The Effect of Phototherapy on Serum Calcium and Magnesium Level in Newborns Gestational Age 36 Weeks and Above

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ABSTRACT

Objective: To investigate the phototherapy effect on serum calcium and magnesium levels of children with gestational age 36 weeks or above.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Department of Pediatric, King Fahad Armed Forces Hospital, Jeddah from Jan to Sep 2019.

Methodology: Total of 200 participants were recruited into the study after obtaining informed consent. Patients' characteristics were obtained from medical record file. Their mothers were interviewed. Before phototherapy, laboratory investigations were done. Phototherapy was performed with conventional method 410-417mm wave length was maintained and patients was kept at distance of 20cm. After phototherapy completion, laboratory investigations were repeated and difference was noted.

Results: Out of 200 patients, 54% were males and 46% were females. Average age of patients was 1.85 ± 0.96 days with range 0-5 days. Decrease in calcium and magnesium levels was observed in 64 (32%) and 49 (24.5%) patients respectively following phototherapy completion. There was statistically significant mean difference in calcium and magnesium levels after phototherapy and bilirubin was also significantly decreased.

Conclusion: Decrease was observed in calcium and magnesium levels following phototherapy. Phototherapy may lead to decrease levels of calcium and magnesium, hence frequent assay warranted. Further investigations should be conducted in our region enrolling only neonates to confirm phototherapy induced hypocalcaemia and hypomagnesaemia.

Keywords: Bilirubin, Calcium, Gestational age, Magnesium, Phototherapy

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INTRODUCTION

Jaundice refers to the yellow-orange skin and sclera discoloration due to high bilirubin levels in the mucous membrane and skin.[1] Among neonates, one of the most prevailing conditions is hyperbilirubinemia which commonly occurs during the neonatal period, particularly within first week of birth.[2] The condition occurs in approximately, 60% and 80% of term and preterm infants respectively.[3] Potential risk factors of severeneonatal jaundice include neonatal sepsis and prematurity.[1] Jaundice is a benign condition but it should be timely assessed because delay in diagnosis and management of severe hyperbilirubinemia may cause acute bilirubin encephalopathy which further increases the risk of kernicterus spectrum disorders (KSD). Bilirubin neurotoxicity causes temporary and permanent brain damage.[4,5] Thus, timely diagnosis and management is of utmost importance.

National Institute of Child Health and Human Development declared phototherapy, as an effective approach to for managing hyperbilirubinemia.[5,6] Even though the phototherapy is widely used non-invasive technique to treat hyperbilirubinemia but various complications are associated with it including dehydration, bronze baby syndrome, skin rash, diarrhea, raised body temperature, ocular injury, hypocalcemia, redistribution of gentoxicity and blood flow.[7]

It is documented in literature that after phototherapy, hypocalcemia occurred among more than 80% and 66.66% preterm and term neonates respectively.[8] Various complications are associated with hypocalcemia in neonates such as tremor, apnea, seizures, tetanus and muscle cramps.[9] There is vital role magnesium in protection of neural system next to hypoxia and neurotoxic effect of bilirubin by obstructing NMDA receptor. Some studiesreported decreasein magnesium levels following phototherapy.[10]

Since timely and effective treatment of hyperbilirubinemia is of utmost importance as it reduces the risk of brain damages and other complications. In addition to this, in our setting phototherapy is considered as the primary management option but some studies documented that phototherapy leads to deficiency in calcium and magnesium levels that may further increase complications in neonates.

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In addition to this, to the best of our knowledge, locally the available data is too scarce. Thus, it is of high importance to uncover the effects the phototherapy on calcium and magnesium levels among children in Saudi Arabia. In the light of available literature, we hypothesized that phototherapy reduces calcium and magnesium levels and the current study was planned to investigate this effect of phototherapy on calcium and magnesium levels among children of gestational age 36 weeks or above.

METHODOLOGY

This cross sectional study was conducted at at Well Baby Nursery department, King Fahad Armed Forces Hospital, Jeddah from January to September, 2019. The study was conducted after acquiring Ethical approval from Hospital Ethics Committee with reference to ERC no. REC 273.

Inclusion Criteria: Neonates with age 0 to 14 days with gestational age 36 weeks or above, diagnosed as neonatal jaundice and requiring phototherapy for at least 48 hours were included in the study.

Exclusion Criteria: Patients with congenital anomalies, serum calcium and serum magnesium less than 2 mmol/1 and 0.65 mmol/1 respectively at baseline, AGPR less than 7 at 5 minutes, neonates with diabetic mothers, mothers received magnesium sulfate and anticonvulsants medications and positive history of exchange transfusion were excluded.

Informed consent was taken from attendants before enrolling patients into the study. WHO sample size calculator was used to estimate sample size. 67% prevalence,[11] 7% margin of error and 95% Confidence interval were used to calculate sample size. The calculated sample size was 174. Drop rate of 15% due to other complications occurring during phototherapy was considered. Therefore, total 200 patients were enrolled into the study using non-probability consecutive sampling technique.

Detailed examination of patients was performed after admission and their characteristics were collected from patients' medical record file. Patients' mothers were also interviewed to record maternal history. Sterilized and disposable syringes were used to draw patients' blood either from feet veins or peripheral and sent to laboratory. Complete blood count, reticulocyte count, Direct Coombs test, serum calcium, albumin and magnesium levels, bilirubin, thyroid profile and G6PD were investigated.

Photo-therapy was performed with the conventional treatment having four blue fluorescent lights. A wave length of range 410-470mm was maintained above the patients' head inside the incubator. A distance of 20cm was maintained from skin surface of patients to lights with complete covering of eyes and genitals. Serum calcium and serum magnesium level were repeated after 12 hours of completion of phototherapy. Patients' who developed other diseases during the treatment were excluded.

All of the collected data was entered into statistical package SPSS-19 to perform statistical analysis. Categorical variables were presented as freq-uency with percentage. Quantitative variables were summarized as mean ± standard deviation. Paired sample t-test was applied to assess difference in calcium and magnesium levels at baseline and after phototherapy. The *p*-value ≤0.05 was taken statistically significant.

RESULTS

Total 200 patients were assessed and enrolled into the study. Average age of patients was 1.85 ± 0.96 days with age range 0-5 days. There were108 (54%) males and 92 females (46%). Majority of neonates (n=134, 67%) were normally delivered while 65 (32.5%) had history of cesarean section and only 1 (0.05%) was ventous as presented in Table-I.

Table-I:Descriptive statistics of study population.

	n(%)			
	Decreased Calcium (n=64)	**Decreased Calcium (n=49)**	**Decreased Ca and Mg (n=22)**	**Overall**
Age (days)	1.60 ± 1.00	1.95 ± 0.95	1.81 ± 1.22	1.85 ± 0.96
Gestation (weeks)	38.51 ± 1.50	38.3 ± 1.37	38.5 ± 1.47	38.43 ± 1.41
Birth Weight (kg)	2.82 ± 0.50	2.75 ± 0.46	2.82 ± 0.48	2.81 ± 0.47
Gender				
Male	40 (62.5)	28 (57.1)	15 (68.2)	108 (54)
Female	24 (37.5)	21 (42.9)	7 (31.8)	92 (46)
Delivery Mode				
ELCS	6 (9.4)	6 (12.2)	4 (18.2)	18 (9)
EMCS	16 (25)	19 (38.8)	9 (40.9)	47(23.5)
SVD	41 (64.1)	24 (49)	9 (40.9)	134 (67)
Ventous	1 (1.6)	-	-	1 (0.5)

After completion of phototherapy, decrease in serum calcium and magnesium levels was observed in 64 (32%) and 49 (24.5%) patients while decrease of both calcium and magnesium was observed in 22(11%) respectively (Figure).

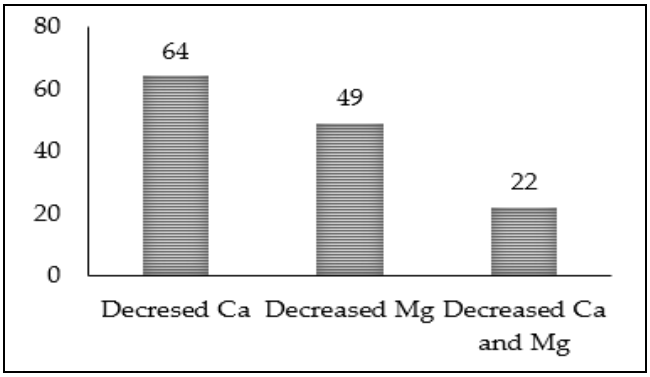

Figure: Frequency of decreased calcium, magnesium and both.

Overall average bilirubin, calcium and magnesium at baseline were 158.51 ± 28.52 Umol/l, 2.30 ± 0.15 mmol/l and 0.78 ± 0.07 mmol/l respectively. After phototherapy overall average bilirubin, calcium and magnesium were 138.23 ± 27.51 Umol/l, 2.39 ± 0.16 mmol/l, 0.79 ± 0.07 mmol/l respectively. We found significant pre and post mean difference for bilirubin (p=0.000), calcium (p=0.000) and magnesium (p=0.000).

Among patients with decreased calcium, significant pre and post mean difference was found for bilirubin (p=0.000) and calcium (p=0.000). Among patients with decreased magnesium, significant pre and post mean difference was found for bilirubin (p=0.000) and magnesium (p=0.000) while among patients with decreased calcium and magnesium, significant pre and post mean difference was found for bilirubin (p=0.003), calcium (p=0.000) and magnesium (p=0.000) as presented in Table-II.

DISCUSSION

During the beginning of neonatal period, hyperbilirubinemia is a frequent occurring problem among term and preterm neonates which is commonly considered as benign condition in infants with high incidence in preterm than in term newborns.[9-12] Globally, neonatal jaundice is common for neonatal morbidity and hospitalization and the potential reason of neonates readmission.[12] Timely diagnosis and treatment of hyperbilirubinemia is essential as the condition may lead to severe hyperbilirubinemia that leads to kernicterus spectrum disorders.

In our health care system, neonates presenting with jaundice primarily managed with phototherapy. But some studies observed decrease in calcium, magnesium and vitamin D levels as side effects of phototherapy. Neonatal hypocalcemia following phototherapy was first observed by Romagnoli *et al,* in 1979.[13]

It was observed in our study that calcium levels were decreased in 32% patients. Another similar study conducted in India reported 26% incidence of hypocalcemia.[12] Significant decrease in calcium levels following 24, 48 and 72 hours of phototherapy was also observed by Barak *et al,* in his study.[14] Reduction in calcium was also evident in an Iranian study that showed after 48 hours of phototherapy the mean reduction in calcium level was 0.34mg/dl.[15] However, in the current on average, there was rise of 0.09 mmol/lin calcium levels after completion of phototherapy. Most likely, the cause of hypocalcemia after phototherapy among neonates is reduction in corticosterone secretion and melatonin levels.[16]

Table-II: Pre and post mean comparison of bilirubin, calciumand magnesium.

	Study Parameters	Mean ± SD		*p*-value
		Before phototherapy	After phototherapy	
Overall (n=200)	Bilirubin (Umol/l)	158.51 ± 28.52	138.23 ± 27.51	<0.01
	Calcium (mmol/l)	2.30 ± 0.15	2.39 ± 0.16	<0.01
	Magnesium (mmol/l)	0.78 ± 0.07	0.79 ± 0.07	<0.01
Decreed Calcium (n=64)	Bilirubin (Umol/l)	152.56 ± 25	135.82 ± 23.23	<0.01
	Calcium (mmol/l)	2.36 ± 0.17	2.27 ± 0.17	<0.01
	Magnesium (mmol/l)	0.77 ± 0.08	0.76 ± 0.07	0.266
Decreased Magnesium (n=49)	Bilirubin (Umol/l)	166.73 ± 32.74	137.18 ± 29.22	<0.01
	Calcium (mmol/l)	2.30 ± 0.17	2.33 ± 0.20	0.201
	Magnesium (mmol/l)	0.80 ± 0.08	0.75 ± 0.07	<0.01
Decreased calcium and Magnesium (n=22)	Bilirubin (Umol/l)	157.31 ± 23.62	136.95 ± 23.78	<0.01
	Calcium (mmol/l)	2.29 ± 0.21	2.20 ± 0.20	<0.01
	Magnesium (mmol/l)	0.79 ± 0.11	0.73 ± 0.08	<0.01

The reduction in magnesium levels was observed in 24.5% in the current study. The finding is consistent with other similar study conducted in India that also observed drop in magnesium levels following phototherapy.[12] Mohammed *et al,* also reported significant decrease in magnesium levels 10. Imani *et al,* and Khosravi *et al* also observed drop in magnesium levels after phototherapy.[17,18] In our study, the slight significant rise of 0.01 Umol/l in magnesium was observed after completion of phototherapy. The current study also found significant decrease in bilirubin levels

which is consistent with other studies.[12,15,19] The possible explanation of rise in magnesium levels in hyperbilirubinemia may be due to the bilirubin toxic effects.[20] However, none of our neonate was symptomatic and does not require any intervention.

Some of the limitations of the present study are that it didn't make compare calcium and magnesium levels separately for preterm and full term neonates. Secondly, maternal practices for neonatal care such as colostrum's discarding or using and maternal level of calcium and magnesium should also be observed to investigate whether frequency of hypocalcemia and hypomagnesemia was differed among babies of healthy and unhealthy mothers following 48 hours of phototherapy.

CONCLUSION

Decrease was observed in calcium and magnesium levels following phototherapy. Phototherapy may lead to decrease levels of calcium and magnesium, hence frequent assay warranted. Further investigations should be conducted in our region enrolling only neonates to confirm phototherapy induced hypocalcemia and hypomagnesemia.

Conflict of Interest: None.

Authors' Contribution

HI: Provided the main idea of research work and research design, collected data and did data analysis followed by data interpretation and wrote research manuscript, NK: Helped in data collection and interpretation and did proof reading of final manuscript.

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