PREVALENCE OF HYPOMAGNESAEMIA AND ITS PROGNOSTIC VALUE IN CRITICALLY-ILL MEDICAL PATIENTS

Sahul Hameed Peer Mohamed1, Gopal Bagialakshmi2, Nagarajan Ragavan3, Rajendran Kapil4, Santhana Krishnan Ramesh Kumar5

1Assistant Professor, Department of General Medicine, Madurai Medical College, Madurai.
2Professor, Department of General Medicine, Madurai Medical College, Madurai.
3Assistant Professor, Department of General Medicine, Madurai Medical College, Madurai.
4Junior Resident, Department of General Medicine, Madurai Medical College, Madurai.
5Scientist (Medical), National Institute for Research in Tuberculosis (ICMR), Madurai.

ABSTRACT

BACKGROUND
Serum magnesium levels in critically-ill ICU patients and its correlation with the prognosis of the patients have been studied. Low serum magnesium levels were seen in critically ill and it was associated increased mortality.

MATERIALS AND METHODS
It is a prospective observational study involving 100 critically-ill medical patients admitted in Intensive Medicine Care Unit of Government Rajaji Hospital, Madurai. A detailed medical history, clinical examination, random blood sugar, serum electrolytes (sodium, potassium, magnesium, calcium), ECG, ABG analysis, complete haemogram and APACHE scoring were done. Chi-square test was used to assess the statistical significance of qualitative data.

RESULTS
Of the 100 patients, 52 (52%) were males and 48 (48%) were females. Age group from 51-60 years contributed as the major study population. On admission, 50% (50/100) patients had hypomagnesaemia, 39% (39/100) had normal serum magnesium levels and 11% had hypermagnesaemia. The hypomagnesaemia group had increased number of days in ICU, increased incidences of ventilatory support and more duration of ventilation and higher mortality compared with normo or hypermagnesaemia group.

CONCLUSION
Hypomagnesaemia in critically-ill medical patients is a poor prognostic indicator in terms of duration of IMCU stay, ventilator dependency and all-cause mortality.

KEYWORDS
Hypomagnesaemia, Critically-Ill Medical Patients.


BACKGROUND
Magnesium is the most abundant intracellular cation after potassium. About 50 percent of the total body magnesium (2000 mEq in the human adult) is distributed in bone remaining in soft tissues. Measurements of serum magnesium does not exactly correlate with body stores because the extracellular fluid has 1% of body magnesium.1 Kidney is major organ maintaining concentration of serum magnesium.2 The thick ascending limb reabsorbs about 60% of the filtered magnesium, proximal convoluted tubule absorbs 20% and the distal convoluted tubule absorbs the remaining 5-10%. Magnesium is primarily absorbed by jejunum and ileum, the absorptive capacity of which can be increased to 70% by 1.25-dihydroxycholecalciferol.1 Serum magnesium although does not exactly correlate with body stores.1

Magnesium monitoring is important in critically-ill patients who are more prone for a myriad of electrolyte abnormalities particularly hypokalaemia, hyponatraemia and hypocalcaemia. The total intracellular magnesium content is 8 to 10 mmol/L (10 to 20 mEq/L). Most of the magnesium in cell is bound to ATP, intracellular nucleotides and enzymes.1 Studies using magnesium-sensitive dyes based on Fura-2 (aminopolycarboxylic acid) indicate that the free cytosolic concentration is 0.6 to 0.8 mmol/L (1.2 to 1.6 mEq/L). Intracellular magnesium forms a complex with adenosine triphosphate and is a cofactor for many enzymes and cotransporters.1 These enzymes and cofactors are necessary for energy metabolism, normal cellular function and all enzyme-catalysed reactions involving nucleotides and ATP.
and replication. 30% of the normal serum magnesium (1.7-2.4 mg/dL) is bound to albumin and 15% is complexed to phosphate and anions. The bone contains one half of the total magnesium (1000 mmol) and only one half is insoluble in the mineral phase.

Changes in the plasma magnesium levels alter cellular magnesium content slowly. The intracellular free magnesium is significantly below electrochemical equilibrium. A type of energy dependant extrusion mechanism exist. The process of active magnesium transport is driven by a favourable transmembrane potential. Magnesium enters the distal convoluted tubule through an apical magnesium channel. Since, the intra and extracellular concentrations of magnesium are comparable, the driving force for magnesium is negligible. Magnesium entry into the cells is the rate limiting step. Magnesium diffuses through the cytosol to be extruded against an electrochemical gradient across the basolateral membrane, which increases in hypokalaemic patients to about 61 to 66% in patients in ICU. Low albumin, malnutrition, aminoglycosides play role. The three basic mechanisms that lead to hypomagnesaemia are redistribution, gastrointestinal loss and renal losses.

The incidence of hypomagnesaemia in hospitalised patients was found to be 12 percent. Low magnesium levels were seen in critically ill and it was significantly associated increased mortality among various diseases. We proposed to assess the prevalence of serum magnesium levels in critically-ill patients and also assess the prognostic significance of serum magnesium in critically-ill medical patients.

**MATERIALS AND METHODS**

The objectives of the study is to assess the prevalence of serum magnesium levels in critically-ill patients and to assess the prognostic significance of serum magnesium in critically-ill medical patients. It was hypothesised that the hypomagnesaemia in critically-ill medical patients was a poor prognostic indicator in terms of duration of IMCU stay, ventilator dependency and all-cause mortality.

**Study Design** - Prospective, descriptive analytical study.

**Study Setting** - The study was conducted at Government Rajaji Hospital from March 2015 to October 2015.

**Study Population** - This study was conducted among 100 critically-ill medical patients admitted in Intensive Medicine Care Unit of Government Rajaji Hospital, Madurai, from March 2015 to October 2015.

**Inclusion Criteria**

Patients suffering from various medical conditions namely pneumonia/interstitial lung disease with respiratory failure, congestive cardiac failure, diabietic ketoacidosis, meningitis, OPC poisoning and snake bite patients requiring ventilator support.

**Exclusion Criteria**

Patients who had received intravenous magnesium prior to transfer to IMCU were excluded.

**Study Protocol and Data Collection**

Eligible patients as per the criteria said above was enrolled to the study. A detailed medical history, clinical examination and relevant laboratory investigations including random blood sugar, serum electrolytes (sodium, potassium, magnesium and calcium), ECG, arterial blood gas analysis and complete haemogram, radiological investigations were performed as indicated in every patient. It was ensured that a blood sample was collected for estimation of serum total magnesium levels on admission to intensive medical care unit. APACHE score was calculated using the APACHE II scoring system. It was ensured that the study did not interfere with the management of patient in the intensive medical care unit. Blood magnesium levels of the subjects was correlated with their prognosis.

**Data Analysis**

The reference range of the normal serum magnesium was fixed between 1.7-2.4 mg/dL. Normal deviate (z) test was applied to find out the significance of difference between two means for quantitative data. Chi-square test was used to assess the statistical significance of qualitative data.

**Ethical Consideration**

The study was approved by Government Rajaji Hospital Ethical Committee. Informed consent was obtained before enrolling subjects to the study.

**RESULTS**

Of the 100 patients, 52 (52%) were males and 48 (48%) were females. Age group from 51-60 years contributed as the major study population. Organophosphorus poisoning was the common critical illness group contributing 21% of the total sample size. The various group of critical illness of the study population is shown in Table 1. Table 2 shows the impact of serum magnesium level on various parameters in study population in ICU patients.

On admission, 50% (50/100) patients had hypomagnesaemia, 39% (39/100) had normal serum magnesium levels and 11% had hypermagnesaemia. The lowest serum magnesium value recorded was 0.7 mg/dL while the highest value was 3.7 mg/dL. The range of duration of stay in intensive medical care unit varied from 4 to 20 days.

The mean duration of IMCU stay in the hypomagnesaemic group is 16.5 days while that of the normomagnesaemic group is 10.4 days, which was statistically significant. The mean duration of ventilator requirement in the hypomagnesaemic group is 11.7 days, while that of normomagnesaemic group is 7.4 days, which is statistically significant. The mean APACHE score of the hypomagnesaemic group was 19.52 while that of the normomagnesaemic group was 9.7 days. The incidence of hypokalaemia in the hypomagnesaemic group was 76%
while in the normomagnesaemic group was 24%, which was statistically significant. The incidence of hyponatraemia in the hypomagnesaemic group was 28% while in the normomagnesaemic group was 12%, which was statistically significant.

The incidence of polymorphic ventricular tachycardia in the hypomagnesaemic group was 8% while in the normomagnesaemic group was 2%. Finally, the mortality rate was also higher in the hypomagnesaemic group, which is 84.2% that was statistically significant. The mortality chart showing the details on mortality in the two groups—hypomagnesaemia and normomagnesaemia—is presented in Table 3a and 3b. Table 4 shows comparison of serum magnesium level among patients requiring ventilator support in ICU.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Type of Critical Illness</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Organophosphorus poisoning</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>Coronary artery disease</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>Diabetic ketoacidosis</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>Meningitis</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>Snake bite</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>ILD with respiratory failure</td>
<td>13</td>
</tr>
<tr>
<td>7</td>
<td>Others</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 1. Type of Critical Illness of Enrolled Study Patients

<table>
<thead>
<tr>
<th>Occurrence</th>
<th>Hypomagnesaemia</th>
<th>Normomagnesaemia</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of hospital stay</td>
<td>16.5 days</td>
<td>10.4 days</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Need for ventilation</td>
<td>41/77 (53.2%)</td>
<td>26/77 (33.7%)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Duration of ventilation</td>
<td>11.7 days</td>
<td>7.4 days</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>APACHE score</td>
<td>19.5±2.5</td>
<td>9.7±2.5</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Hypokalaemia</td>
<td>38/50 (76%)</td>
<td>12/50 (24%)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Hypoponatraemia</td>
<td>32/50 (64%)</td>
<td>14/50 (28%)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Hypocalcaemia</td>
<td>19/50 (38%)</td>
<td>6/50 (12%)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>4/50 (8%)</td>
<td>1/50 (2%)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>16/19 (84%)</td>
<td>3/19 (15.79%)</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

Table 2. Comparison of Hypomagnesaemia and Normomagnesaemia Group of Patients among the Study Population on Various Parameters

DISCUSSION

Our study showed that patients with low serum magnesium had longer duration of hospital stay, higher mortality rate and higher incidence of dyselectrolytaemia (hypokalaemia, hypoponatraemia, hypocalcaemia). Hypokalaemia is usually refractory to correction in the background of hypomagnesaemia. Magnesium depletion predisposes to hypophosphataemia, which is the underlying cause for
longer ventilator stay. A higher mortality rate was detected in hypomagnesaemic patients as compared to normomagnesaemic patients by Chernow et al (41% vs. 13%) and Rubiez et al (46% vs. 25%), respectively. The mortality rate in our study was similar to these studies.

The cause for high mortality in the hypomagnesaemic group could be multifactorial. The foremost contributing factor is the primary disease itself followed by other electrolyte abnormalities (particularly hypokalaemia, which predisposes to polymorphic ventricular tachycardia), ventilator associated complications, hospital-acquired infections in the order of hierarchy.

In the study carried out by Soliman et al and Limaye et al, there was no difference in the length of ICU stay among the hypo as well as normal magnesium groups whereas in our study hypomagnesaemia had a prolonged stay.

The main implications of the study is that it has been made clear that magnesium monitoring in the intensive care setting can be a diagnostic tool for recalcitrant hypokalaemia, decrease the duration of ventilator stay, decrease in the morbidity and mortality; if suspected and detected, decrease the incidence of ventricular tachycardia.

Limitations
The mortality rate, duration of hospital stay, need for ventilator stay were all high in the group of patients with coronary artery disease. Most of the patients of coronary artery disease were on long-term diuretics, which could result in hypomagnesaemia. Moreover, the disease process itself is more contributory for the morbidity rather than hypomagnesaemia per se. Next, the major population of the study group is contributed by the age group of 51-60 yrs. Higher age itself is a risk factor for developing multiple dyselectrolytaemias.

CONCLUSION
Magnesium though is most understudied electrolyte has critical implications in the ICU setting.

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