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Original Research Article

Investigating the Impact of Phototherapy on Serum Magnesium Levels in Full-Term Neonates with Hyperbilirubinemia

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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 Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India receiving phototherapy for the period of 2 years. After approval of the ethical committee, 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 5.2 ± 1.4 days. There were 68 (34%) neonates delivered by normal vaginal delivery and 132 (66%) neonates delivered by cesarean section. Mean birth weight was 3.1 kg. 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. Serum total magnesium level in single and double phototherapy decreases after treatment, but this decrease is significant only in the double phototherapy group (P = 0.022). In the intensive group, this parameter has slightly increased, which was not statistically significant (P = 0.530). 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

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 [1,2] 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. [3,4] 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. [5,6] Intensive phototherapy can also shorten the total phototherapy time and period of hospital stay. [7,8] Phototherapy may produce a transient rash, transit green stools, lethargy, or abdominal distension. [9] Sometimes, there is an increase skin and muscle blood flow, insensible water loss, skin temperature, heart, and respiratory rates. So, neonates undergoing phototherapy are at a higher risk of electrolyte changes.

Hyperbilirubinemia is a substantial clinical problem that is the most common cause of newborn hospitalization. Neonatal jaundice is defined as a total serum bilirubin level above 5 mg per dl (86 μmol/l) or total serum bilirubin more than 95th percentile. Jaundice affects at least 60% of full-term and 80% of preterm neonates.[2] There are two main types of jaundice in neonates, indirect hyperbilirubinemia (nonconjugated) and direct hyperbilirubinemia (conjunctival). Direct hyperbilirubinemia does not lead to neurotoxicity, while indirect hyperbilirubinemia is toxic and harmful for the brain. When indirect bilirubin reaches a toxic level for neuronal cells, it deposits in the nerve membrane and causes permanent neurological damage to the central nervous system. [9-13] There was a positive relation between serum magnesium and bilirubin levels, and it was propounded that rising of magnesium in hyperbilirubinemia might be a compensatory mechanism against toxic effects of bilirubin. [14] Therefore, measurement of ionized magnesium provides an accurate assessment of the unbound form of magnesium. [15] Phototherapy is the safest and commonly used treatment option for neonatal jaundice. Phototherapy leads to some adverse complications, but the potential complications of phototherapy are hypocalcemia and hypomagnesemia. [16] The mechanism of hypomagnesemia following phototherapy has been explained as unconjugated bilirubin gets deposited on the outer membrane of the neurons and causes bilirubin toxicity. To prevent the deposition of bilirubin in the outer membrane, intracellular magnesium goes out from the neurons, erythrocytes, and cardiocytes and gets deposit in the outer membrane. Cells get damage as intracellular magnesium goes out from the cells and plasma ionized magnesium goes up. So, this protective mechanism itself causes neuronal and cardiac damage. Phototherapy reduces bilirubin. As a result of this, the movement of magnesium from intracellular to extracellular is stopped, and this leads to decrease in the plasma ionized magnesium and serum magnesium also. [17]

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 Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India receiving phototherapy for the period of 2 years. After approval of the ethical committee, 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.[18]

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	5.2±1.4
Gestational days (weeks) Mean±SD	37±0.8
Birth weight (kg) Mean±SD	3.1±0.3

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 5.2 ± 1.4 days. There were 68 (34%) neonates delivered by normal vaginal delivery and 132 (66%) neonates delivered by cesarean section. Mean birth weight was 3.1 kg.

Table 2: Total serum bilirubin levels before and after single, double, and intensive phototherapy

Phototherapy types	Before	After	p-value
Single	15.30 ± 0.5	8.42 ± 1.48	<0.001
Double	18.32 ± 0.72	8.75 ± 1.42	<0.001
Intensive	20.64 ± 2.44	9.20 ± 1.22	<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	p-value
Single	2.07 ±0.32	2.00 ± 0.34	0.525
Double	2.20 ±0.38	2.08 ± 0.32	0.022
Intensive	2.04 ± 0.36	2.05 ± 0.28	0.530

Serum total magnesium level in single and double phototherapy decreases after treatment, but this decrease is significant only in the double phototherapy group (P = 0.022). In the intensive group, this parameter has slightly increased, which was not statistically significant (P = 0.530). 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		14	0	50	15	0.540
Double	6	50	40	6	52	15	0.004
Intensive	4	60	26	4	40	15	0.944

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 [19,20] 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. [21] 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. [22,23] 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. [25]

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 5.2 ± 1.4 days. There were 68 (34%) neonates delivered by normal vaginal delivery and 132 (66%) neonates delivered by cesarean section. Mean birth weight was 3.1 kg. 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. [14]

Serum total magnesium level in single and double phototherapy decreases after treatment, but this decrease is significant only in the double phototherapy group (P = 0.022). In the intensive group, this parameter has slightly increased, which was not statistically significant (P = 0.530). 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. Subhashini et al [26] 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 [27] 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. [28]

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.[29] 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[30] 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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