)] . A transient decrease in total serum calcium in newborns with indirect hyperbilirubinemia, while under phototherapy was reported by many authors [(1,2,5-13)].

Objective: This study aimed to evaluate the effect of different types of phototherapy on serum calcium of both preterm and full-term infants with indirect hyperbilirubinemia, in either supine or prone position.

MATERIAL AND METHODS

This was a cross sectional study that was conducted between March 2016 and November 2017 at the level III neonatal intensive care unit and pediatric ward at Prince Hashem Military Hospital and Al-Qurayyat General Hospital, Al-Jouf. A total of 100 newborns candidate for phototherapy (50 preterm and 50 full terms) were divided into two main groups using the odd (group A) and equal numbers (group B) according to the sequence of admission: **A-** infants with indirect hyperbilirubinemia need therapeutic phototherapy (25 preterm infants and 25 full term infants) and **B-** (control group) infants with total serum bilirubin need no therapeutic, but prophylactic phototherapy (25 preterm infants and 25 full term infants). Blue and white light phototherapy were equally used for different infants of both groups. In each group, half of the infants were managed mostly in prone position, while the other half was managed in supine position. Total serum bilirubin, serum calcium, total protein and serum albumin were taken on daily base. Corrected and ionized serum calcium were calculated before the initiation of phototherapy, for the subsequent 3- 5 days of phototherapy and 2 days after termination of phototherapy.

The following inclusion criteria were accepted: infants with normal total serum calcium, of more than 28 weeks gestational age, more than 850 grams birth weight, less than 14 days of life and who started to have indirect hyperbilirubinemia after the second day of life or more.

The infants excluded from the study if met any of the following criteria: infants with direct hyperbilirubinemia, infants received calcium gluconate either intravenously or orally before the initiation of phototherapy. Moreover, those who needed exchange transfusion or blood transfusion for any reason, those who given sodium bicarbonate to correct metabolic acidosis, infants on total parenteral nutrition, those with congenital heart defects, infants of diabetic mothers, infants with refractory hypocalcemia and dysmorphic infants.

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Infants included in the study rounded daily by the attending neonatologist and pediatricians and managed accordingly. Equally important, blood samples have been taken daily by a registered nurse and sent to the local laboratory at both Prince Hashem Military and Al-Qurayyat General Hospital. The results were followed and calculated almost using computerized electronic calculators by the neonatologists and pediatricians participating in this study. We considered hypocalcemia as a total serum calcium of <7 mg/dl in premature infants and as a total serum calcium of <7.5 mg/dl in full-term babies and ionized calcium < 4 mg/dl in both.The patient was the unit of analysis in this study. SPSS version 17 was used for analyzing data. Furthermore, a descriptive statistical study was carried out on the measurements of variables collected. Statistically, significant differences between groups were tested using the Chi-squire test when concerning proportions. The level of significance was set at $P<0.05$.

The study was done after approval of ethical board of Al-Qurayat General Hospital .

RESULTS

Of total 100 newborn infants were included in this study; 31 (31%) developed hypocalcemia, of them 20 (20%) preterm and 11 (11%) full term infants. Of all infants who developed hypocalcemia 2 (6.6%) had symptomatic hypocalcemia (a full term who developed convulsion and a preterm infant who developed severe apnea required intubation).

Table 1: main results of the study

	Therapeutic phototherapy		Prophylactic phototherapy		Supine position		Prone position		White light		Blue light	
	Total	ca↓	Total	ca↓	Total	ca↓	Total	ca↓	Total	ca↓	Total	ca↓
Full term infants	25	6 (31.5%)	25	5 (41.6%)	26	5 (35.7%)	24	6 (35.2%)	26	4 (33.3%)	24	7 (36.8%)
Preterm infants	25	13 (68.4%)	25	7 (58.3%)	26	9 (64.2%)	24	11 (64.7%)	26	8 (66.6%)	24	12 (63.1%)

Table2: hypocalcemia pregnancy duration cross tabulation count

		Pregnancy type		Total
		Premature	Full term	
Calcium	Normal level	30	39	69
	Hypocalcemia	20	11	31
Total		50	50	100

(χ^2 test., $p < 0.05$)

Table 3: hypocalcemia photo type cross tabulation count

		Photo type		Total
		White	Blue	
Calcium	Normal level	37	32	69
	Hypocalcemia	12	19	31
Total		49	51	100

(χ^2 test, $p > 0.05$)

Table 4: hypocalcemia patient position cross tabulation count

		Patient position		Total
		Supine	Prone	
Calcium	normal level	37	32	69
	hypocalcemia	14	17	31
Total		51	49	100

(χ^2 test, $p > 0.05$)

As shown in **table 1**of 50 infants who received therapeutic phototherapy 19 (38%) developed hypocalcemia where of the 50 infants who received prophylactic phototherapy; 12 (24%) developed hypocalcemia to explain, of total 10 infants who received extensive phototherapy 6 (60%) developed hypocalcemia (of them 4 (66.6%) preterm and 2 (33.3%) full term infants). Where of 90 infants who managed with single phototherapy 25 (27.7%) have had hypocalcemia (16 (64%) preterm and 9 (36%) full term infants).

Furthermore, 48 infants (24 preterm and 24 full term infants) who managed in prone position 17 (35.4%) developed hypocalcemia. Where, 14 (26.9%) of total 52 (26 preterm and 26 full terms) infants who received phototherapy in supine position developed hypocalcemia.

Whilst, 50 infants (26 preterm and 26 full terms) who managed under white light 12 (24%) have had hypocalcemia, where of 50 infants in whom blue light phototherapy was used 19 (38%) infants developed hypocalcemia.

Figures 1&2 illustrated that almost hypocalcemia developed after 48-72 hours of phototherapy initiation, and each extra 24 hours associated with 0.4 mg/dl decreased in total serum calcium. Total serum calcium returns back to levels above 8 mg/dl after 24 -48 hours of phototherapy discontinuation.

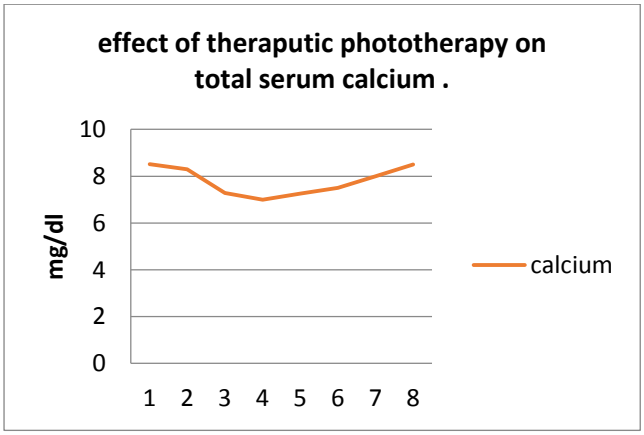

Figure1: effect of therapeutic phototherapy on total serum calcium over time (days).

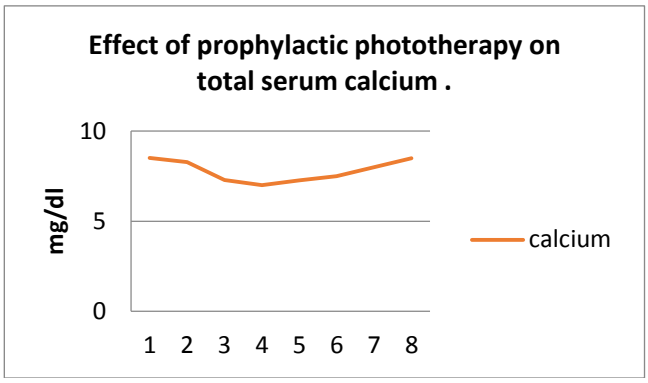

Figure 2: effect of prophylactic phototherapy on total serum calcium over time (days).

DISCUSSION

This study showed that phototherapy induced hypocalcemia in newborn infants is a fact. (31 %) of total 100 newborns who received phototherapy for hyperbilirubinemia developed hypocalcemia. The significant fall in total serum calcium in both term and preterm infants during phototherapy was comparable to earlier studies [8,10,11]. Both the ionized portion of calcium and the corrected calcium levels were also low. Normal total protein and albumin levels in all infants who included in this study and who developed hypocalcemia made hypoalbuminemia unlikely to be the cause of the observed decrease in total serum calcium during our study.Thus, data from our study showed that newborn infants who received extensive phototherapy developed lower levels of serum calcium than those who received single phototherapy a fact which supporting the effect of phototherapy on calcium level and not mentioned in other studies [1,2&5-13].

Our observation showed a relation between the level of total serum bilirubin and the decrease in the level of total serum calcium can be found as shown by the difference in the occurrence of hypocalcemia in both main groups (A (38%) and B (24%)). This fact is not in agreement with results of other authors [1,2 &5-13] who studied the effects of phototherapy on serum calcium. Moreover, this relation could be explained by prolonged duration and more extensive phototherapy needed when high levels of total serum bilirubin were observed.

In addition, when subjects cross tabulated for calcium level and duration of pregnancy as shown in (**Table 2**), we found that preterm infants who received phototherapy developed more and lower total serum calcium than did the full term ones (40 % and 22 % respectively), which is clinically and statistically significant ($p < 0.05$), and this could be explained by the fact that premature infants are born

for hypocalcemia [1]**.** Above all, the difference in this study was statistically not significant ($p > 0.05$), but for unclear reason . The frequency of phototherapy induced hypocalcemia found to be higher among the newborns who managed by the blue light phototherapy than those who managed using the white light phototherapy (19 % and 12 % respectively) and this makes our study different from other studies [5-11] who suggested more prevalence of hypocalcemia associated with the use of white light phototherapy. Thus, we recommend the use of white light phototherapy for the treatment of indirect hyperbilirubinemia of the newborn infants.

Equally important, we did not find big difference in the occurrence of phototherapy induced hypocalcemia among the newborn infants who managed in either supine (14%) or prone position (17%) and this was statistically not significant ($p > 0.05$). The fact that makes the dogmas that explaining the occurrence of hypocalcemia by the direct inhibitory effect of phototherapy light on the pineal body under the uncovered occipital area, that causes increase calcium uptake by bone after the blocking effect of melatonin decreases (as hypothesized by other authors [5-12]) weak and calls for further research to understand the exact mechanism that stand behind the decrease in the total serum calcium caused by phototherapy.

So, our study showed that there was a relation between the decrease in the calcium level and the duration of phototherapy; moreover an observation which not studied by other authors beforehand. Also, to reach almost the initial total serum calcium it needs 24-48 hours after discontinuation of phototherapy.Two infants (6.6% of total 31 infants who had low calcium levels during phototherapy) developed symptomatic hypocalcemia (of them premature infants who develop severe apnea needed intubation and ventilatory support in addition to intravenous calcium gluconate, and a full-term baby who had focal convulsions which responded to intravenous calcium gluconate. Both cases underwent full work- up for the events and no cause could be identified but low serum calcium.Indeed, this fact makes us think seriously about the role of the prophylactic calcium during phototherapy to decrease the occurrence of both symptomatic and asymptomatic hypocalcemia.

Although, it was not the aim of our study, but we found that the decrease in the total serum bilirubin is not affected by the position of the newborn infant while on phototherapy.

Hence, our study has a major limitation that we did not study the effects of phototherapy on urinary calcium excretion, as this was suggested by **Hooman and Honarpisheh** [13] to be the cause that stands behind the hypocalcemia that induced by phototherapy.

CONCLUSION

Phototherapy induced hypocalcemia in both full term and premature infants. In addition to the common practice of monitoring the total serum bilirubin and PCV in all newborns on phototherapy, it is important to monitor the total serum calcium on daily base.

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