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Original Research Article

Study to Determine the Effect of Phototherapy on Serum Magnesium Level in Term Neonates with Hyperbilirubinemia: An Observational Study

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Abstract

Aim: The aim of the present study was to determine the effect of phototherapy on serum magnesium level in term neonates with hyperbilirubinemia.

Material & methods: A prospective hospital-based comparative study was conducted on 200 eligible neonates admitted in the Department of Neonatology, receiving phototherapy for the period of one year. informed consent was obtained from the parents of the selected neonates. This study included 200 full-term neonates who were subjected to phototherapy for treating neonatal hyperbilirubinemia according to the guidelines of the American Academy of Pediatrics.

Results: Our study included 200 full-term neonates with jaundice who received phototherapy for treating neonatal indirect hyperbilirubinemia, comprising 130 (65%) males, and 70 (35%) females, with the mean gestational age of 37 ± 0.8 weeks and mean postnatal age of 5.4 ± 1.3 days. There were 68 (34%) neonates delivered by normal vaginal delivery and 132 (66%) neonates delivered by cesarean section. Mean birth weight was 3.2 kg. Subjects have a mean intrauterine age of 38.45 weeks and a jaundice onset age of 3.67 days. The mean difference of jaundice onset age, intrauterine age, admission weight and mother's age were not significant. Serum total magnesium level in single and double phototherapy decreases after treatment, but this decrease is significant only in the double phototherapy group (P = 0.032). In the intensive group, this parameter has slightly increased, which is not statistically significant (P = 0.575). The serum total magnesium level and its changes were reported in three groups before and after phototherapy. The serum magnesium level in new borns before treatment was normal in all three treatment groups. The status of each patient showed that single, double, and intensive phototherapy groups have magnesium content of more than 2.2 mg/dl, respectively.

Conclusion: In the present study, the serum magnesium level showed a significant reduction only in the double phototherapy method and remained in the normal range in the other two groups. On the other hand, in all three treatment groups, the level of serum magnesium before the treatment was normal and did not increase significantly.

Keywords: Hyperbilirubinemia, Magnesium, Phototherapy

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Introduction

In neonates, jaundice is a common occurrence that requires immediate medical attention. Unconjugated bilirubin deposits in the skin, nail bed, and sclera of babies with jaundice, turning the skin, nail bed, and sclera yellow. [1] Neonates appear jaundiced when it exceeds 7 mg/dl; clinical jaundice affects one-quarter to half of all term infants, and higher percentages are typical in infants born before term. Furthermore, the maximum blood bilirubin level in well-term newborns is over 12.9 mg/dl in 6.1 percent of them. [2] Hyperbilirubinemia is a serious medical condition that is the leading cause of infant hospitalisation in Southeast Asia. [3] Indirect hyperbilirubinemia (nonconjugated) and direct hyperbilirubinemia (conjugated) are the two kinds of jaundice in newborns (conjugated). Direct hyperbilirubinemia has little effect on the brain, whereas indirect hyperbilirubinemia is toxic and detrimental.

When indirect bilirubin levels in neuronal cells reach dangerously high levels, it accumulates in the nerve membrane, permanently harming the central nervous system. [3] Bilirubin build-up in the neurons of the brain basal ganglia causes encephalopathy, Kernicterus, and athetoid cerebral palsy. High bilirubin levels in newborns, in contrast to adult jaundice, impair the neurological system, which is linked to the neonate's blood-brain barrier not fully maturing. [4-7] Magnesium is the body's fourth most abundant element, with the vast bulk of it stored in intracellular compartments. The relationship between extracellular magnesium concentrations and manifestation, on the other hand, is important to doctors. The gastrointestinal, skeletal, and renal systems are the main organ systems involved with magnesium homeostasis, despite the fact that the regulators regulating these organs at the cellular level are still unknown. Hypermagnesemia is uncommon, occurring largely in the elderly and those with renal failure, and there is evidence that plasma ionised Mg levels are linked to the severity of hyperbilirubinemia in infants. [2]

Bilirubin deposition in neurons results in irreversible neuronal damage. Bilirubin binds to the phospholipids of NMDA receptors that are found in plasma membranes. Magnesium is an NMDA antagonist that inhibits bilirubin's neurotoxic effects. Phototherapy has been linked to a number of side effects in the treatment of neonatal hyperbilirubinemia, but nothing is known about how it affects serum magnesium levels. [2]

The most commonly used treatment for hyperbilirubinemia is phototherapy. Phototherapy has minor complications including hyperthermia, fever, diarrhea effects on blood cells, cytokines, and vitamins, as well as ocular and dermatological complication. Magnesium plays a role in protecting the neural system against hypoxia and neurotoxic effects of bilirubin, through blocking N-methyl-D-aspartate (NMDA) receptor. Bilirubin leads to hyperactivity of the NMDA receptor and exerts neurotoxic effects through binding to NMDA, which has a key role in synaptic physiologic functions and memory. [8] Therefore, this study was carried out to determine the effect of phototherapy on serum magnesium level in term neonates with hyperbilirubinemia.

Materials & Methods

A prospective hospital-based comparative study was conducted on 200 eligible neonates admitted in the Department of Neonatology, Yashvi Children Hospital, Patna, Bihar, India, receiving phototherapy for the period of one year. informed consent was obtained from the parents of the selected neonates. This study included 200 full-term neonates who were subjected to phototherapy for treating neonatal hyperbilir-ubinemia according to the guidelines of the American Academy of Pediatrics. [9]

Exclusion Criteria

- Neonates who had direct bilirubin more than 20%, exchange transfusion cases.
- Neonates with cephalohematoma, congenital malformation.
- Inborn errors of metabolism and sepsis.
- Neonates whose mothers received magnesium sulfate or oxytocin at any time during gestation,
- Intrauterine growth retardation,
- Infants of diabetic mothers,
- Neonates on intravenous fluid,
- Hypocalcemia
- Hypomagnesemia before starting phototherapy, and
- Hemolytic hyperbilirubinemia.

Each neonate was subjected to detailed history taking (gestational age, mode of delivery, detailed prenatal, natal history, age on admission, and day of onset of jaundice, family history of neonatal jaundice) and clinical examination.

Before starting phototherapy, venous blood sample was sent for serum magnesium (total and ionized), and it was considered as control. Serial measurements of (total–ionized) serum magnesium levels were done at 48 h after phototherapy and after termination of phototherapy Laboratory investigations included serial measurements of total serum bilirubin levels (at admission, 48 h after phototherapy and at discharge), blood groups and rhesus factor to infant and mother, reticulocytic count, serum calcium, complete blood count, C-reactive protein, liver function test, and Coombs test. Thereafter, all data were tabulated and analyzed statistically to detect the effect of phototherapy on the serum magnesium level.

Statistical Analysis

The collected data were revised, coded, tabulated, and introduced to a computer software using (IBM Corp.Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, New York: IBM Corp.). Shapiro test was done to test the normality of data distribution. Paired sample t test was used to assess changes over time. The correlation coefficient defines the strength and direction of the linear relationship between two variables. P value is significant if less than 0.05 at confidence interval 95%.

Results

Table 1: Demographic details

Gender	**N%**
Male	130 (65)
Female	70 (35)
Mode of delivery	
NVD	68 (34)
LSCS	132 (66)
Neonatal age (days) Mean±SD	5.4±1.3
Gestational days (weeks) Mean±SD	37±0.8
Birth weight (kg) Mean±SD	3.2±0.2

Our study included 200 full-term neonates with jaundice who received phototherapy for treating neonatal indirect hyperbilirubinemia, comprising 130 (65%) males, and 70 (35%) females, with the mean gestational age of 37 ± 0.8 weeks and mean postnatal age of 5.4 ± 1.3 days. There were 68 (34%) neonates delivered by normal vaginal delivery and 132 (66%) neonates delivered by cesarean section. Mean birth weight was 3.2 kg.

Table 2: Characteristics of neonates for the treatment groups

Variable	Single		Double		Intensive		
	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	P value
Jaundice onset age (day)	3.60 ± 1.75	2-12	3.16 ± 1.40	2-9	3.14 ± 1.52	2-10	0.420
Intrauterine age (week)	38.45 ± 0.50	38-40	38.42 ± 0.85	38-41	38.72 ± 0.72	38-41	0.030
Admission weight (gr)	2684 ± 320	2500-3900	3246 ± 340	2500-4150	3165 ± 356	2500-4000	0.160
Mother's age (year)	27.46 ± 4.32	17-39	28.47 ± 5.30	16-40	29:32 ± 5.25	16-42	0.120

Subjects have a mean intrauterine age of 38.45 weeks and a jaundice onset age of 3.67 days. The mean difference of jaundice onset age, intrauterine age, admission weight and mother's age were not significant.

Table 3: Total serum bilirubin levels before and after single, double, and intensive phototherapy

Phototherapy types	Before		After	Differences (mg/dl)	
		Mean±SD			
Single		16.32 ± 0.6	8.40 ± 1:40	−7:92 ± 1:56	<0.001
Double		18.36 ± 0.70	8.75 ± 1:42	−9:61 ± 1:65	<0.001
Intensive		20.60 ± 2.40	9.20 ± 1.22	−11.4 ± 2:73	<0.001

The amount of total serum bilirubin decreases in all groups.

Table 4: Serum magnesium levels before and after single, double, and intensive phototherapy

Phototherapy types	Before	After	Differences (mg/dl)	
		Mean±SD		
Single	2.05 ±0.30	2.00 ± 0.30	−005 ± 0.25	0.590
	2.18 ±0.36	2.08 ± 0.32	−0.1 ±0.42	0.032
Double				
Intensive	2.02 ± 0.35	2.05 ± 0.28	0.03 ± 0.30	0.575

Serum total magnesium level in single and double phototherapy decreases after treatment, but this decrease is significant only in the double phototherapy group (P = 0.032). In the intensive group, this parameter has slightly increased, which is not statistically significant (P = 0.575). The serum total magnesium level and its changes were reported in three groups before and after phototherapy.

Table 5: Serum magnesium status before and after phototherapy in three treatment groups

Phototherapy types	<1.5 N	1.5-2.2 N	<2.2 N	<1.5 N	1.5-2.2 N	<2.2 N	P
Single	0	0	14	0	50	16	0.565
Double	6	50	40	6	52	16	0.003
Intensive	4	60	26	4	40	16	0.942

The serum magnesium level in new borns before treatment was normal in all three treatment groups. The status of each patient showed that single, double, and intensive phototherapy groups have magnesium content of more than 2.2 mg/dl, respectively.

Discussion

Neonatal hyperbilirubinemia (NH) is the commonest clinical problem occurring during the first week of life, as more than two thirds of newborns develop clinical jaundice [10,11] that can be treated by phototherapy, exchange transfusion, or by pharmacologic agents. Phototherapy is the most common intervention in therapy used as it is relatively safe and non-invasive. [3,12] The conventionally used light sources in phototherapy are fluorescent tubes and halogen spotlights. However, they cannot be placed close to the infant as they produce considerable amount of heat. Due to this limitation, light-emitting diodes (LEDs) have been used as alternatives as they produce low heat rendering them safe to be placed very close to the infant. [13,14] Jaundice is the most common condition that requires medical attention and hospital readmission in newborns. The yellowish coloration of the skin and sclera in newborns with jaundice is the result of the accumulation of unconjugated bilirubin. [15]

Our study included 200 full-term neonates with jaundice who received phototherapy for treating neonatal indirect hyperbilirubinemia, comprising 130 (65%) males, and 70 (35%) females, with the mean gestational age of 37 ± 0.8 weeks and mean postnatal age of 5.4 ± 1.3 days. There were 68 (34%) neonates delivered by normal vaginal delivery and 132 (66%) neonates delivered by cesarean section. Mean birth weight was 3.2 kg. Subjects have a mean intrauterine age of 38.45 weeks and a jaundice onset age of 3.67 days. The mean difference of jaundice onset age, intrauterine age, admission weight and mother's age were not significant. The mean difference of jaundice onset age, intrauterine age, admission weight and mother's age were not significant. The amount of total serum bilirubin decreases in all groups. Our study showed that there was a statistically significant positive correlation between total bilirubin and magnesium (total and ionized) in all studied neonates. This agreed with the study done by Sapkota. [16]

Serum total magnesium level in single and double phototherapy decreases after treatment, but this decrease is significant only in the double phototherapy group (P = 0.032). In the intensive group, this parameter has slightly increased, which is not statistically significant (P = 0.575). The serum total magnesium level and its changes were reported in three groups before and after phototherapy. The serum magnesium level in new borns before treatment was normal in all three treatment groups. The study by Meghana [17] concluded that average magnesium value noted before phototherapy was 2.8 mg/dl and after phototherapy was 1.7 mg/dl, showing a significant difference. Subhashini et al [18] observed that serum magnesium levels before phototherapy in newborns were increased. There was a significant decrease in the level of magnesium after phototherapy, but none reached hypomagnesemia. Bezboruah and Majumder [19] discovered only a significant reduction of mean serum magnesium value following phototherapy.

The status of each patient showed that single, double, and intensive phototherapy groups have magnesium content of more than 2.2 mg/dl, respectively. In our study, serum magnesium level showed a significant reduction after phototherapy in double phototherapy, but this difference did not show significant changes in both single and intensive phototherapy methods. The reason for insignificant findings in single and intensive phototherapy methods may be a delay in blood sampling due to ethical issues because in our study, no additional blood sampling was performed. Reduced serum magnesium levels after double phototherapy are probably due to increased levels of plasma magnesium in association with hyperbilirubinemia, in which after phototherapy, the magnesium level decreases in association with bilirubin reduction. Since only 1% of the body's magnesium is extracellular, most of these changes are due to the displacement of magnesium between the inside and outside of the cell. Therefore, with increasing bilirubin, plasma levels of magnesium also increase as a result of cellular degradation or as a defense mechanism. In Khosravi et al.'s study, the total serum magnesium levels decreased significantly after phototherapy; it is similar to our results in double phototherapy methods. [20]

In a study, Sarici et al.'s reported that in the severe hyperbilirubinemia group, serum ionized magnesium levels were significantly higher in comparison to the moderate hyperbilirubinemia group. [21] But our results revealed that the serum magnesium level was normal in all three groups before the treatment, and there was no increase in serum magnesium level. In Sarici et al.'s study, the increase in magnesium levels in severe hyperbilirubinemia was caused by magnesium leakage from damaged neurons and red blood cells to exert its protective effect on the nervous system. Shahriarpanah et al [22] found that the serum level of magnesium decreased through relieving hyperbilirubinemia, and the increase in the plasma level of magnesium might be owing to synchronization with hyperbilirubinemia too.

Conclusion

Bilirubin exerts its neurotoxicity effect by binding to the NMDA receptor in the neural synapse. Magnesium is one of the most important inhibitors of the NMDA receptor. The body increases the level of extracellular magnesium to reduce the neurotoxicity effects of bilirubin as a defense mechanism. In the present study, the serum magnesium level showed a significant reduction only in the double phototherapy method and remained in the normal range in the other two groups. On the other hand, in all three treatment groups, the level of serum magnesium before the treatment was normal and did not increase significantly.

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