Original Article

Effect of Phototherapy on Total Serum Magnesium Level in Neonatal Jaundice

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ABSTRACT

Introduction: Neonatal jaundice is a common cause of morbidity encountered in the first week of life. Most preterm neonates develop clinical jaundice, and among term neonates, around eighty-five percent develop jaundice. Peak total bilirubin level >12.9 mg/dl is found in 6.1% of well-term newborns. Three percent of normal term infants have a total bilirubin level >15 mg/dl. Phototherapy is one of the main modalities of treatment of hyperbilirubinemia. A decrease in serum magnesium level is thought to be one of the side effects of phototherapy in neonatal jaundice.

Objective: The objective of this study was to evaluate the difference in serum magnesium levels before and after phototherapy in neonates.

Methods: A Descriptive study was conducted in the Neonatal Intensive Care Unit (NICU) and emergency ward of Kanti Children's Hospital (KCH). Any neonate admitted with the diagnosis of neonatal jaundice in phototherapy and meeting inclusion criteria were included in the study. Data were analyzed using Statistical Package for Social Sciences (SPSS).

Results: A Total of 54 neonates that needed phototherapy were enrolled in the study. The mean serum magnesium level before phototherapy was 2.02 ±0.25 mg/dl and it was 1.77 ±0.29 mg/dl after phototherapy. The difference was statistically significant with the p-value of <0.001 in both sexes and age groups of five days and lower.

Conclusion:The mean serum magnesium level along with the mean total serum bilirubin level reduced significantly after phototherapy in neonates with hyperbilirubinemia irrespective of age, sex, and type of phototherapy.

Keywords: jaundice; phototherapy; magnesium; neonate

ARTICLE INFORMATION	Source of Support: Self	Conflict of Interest: None
Received: 3 January 2022	Accepted: 25 April 2022	Published Online: 30 April 2022

INTRODUCTION

Jaundice is a yellowish discoloration of the sclera and mucous membrane. Serum total bilirubin is higher in the newborn in comparison with adults and is greater than 1mg/dl. Most preterm neonates develop clinical jaundice and among term neonates, around eighty-five percent develop jaundice. In terms of well newborn, 6.1% of having a peak total serum bilirubin level >12.9 mg/dl and in 3% of normal term newborn total bilirubin level is >15 mg/dl. Among the cause of morbidity in the first week of life in a neonate, neonatal jaundice is a common cause.[1]

Among the cation in our body, magnesium is the fourth most abundant which is stored intracellularly. The kidney, bone, and gut play a vital role in the homeostasis of magnesium. Different

studies suggest that there is a positive relationship between severity of hyperbilirubinemia in the neonate and plasma ionized magnesium level.[2]

When a neonate is kept in phototherapy, transcranial illumination leads to alteration in the function of the pineal gland which will result in decreased secretion of melatonin which is essential to stimulate secretion of cortisone. Cortisone increases the absorption of calcium and magnesium in the gut and kidney. Therefore, a decrease in cortisone level leads to hypomagnesemia and hypocalcemia. Glutamate receptors NMDA (N-Methyl-D-Aspartate) which are phospholipid of the plasma membrane have an affinity to bilirubin. When NMDA receptors are activated it may cause injury to neurons. NMDA antagonist magnesium though can lead to a decrease in neurotoxic sequelae.[3]

Initial management in neonatal jaundice is phototherapy, but it also has negative consequences, among them hypomagnesemia is one. Studies have shown that phototherapy may decrease the serum magnesium level.[4,5] The decrease in serum magnesium level could be due to phototherapy and it may have clinical consequences. There is a correlation between serum magnesium and total bilirubin levels before and after phototherapy.[6]

Magnesium may have the possibility of a neuroprotective role in neonates with hyperbilirubinemia.[7] It has been shown that postnatal magnesium sulfate administration has a neuroprotective effect from bilirubin toxicity.[8,9] Magnesium sulfate when given antenatally, has a protective effect and prevents brain damage in neonates who are preterm.[10] So, if supplement magnesium could be given before phototherapy it may help to prevent neuronal damage, may prevent kernicterus, and also increase serum magnesium level.

METHODOLOGY:

A hospital-based descriptive study was conducted in the emergency ward and neonatal intensive care unit of Kanti Children's Hospital (KCH) from August 2019 - July 2020. Any neonate admitted with a diagnosis of neonatal jaundice in phototherapy and meeting inclusion criteria were taken as cases. Neonates with jaundice requiring phototherapy in KCH emergency ward NICU and NIMCU were included for the study; and neonates with exchange transfusion history, with seizure and if a mother was antenatally administered magnesium sulfate at any time during gestation were excluded from the study. A blood sample (2ml)was taken before and after phototherapy. Following the collection, the blood sample was centrifuged in a centrifuge machine of Kokusan Corporation, at the rate of 3000-4000 rpm for 30 minutes. Then, the separated serum was collected in the serum sample cup, and then the separated serum was kept in the sample port of the Automated electrolyte Analyser of E-Lyte Plus(High technology inc.20 Alice Agnew Dr. North Attleboro, MA02763 USA). Then, the Automated Analyser finally displayed the result of serum magnesium level in the monitor. Sample size was calculated having Z value of 1.96 at 95% confidence interval, *p* value of 10% and tolerable error was 0.09 and it was 48,54 cases were enrolled for the study. [11]

Serum magnesium and serum bilirubin level were recorded before and after phototherapy and data were analyzed using Statistical Package for Social Sciences (SPSS) version 16. Qualitative parametric variables were compared using the Chi-Square test and qualitative non - parametric values were compared using the independent sample t-test. When p values were less than 0.05 it was considered significant.

RESULTS

During the study period of one year, 54 children who met inclusion criteria were enrolled in the study. The age group was categorized as neonates less than 5 days and 5 days and more. The mean age of neonates in the study group was 6.15±3.78 days with the range of 3 days to 28 days. The study group of <5 days was 21 (38.9%) and ≥5 days were 33 (61.1%). Among 54 neonates, 37 were male and 17 were female. Total mean serum bilirubin level reduced from phototherapy level to non-phototherapy level in both the age groups after phototherapy. This fall in total serum bilirubin level is statistically significant (p-value <0.001). (table 1)

Table 1: Total mean serum bilirubin level of participants by age before and after phototherapy

Age of neonates (in days)	Total mean serum bilirubin level	Mean	SD	*p*-value
<5 days (n=21)	Before phototherapy	19.29	2.32	<0.001
	After phototherapy	13.33	1.67	
≥5 days (n=33)	Before phototherapy	20.27	1.59	<0.001
	After phototherapy	14.17	2.12	

Table 2: Mean serum magnesium level of neonates by age before and after phototherapy

Age of neonates (in days)	Serum magnesium level	Mean	SD	*P-value*
<5 days (n=21)	Before phototherapy	1.97	0.25	<0.001
	After phototherapy	1.70	0.24	
≥5 days (n=33)	Before phototherapy	2.06	0.24	<0.001
	After phototherapy	1.81	0.31	

In our study, the mean serum magnesium level before phototherapy in less than 5 days neonate was 1.97 ± 0.25 and in more than 5 days it was 2.06 ± 0.24 with a p-value of <0.001. Mean serum magnesium level after phototherapy in less than 5 days was 1.70 ±0.24 and in more than 5 days it was 1.81 ± 0.31 with the *p*-value of <0.001 which is statistically significant. (table 2)

In this study, it was found that the mean serum magnesium level in both male and female newborn babies fell after phototherapy . This fall in serum magnesium level in both sexes is found to be statistically significant with a p-value of <0.001. (table 3)

Table 3: Mean serum magnesium level of neonates by sex before and after phototherapy

Sex of neonates	Mean serum magnesium level	Mean	SD	*p*-value
Male (n=37)	Before phototherapy	2.01	0.24	<0.001
	After phototherapy	1.79	0.29	
Female (n=17)	Before phototherapy	2.06	0.27	<0.001
	After phototherapy	1.72	0.28	

DISCUSSION

In terms and mostly in preterm neonates, hyperbilirubinemia is a common problem. Keeping neonates in phototherapy is one of the main modalities of treatment of hyperbilirubinemia in neonates who are in the phototherapy range. While considering phototherapy as a treatment option it is effective and safe. Adverse reactions due to phototherapy are minimal and there are no such long-term adverse reactions due to phototherapy.[12]

The body has a keen system for maintaining the function and maturation of our brain. An example of this is the thyroid hormone which has a role in the maturation of the brain prenatally and in neonatal life. When these hormones lack it results in congenital hypothyroidism which results in impaired growth and development of the brain and other adverse sequelae in neonates.[13-15]

Our study subjects have a male to female ratio of 2.1: 1. A study[7] showed male preponderance with the male to female ratio of 1.3: 1. This male preponderance may be to the fact that male neonates are affected by neonatal jaundice more than female neonates. It may also be to the fact that the male children are given more attention than the female children as far as health-seeking behavior is concerned in our part of the world. The demographic health survey shows an almost similar number of male and female children in our country.

Five days and older neonates predominated the less than five days old neonates in this study. These findings were parallel with the findings of study[3] where the mean age of neonates in the study group was 6.15±3.78 days with the range of 3 days to 28 days. This is most probably due to the occurrence of pathological jaundice in first 24 hours

which is rare and physiological jaundice occurs after 24 hours and mostly requires phototherapy.

Table 4: Demographic profile of participants

Age	Frequency	Percent
<5 days	21	38.9
≥5 days	33	61.1
Total	54	100
Sex of child		
Male	37	68.5
Female	17	31.5
Total	54	100
Gestational age		
<35 weeks	8	14.8
35 to 37 weeks	6	11.1
≥ 37 weeks	40	74.1
Total	54	100
locality of child		
Inside valley	29	53.7
Outside valley	25	46.3
Total	54	100

The present study revealed that mean total serum bilirubin level reduced to 13.33±1.67 mg/dl from 19.29±2.32 mg/dl in neonates less than 5 days old and to 14.17 ±2.12 mg/dl from 20.27±1.59 mg/dl in 5 days or older neonates after phototherapy. These falls in total mean serum bilirubin levels in both age groups are found to be statistically significant with the p-value of <0.001. Similar findings were observed by different studies[2, 16,17,18], the discrepancies observed by these studies were the level of statistical significance. These discrepancies might be due to differences in sample size, type of phototherapy machines used, body surface area of neonates exposed to phototherapy,etc. Based on the findings of all these studies it can be concluded that phototherapy is one of the main modalities of treatment of hyperbilirubinemia in neonates.

This study had an aim to look for a change in serum magnesium level before and after phototherapy in neonates with hyperbilirubinemia. Mean serum magnesium level before phototherapy was 2.02 ±0.25 mg/dl and it was 1.77 ±0.29 mg/dl after keeping in phototherapy; the fall was statistically significant with the p-value of <0.001. This finding is consistent with the observations made by other studies[6,17]. However, significant levels were lesser in their findings with the p-values of 0.002 and 0.047 respectively. These discrepancies in the p-values might be because of sample size or other factors like the weight of the neonates, gestational age, etc.

Study findings showed that the mean serum magnesium level fell from 1.97 ± 0.25mg/dl to 1.70 ±0.24 mg/dl in less than 5 days old neonates and from 2.06± 0.24mg/dl to 1.81 ±0.31mg/dl in 5 days and older neonates after phototherapy. These falls in serum magnesium levels are statistically significant (p-values <0.001) in both age groups. Similar observations of fall in serum magnesium levels after phototherapy[3] were observed in both the age groups of neonates with hyperbilirubinemia. The statistical significance found by them was even stronger than in our study (p-values <0.0001vs <0.001).

The present study looked at the fall in serum magnesium level to hypomagnesemia level after phototherapy. Normal serum magnesium level is defined as the level between 1.2-2.6 mg/dl for 0-6 days old neonates and 1.6-2.6 mg/dl for 7-28 days old neonates. A Level below this age-specific range is considered hypomagnesemia. Hypomagnesaemia was observed only in 5 neonates in our study. It was also seen in this study that the occurrence of hypomagnesemia was not significantly different (p-value=1) in neonates who underwent single surface phototherapy or double surface phototherapy. Furthermore, there was no significant difference in changes in serum magnesium level on the use of single or double surface phototherapy type. Clinical features of hypomagnesemia were not considered in our study. It would have been useful to study clinical manifestations of hypomagnesemia for clinical purposes.

It is argued by a study[7] that the increase in magnesium level may be associated with the increase in serum bilirubin level as a compensatory mechanism in neonates as the magnesium may have the possibility of a neuroprotective role in neonates with hyperbilirubinemia. It was shown by study[8,9] that giving magnesium sulfate had a neuroprotective role and prevents toxicity caused by a high level of bilirubin. It was also hypothesized[19] that the increase in plasma ionized magnesium level can be due to movement of magnesium from the intracellular compartment to extracellular which

may be the result of injury to cells like neurons and erythrocytes due to hyperbilirubinemia. This increase in magnesium level has a neuroprotective role against the emerging toxicity risk of increasing serum bilirubin level. Study[20] found that to overcome the toxicity of hyperbilirubinemia there is a change in magnesium level as a compensatory mechanism that helps in neuroprotection. There is a benefit and protective effect when magnesium sulfate is administered antenatally and protects preterm neonates from brain damage[10]. This protective effect was considered to be due to increased cerebral blood flow after $MgSO_4$ administration.[10]

The previous study[6] showed that the levels of magnesium in neonates with severe hyperbilirubinemia were higher than the mild hyperbilirubinemia group (p-value = 0.03) before phototherapy. There was a mild correlation between serum magnesium and total bilirubin levels before (r=0.315, p-value= 0.001) and after phototherapy (r=0.314, p-value = 0.004). They concluded that phototherapy could reduce total magnesium and total bilirubin serum levels in the same direction. This is true with the findings of our study. However, the severity of hyperbilirubinemia was not graded and a correlation between the serum magnesium level and bilirubin level before and after phototherapy was not done in our study.

Limitations: The study was conducted over period of one year and the sample size was only 54, which is small and does not represent the general population of the country. The only serum magnesium level was measured, if ionized magnesium would have been measured result had been more accurate. But due to the unavailability of the test, it could not have been measured.

CONCLUSION

The mean serum magnesium level along with the mean total serum bilirubin level reduced significantly after phototherapy in neonates with hyperbilirubinemia irrespective of age, sex, and type of phototherapy. It is recommended to monitor serum magnesium levels during phototherapy in neonates with hyperbilirubinemia and to conduct the study on a larger scale.

Acknowledgement: I would like to acknowledge Prof. Dr. Ganesh Kumar Rai for his constant support and guidance for the completion of this research work.

REFERENCES

1. Eichenwald E, Hansen, A., Martin, C. and Stark, A. (n.d.). Cloherty and Stark's manual of neonatal care: wolters kluwer; 2018. 8th ed.
2. Ravichander B, Kundu S. Effect of double surface photo-therapy on serum magnesium levels in term and late preterm neonates. Journal of Evidence-Based Medical- Healthcare [JEBMH]. 2018;5(4):315-8. https://doi.org/10.18410/jebmh/2018/63 [Google]
3. Karambin MM, Heidarzadeh A, Norouzi H, Dalili S. New insight into the effect of phototherapy on serum magnesium level. Iranian Journal of Neonatology IJN. 2017 Sep 1;8(3):44-7. [Google Scholar]
4. Ilves P, Kiisk M, Soopold T, Talvik T. Serum total magnesium and ionized calcium concentrations in asphyxiated term newborn infants with hypoxic-ischaemic encephalopathy. Acta Paediatrica. 2000 Jun;89(6):680-5. https://doi.org/10.1111/j.1651-2227.2000.tb00364.x [Pubmed]
5. Engel RR, Elin RJ. Hypermagnesemia from birth asphyxia. The Journal of pediatrics. 1970 Oct 1;77(4):631-7.https://doi.org/10.1016/S0022-3476(70)80205-0 [Google Scholar]
6. Imani M, Rezaee-pour M, Mohamdi M, Shiri M, Noroozifar M, Mahmodi NJRJoMS. Study of relationship between total Magnesium and total bilirubin levels in neonates' sera before and after phototherapy. 2012;19(100). [Google Scholar]
7. Mehta R, Petrova A. Ionized magnesium and gestational age. The Indian Journal of Pediatrics. 2007 Nov;74(11):1025-8. [Pubmed]
8. Bhat MA, Charoo BA, Bhat JI, Ahmad SM, Ali SW. Magnesium sulfate in severe perinatal asphyxia: a randomized, placebo-controlled trial. Pediatrics. 2009 May 1;123(5):e764 .https://doi.org/10.1542/peds.2007-3642 [Pubmed]

9. Gathwala G, Khera A, Singh J, Balhara B. Magnesium for neuroprotection in birth asphyxia. Journal of pediatric neurosciences. 2010 Jul;5(2):102. [Pubmed]
10. Imamoglu EY, Gursoy T, Karatekin G, Ovali F. Effects of antenatal magnesium sulfate treatment on cerebral blood flow velocities in preterm neonates. Journal of Perinatology. 2014 Mar;34(3):192-6. https://doi.org/10.1038/jp.2013.182 [Pubmed]
11. Shrestha S, Budhathoki S, Sanjel S, Sindan N, Kayastha N, Shrestha A.Effect of Phototherapy on serum calcium level in neonatal hyperbilirubinemia. Journal of Karnali Academy of Health Sciences.2021;4(2)
12. Gregory MLP MC, Cloherty JP. Neonatal hyperbilirubinemia. In: Cloherty JP, Eichenwald EC and Stark AR (eds). Manual of Neonatal Care, 7th ed. Chapter 26, Lippincott-Raven Philadelphia 2012. 304-339.
13. Dalili S, Rezvany SM, Dadashi A, Medghalchi A, Mohammadi H, Dalili H, Mirzanejad M, Gholamnezhad H, Amirhakimi A. Congenital hypothyroidism: a review of the risk factors. Acta Medica Iranica. 2012:735-9. [Full Text]
14. Karamifar H DS, Karamizadeh Z, Amirhakimi G, Dalili H. Autoimmune polyglandular syndrome type 2: an unusual presentation. Acta Medica Iranica. 2010;48(3):196-7. [Pubmed]
15. Dalili S, Mohtasham-Amiri Z, Rezvani SM, Dadashi A, Medghalchi A, Hoseini S, Gholami-Nezhad H, Amirhaki A. The prevalence of Iodine Deficiency Disorder in two different populations in Northern Province of Iran: a comparison using different indicators recommended by WHO. Acta Medica Iranica. 2012:822-6. [Google Scholar]
16. NK. S. Effect of phototherapy on serum bilirubin and ionized magnesium level in hyperbilirubinemic neonates. Innovare Journal of Medical Science. 2017:10-1. [Full Text]
17. El Frargy MS, El-sharkawy HM, Attia GF. Study of Serum Magnesium Levels in Neonatal Jaundice: The Effect of Phototherapy. Current Pediatric Research. 2016. [Full Text
18. Shahriarpanah S, Tehrani FH, Davati A, Ansari I. Effect of phototherapy on serum level of calcium, magnesium and vitamin D in infants with hyperbilirubinemia. Iranian Journal of pathology. 2018;13(3):357.[Pubmed]
19. Mohsen AH, Afify MF, Allam E, Abdelkarem H. Role of magnesium ion in neonatal jaundice. Life science journal-acta zhengzhou university overseas edition. 2012 Jan 1;9(3). [Full Text]
20. Sarici SU SM, Erdem G, et al. Evaluation of plasma ionized magnesium levels in neonatal hyperbilirubinemia. Pediatr Res 2004; 55: 243-247. https://doi.org/10.1203/01.PDR.0000103874.01584.F3 [Pubmed]