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Original Article

New Insight into the Effect of Phototherapy on Serum Magnesium Level

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ABSTRACT

***Background*:** Jaundice is one of the most common findings in the neonatal period. In almost all the cases, neonatal jaundice occurs due to the elevated level of unconjugated bilirubin. Evidence is scarce regarding the association between magnesium and bilirubin levels in neonatal hyperbilirubinemia. The present study aimed to investigate serum magnesium levels before and after phototherapy.

***Methods*:** This observational study was conducted on 65 neonates with jaundice, who were admitted to 17 Shahrivar Hospital of Rasht, Iran during September 2011-2012. Neonates with total serum bilirubin level of >20 mg/dL underwent phototherapy with 12 lamps. Magnesium levels were measured before and 24 hours after phototherapy. Data analysis was performed in SPSS version 19 using descriptive statistics (mean and standard deviation) and paired t-test at 95% confidence interval, and P-value of less than 0.05 was considered statistically significant.

***Results*:** In total, 65 neonates, including 37 boys (56.9%) and 28 girls (43.1%), were enrolled in the study. Mean magnesium level was significantly higher before phototherapy (2.07±0.33) compared to after phototherapy (1.81±0.27) (P<0.0001).

Conclusion: According to the results, mean magnesium level was significantly higher before phototherapy compared to after phototherapy. However, physiological characteristics of magnesium were not assessed. It seems that the findings of the present study could lay the groundwork for further investigation in this regard.

Keywords: Jaundice, Neonate, Magnesium, Phototherapy

Introduction

Jaundice is one of the most common manifestations in the neonatal period. Neonatal jaundice occurs due to the elevated levels of unconjugated bilirubin (UCB) (1) and may induce neurological sequelae, such as encephalopathy. Currently, the molecular mechanism of UCB that induces neurotoxicity has been elucidated incompletely (2). It seems that UCB may occur due to the affinity of bilirubin molecules to the phospholipids of the plasma membrane (3) or through activated oxidative stress and different pathways (2). Moreover, bilirubin may induce excitotoxicity mechanisms, contributing to neuronal injuries.

Bilirubin exhibits an affinity for the phospholipids of the plasma membrane, such as the N-methyl-D-aspartate (NMDA) receptors. Therefore, it seems that the activation of NMDA receptors may induce neuronal injury, which could be blocked by the antagonists of the NMDA receptors. According to the literature, magnesium is an NMDA antagonist, which could decrease the neurotoxic effects of bilirubin (4).

Evidence suggests that the protective effects of antenatal MgSO4 administration in ischemic events and hypoxic brain damage are due to the increased risk of middle cerebral artery (5). Although we were not able to assess the physiological characteristics of magnesium, it seems that our findings could lay the groundwork for further investigation in this regard. The present study aimed to evaluate the total serum magnesium level in icteric neonates before and after phototherapy.

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Methods

This observational study was conducted on 65 neonates with severe jaundice hospitalized in 17 Shahrivar Hospital of Rasht, Iran during September 2011-2012. Inclusion criteria were as follows: 1) age of less than four weeks; 2) UCB and direct bilirubin of less than 1.5 mg/dL; 3) absence of congenital metabolic disorders; 4) no evidence of neonatal sepsis and 5) no administration of maternal magnesium sulfate. Selected patients were assessed by clinicians to indicate metabolic disorders.

All the neonates with the total bilirubin level of >20 mg/dL underwent phototherapy with the same device containing 12 lamps (model: Epi Intenzio, 450 nanometers). Serum magnesium levels were measured before and 24 hours after phototherapy by photometric methods using the Biotecnica BT-2000 Plus Chemistry Analyzer.

Data were collected from the hospital information system, including age, gender, gestational age, duration of jaundice, and weight on admission. Data analysis was performed in SPSS version 19.0 using descriptive statistics (mean and standard deviation) and paired t-test with 95% confidence interval. In this study, P-value of less than 0.05 was considered statistically significant.

Results

In total, 65 neonates, including 37 boys (56.9%) and 28 girls (43.1%), were enrolled in the study (Table 1).

According to the results, mean magnesium level was significantly higher before phototherapy (2.07±0.33) compared to after phototherapy (1.81±0.27) (P<0.0001). Mean magnesium level in terms of the age, gender, and bilirubin levels before and after phototherapy is presented in Table 2.

Discussion

The human body has a competitive system for maintaining the efficacy and maturity of the brain. For instance, thyroid hormones have a significant effect on the prenatal and neonatal maturity of the brain, and lack of these hormones may lead to the congenital hypothyroidism of the brain and the associated complications in neonates (6-9).

Similar to hormones, changes in electrolytes (e.g., magnesium) play a pivotal role in maintaining proper brain function. Generalized cellular damage caused by hypoxic-ischemic encephalopathy and perinatal asphyxia may increase the serum levels of magnesium. Although Ilves et al. (2000) and Engel et al. (1999) have previously investigated the effect of phototherapy on magnesium levels, findings of the current study could help clinicians in the prognosis of the high-risk patients for brain damage (10, 11).

In a research in this regard, Imamoglu et al. (2014) reported the significant protective effect of antenatal MgSO4 administration against hypoxic-ischemic brain damage in preterm neonates. Accordingly, these effects were resulted from the increased cerebral blood flow after MgSO4 administration (5). Similarly, Sarici et al. (2004) confirmed the remarkable neuroprotective effects of magnesium as a compensatory mechanism against the risk of toxicity associated with increased serum bilirubin. Furthermore, the researchers stated that increased plasma ionized

Table 1. Demographic Characteristics of Neonates

Variable	Mean±SD	Minimum	Maximum
Age (day)	6.15±3.78	3	28
Birth Weight (g)	442.5±3221	2200	4300
Gestational Age (week)	0.69±38.26	35	39
Bilirubin Level (mg/dL)	21.48±1.67	20	27

Table 2. Comparison of Mean Magnesium Level before and after Phototherapy

		N	Mean	SD	P-value
Total	Before Phototherapy	65	2.07	0.33	<0.0001
	After Phototherapy	65	1.81	0.27	
Age (<5 days)	Before Phototherapy	43	2.09	0.34	<0.0001
	After Phototherapy	43	1.83	0.27	
Age (>5 days)	Before Phototherapy	22	2.03	0.33	<0.0001
	After Phototherapy	22	1.76	0.26	
Boys	Before Phototherapy	37	2.07	0.39	<0.0001
	After Phototherapy	37	1.79	0.29	
Girls	Before Phototherapy	28	2.08	0.26	<0.0001
	After Phototherapy	28	1.83	0.24	
Br (<22 mg/dL)	Before Phototherapy	48	2.06	0.361	<0.0001
	After Phototherapy	48	1.81	0.28	
Br (>22 mg/dL)	Before Phototherapy	17	2.11	0.4	<0.001
	After Phototherapy	17	1.8	0.24	

magnesium may be due to generalized cellular damage to the neurons and erythrocytes. Therefore, they concluded that neurologic outcomes could be improved (12).

In another study in this regard, Okhravi et al. (2015) recommended auditory brainstem responses for bilirubin neurotoxicity screening in all the patients with hyperbilirubinemia (13). However, in the mentioned study, it was assumed that increased level of magnesium could be used as a screening test or treatment method before brainstem dysfunction in order to prevent bilirubin neurotoxicity.

Deposition of bilirubin in the neurons may cause permanent neuronal injury. As mentioned earlier in the article, bilirubin exhibits an affinity for the phospholipids of the plasma membrane, such as the NMDA receptors. Magnesium is an NMDA antagonist, which acts against the neurotoxic effects of bilirubin (12). According to the results obtained by Naylor et al. (2013), excitotoxicity (e.g., *status epilepticus*) could be caused by NMDAR hyperactivity (14). On the other hand, Imamoglu (2015) claimed that bilirubin-induced neurologic dysfunction and NMDAR hyperactivity might occur due to the same cause (15).

Since magnesium is an NMDA antagonist acting against the neurotoxic effects of bilirubin (12), we hypothesized increased extracellular magnesium as a compensatory mechanism in the neonates with hyperbilirubinemia after phototherapy. Therefore, it is recommended that NMDA antagonists be further investigated.

In the current research, pre- and post-phototherapy serum magnesium levels were compared in the neonates with hyperbilirubinemia. According to the results, mean magnesium level was significantly higher before phototherapy (2.07±0.33) compared to after phototherapy. This finding is consistent with the results obtained by Khosravi et al. (4) and Imani et al. (16), who reported that phototherapy could significantly decrease serum magnesium and bilirubin levels (4, 16).

Although we were not able to assess the physiological characteristics of magnesium in the current research, our findings could lay the groundwork for further investigations in this regard.

Conclusion

According to the results, mean magnesium level was significantly higher before phototherapy compared to after phototherapy. However, physiological characteristics of magnesium were not assessed. It seems that the findings of the present study could lay the groundwork for further investigation in this regard.

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Conflicts of interests

None declared.

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