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Biochemistry

STUDY OF SERUM MAGNESIUM LEVEL IN NEONATAL HYPERBILIRUBINEMIA- A HOSPITAL BASED STUDY

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ABSTRACT Neonatal hyperbilirubinemia is the most common clinical condition that requires medical attention and hospital readmission in newborns. It is the yellowish discoloration of skin and sclera due to bilirubin. Deposition of unbounded bilirubin in the neuron membrane causes permanent neuronal injury. Magnesium, a principally intracellular ion, increases in plasma may be due to extracellular movement resulting from generalized cellular injury including neurons and erythrocytes.

The aim of the study was to estimate and find the correlation between plasma magnesium and serum bilirubin levels in neonatal hyperbilirubinemia. Blood samples were collected from 30 full term neonates who were admitted with jaundice over a period from September 2017 to February 2018 in neonatology unit, department of pediatrics, Jorhat Medical College & Hospital. There was a positive correlation between the plasma magnesium level and serum bilirubin level ($r = 0.987$ and P value is significant <0.0001). The study highlights the possibility of a neuroprotective role or compensatory mechanism of magnesium against the toxicity of increasing serum bilirubin.

KEYWORDS : Magnesium, Bilirubin, Hyperbilirubinemia

INTRODUCTION:

Neonatal hyperbilirubinemia is a life threatening disorder encountered during the neonatal period, especially in the first week of life. [1,2] When the total serum bilirubin rises above the 95th percentile for age during the first week of life, it will be considered as hyperbilirubinemia. [3,4]

Bilirubin is not merely a harmful molecule that has dire consequences, but bilirubin like uric acid is an important antioxidant circulating in biologic system of neonate .[5-7] However, high bilirubin levels can be toxic for central nervous system development and may cause behavioral and neurological impairment (Neurotoxicity or Kernicterus) even in term newborns.[8-10] Five to ten percent of newborns develop jaundice required the management of hyperbilirubinemia.[11] Neonatal jaundice may be on account of different parameters such as birth weight, gestational age, premature rupture of membranes, maternal infectious diseases or other illness during pregnancy, having different sources of origin, hence having different types.[12]

Deposition of unbound bilirubin or its acid form in the neuron membrane causes permanent neuronal injury with a distinctive regional topography throughout the CNS. Considering the affinity of bilirubin molecule to phospholipids of the plasma membrane, the sequence of membrane events initiated by bilirubin molecules damages all adjacent membrane-bound enzymes and receptors. However, distant plasma membrane structures such as N-Methyl-D-Aspartate (NMDA) receptor/ion channel complex located within neuronal membranes on the synaptic surface of neurons are disrupted as well. Increased and prolonged activation of NMDA receptor as in perinatal asphyxia and hypoxic ischemic encephalopathy (HIE). However, it has been shown in newborn piglets that bilirubin also increases activation of the NMDA receptor by modifying its binding characteristics, increases the receptor's affinity for NMDA receptor antagonists, and thus results in neuronal injury. Bilirubin-induced neurotoxicity may share common features with HIE-induced brain injury by mechanisms mediated by the NMDA receptor. The observations that both bilirubin-induced and HIE-induced neuronal injury can be blocked by the administration of a potent NMDA receptor antagonist MK-801 (dizocilpine) further support the hypothesis that similar excitotoxic mechanisms contribute to the neuronal injury caused by both bilirubin and hypoxia.[13-20]

Magnesium is the fourth most plentiful cation in the body and the second most prevalent intracellular cation. However, the extracellular concentration of magnesium that is of interest to the clinician is due to its association in manifestation. The major organs system concerned with magnesium homeostasis are the gastrointestinal, skeletal, and renal, but the regulators influencing these organs at the cellular level yet unsettled. Within the cell, most of the magnesium is bound to proteins and negatively charged molecules; 80 % of cystolic magnesium is bound to ATP and Mg ATP is the substrate for numerous enzymes. The nucleus, mitochondria, and endoplasmic reticulum contain significant amounts of magnesium. Reducing the serum magnesium concentration decreases the threshold of axonal stimulation and increases nerve conduction velocity. Magnesium also influences the release of neurotransmitter at the neuromuscular junction by competitively inhibiting the entry of calcium in the pre-synaptic nerve terminal. Reducing the serum magnesium concentration results in increased neuromuscular excitability. [21-23]

With this background in mind, a study was planned and undertaken among a group of 30 numbers of infants undergoing treatment in the neonatalogy wing of the department of pediatrics, JMCH with neonatal jaundice.

MATERIALS AND METHODS:

The study was conducted on 30 full term neonates who were admitted with jaundice over a period from September 2017 to February 2018 in the neonatology unit, department of pediatrics, JMCH.

Inclusion criteria:

Full-term neonates with pathological hyperbilirubinemia (neonatal hyperbilirubinemia was diagnosed when newborn infant has a peak bilirubin level from 7 to 20 mg/dl in serum within 10 days of birth in terms) and having unconjugated bilirubin/total bilirubin ≥80%.

Exclusion criteria:

1. Exchange transfusion cases.
2. Neonates with cephalohematoma, congenital malformation, inborn errors of metabolism, sepsis or whose mother was antenatally administered magnesium sulfate during gestation.
3. Hemolytic hyperbilirubinemia.

SAMPLE COLLECTION:

Blood samples were obtained from infants during veinpuncture and centrifuged at 3000 rpm for 10 minutes at room temperature. Then concentration of plasma magnesium and serum bilirubin was determined using Vitros 250 dry chemistry autoanalyser (ortho-clinical diagnostics- Johnson & Johnson).

Quality Control: Adequate laboratory parameters were followed.
Statistical Analysis: Done in Microsoft excel.

RESULTS AND OBSERVATIONS:

Total number of cases	Plasma Magnesium mg/dL (Mean±SD)	Serum Bilirubin Mg/dL (Mean±SD)	P value	r value
30	2.74±0.43	12.50±3.85	< 0.0001	0.987

Table 1: Table showing plasma magnesium and serum bilirubin among all the cases and comparative P value and r (correlation coefficient) value

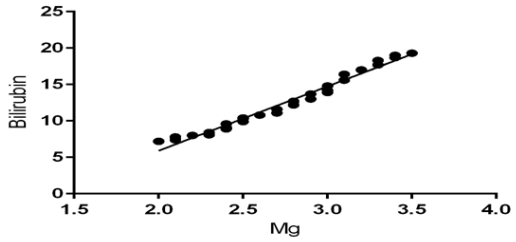

Fig: Scatter diagram showing the correlation between the plasma magnesium mg/dL (X-axis) and serum bilirubin mg/dL (Y-axis)

In the present study there was a positive correlation between the plasma magnesium level and serum bilirubin level (r = 0.987 and P value is significant <0.0001).

DISCUSSION:

Hyperbilirubinemia poses a risk for development of kernicterus (acute bilirubin encephalopathy),which refers to a neurological syndrome that results in brain damage owing to deposition of bilirubin in the basal ganglia and brainstem nuclei, to compensate this effects extracellular movement of Mg, resulting from generalized cellular injury including neurons and erythrocytes with possibility of a neuroprotective effect.[23,24]

Magnesium (Mg++) ion, like MK-801(dizocilpine), is one of the most important antagonistic regulators of the NMDA receptor/ion channel complex.[24,25] It protects the CNS against hypoxia and exerts its neuroprotective effects by blocking excitotoxic and NMDA receptor–mediated neuronal injury mechanisms.[24-29] Many physiologic functions of Mg ions seem to act against or compensate for the neurotoxic effects of bilirubin molecules.[30,31]

In the present study, performed with varying degrees of hyperbilirubinemia, we demonstrated a positive correlation between plasma magnesium and severity of hyperbilirubinemia. This suggests that increase in plasma magnesium may be due to extracellular movement of intracellular magnesium.

In concord of our study, Afify et al., 2012 [32] reported that the plasma magnesium levels were significantly higher in jaundiced neonates compared to controls and this may be due to mild hemolysis. Also, the increased magnesium levels may be due to the extracellular movement of intracellular magnesium secondary to cellular injury caused by high bilirubin levels that may cause neuronal and generalized cellular injury. They reported that magnesium levels were significantly higher in jaundiced neonates than controls and postulated that the plasma levels of magnesium become higher in serum depending on the existence of mild hemolysis in neonates, the fact that magnesium is high in erythrocytes, especially reticulocytes than in serum concentrations, so its serum levels increase after hemolytic.

In the contrary from our results are Tuncer et al., 1972 [33], who reported lower serum total magnesium concentrations in both umbilical cord and maternal blood of neonates with hyperbilirubinemia, when compared with normal neonates and they postulated that hypomagnesaemia may result from intracellular shift of magnesium ions, this difference may be due to different methodology and the source (maternal and cord blood) of blood samples.

In harmony with our study, Sarici et al. [34] found a positive correlation between plasma Mg and the severity of hyperbilirubinemia in full-term newborns with neonatal jaundice.

Mehta and Petrova [35] suggested the possibility of a neuroprotective role or a compensatory mechanism in plasma ionized Mg increase against emerging toxicity risk of increasing serum bilirubin values and this agreed with our results.

CONCLUSION:

From the present study it is observed that neonates with hyperbilirubinemia had significant higher magnesium levels. This may be due to physiological compensatory mechanism that counters toxic effect of bilirubin. Determination of exact pathophysiological process responsible for elevation of plasma magnesium level in relation to hyperbilirubinemia will make it possible to early postnatal magnesium measurement in predicting the development of significant hyperbilirubinemia. The value of magnesium treatment in the therapy of neonatal hyperbilirubinemia deserves further studies.

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