Original Research Article

Correlation of serum magnesium levels with renal parameters in patients with acute kidney injury

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ABSTRACT

Background: Acute kidney injury is a common problem with various causes and consequences like electrolyte disturbances in the form of hypocalcaemia, hypokalaemia, hyperkalaemia depending on the phase. Hypomagnesaemia is one of the most common electrolyte disturbance found in hospitalized patients especially in the critically ill patients. Prevalence of hypomagnesemia varies from 11 to 65% in different studies. Hence, we decided to conduct a study to evaluate correlation of serum magnesium levels in AKI.

Methods: A cross-sectional, hospital based time bound study was conducted between November 2016 and August 2018 with a sample of 100 patients aged 18-65 years and who had AKI were included and patients with diabetes mellitus, multi-organ dysfunction, obstructive uropathy and drug induced AKI were excluded from study. The decrease in magnesium <1.7 mg/L was defined as hypomagnesaemia. AKI was defined as per AKIN criteria. Day 1, day 3 and day 6 magnesium levels were measured.

Results: Prevalence of hypomagnesaemia was 53%, 30% and 36% on day 1, day 3 and day 6 respectively. It was observed that there was a positive correlation between serum magnesium, and serum creatinine. Normomagnesaemia and hypermagnesemia on day 1, 3 and 6 were significantly associated with recovery of AKI (p<0.001).

Conclusions: The prevalence of hypomagnesemia was significantly higher in AKI patients and normal magnesium and hypermagnesium on day 1, 3 and day 6 was associated with recovery than non-recovery. Hypomagnesemia was associated more with non-recovery then recovery.

Keywords: Acute kidney injury, Serum creatinine, Serum magnesium

INTRODUCTION

Acute kidney injury (AKI), a syndrome with multiple aetiologies, affects approximately 5.7% of all hospitalized patients. According to studies the incidence of AKI approaches 200 cases/million adult patients. AKI defined by acute kidney injury network as an increase in serum creatinine of more than or equal to 0.3 mg/dl, or a percentage increase in serum creatinine of more than or equal to 50% (1.5 folds) increase from baseline, or a reduction in urine output <0.5 ml/kg/hr for more than 6 hours. Electrolyte imbalances like hypomagnesaemia, hypokalaemia and hypophosphatemia are commonly seen in AKI. Although magnesium deficiency is a common clinical problem, serum magnesium levels are overlooked in recovering AKI cases.

Magnesium competes with calcium transport system in the cell membranes, which diminishes the intracellular calcium concentration, resulting in relaxation of smooth muscle cells. In mesangial cells in culture, magnesium inhibits the contraction induced by cyclosporine and
angiotensin 2, while hypomagnesaemia potentiates the post ischemic renal injury in rats. In addition, hypomagnesaemia decreases the GFR and the RBF in zidovudine treated rats. It may be helpful in relaxing the smooth muscle by stimulating the release of NO and also induces a peripheral vasodilator effect.  

Magnesium deficiency may also produce neuromuscular manifestation such as myoclonic jerks paraesthesia, dysarthria and neuropsychiatric manifestation like agitation anxiety and depression. The purpose of the current study is to correlate serum magnesium levels with renal parameters in patients with AKI.

**Aims and objectives**

To estimate the level of serum magnesium in patients with acute kidney injury and to evaluate the correlation of serum magnesium with serum creatinine in patient with acute kidney injury.

**METHODS**

A total of 100 patients from those attending medicine OPD and getting admitted in medicine ward, Victoria and Bowring hospital, attached to Bangalore medical college and research institute, during the period of 1 November 2016 to 30 August 2018 were taken for study, if they satisfied all the inclusion and exclusion criteria.

**Inclusion criteria**

All patients satisfying acute kidney injury network guideline, who gave informed consent, aged more than 18 years.

**Exclusion criteria**

Patients with multi organ failure, drug induced AKI, obstructive uropathy, chronic alcoholic patients, type 2 diabetes mellitus and elderly patients with more than 65 years of age.

Data was collected from outpatient and inpatients admitted in Victoria and Bowring hospital, Bangalore. Patients were selected according to inclusion and exclusion criteria mentioned below. Hypomagnesaemia was defined as serum magnesium <1.7 mg/dl (normal range 1.7-2.2 mg/dl). Blood samples were collected to measure CBC, RFT, serum electrolyte, RBS and serum magnesium levels on 0, 3 and 6 days (or day of discharge), serum magnesium was estimated by automated analyzer method. The sample size calculation was done using formula:

\[ n = \frac{z^2 \times \sigma^2}{d^2} = \frac{(1.96)^2 \times (0.41)^2}{(0.08)^2} = \frac{0.645}{0.0064} = 100.7 \]

Where, \( z = 1.96, \sigma = 0.41, d = \text{precision} = 0.08 \)

**Statistical analysis**

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Pearson correlation was done to find the correlation between two quantitative variables and qualitative variables respectively.

**RESULTS**

Mean age of patients was observed as 43.07±13.38 years. 25% were in the age group 21 to 30 years, 21% were in the age group 31 to 40 years, 25% were in the age group 41 to 50 years, 17% were in the age group 51 to 60 years and 12% were in the age group 61 to 70 years. Sex distribution was observed as, male 70% and female 30%.

**Serum creatinine distribution among subjects**

At baseline mean serum creatinine was observed as 4.6±2.7 mg/dl, on day 1 mean serum creatinine was 4.8±2.7 mg/dl, on day 3 mean serum creatinine was noted as 4.5±3.0 mg/dl and on day 6 mean serum creatinine was found to be 4.1±3.5 mg/dl. There was significant difference in mean serum creatinine on day 1 compared to baseline value. At day 3 and day 6 there was no significant difference in serum creatinine compared to baseline.

**Table 1: Correlation between serum creatinine and serum magnesium on day 1.**

| Variables     | Serum creatinine | Serum magnesium |
|---------------|------------------|-----------------|
| Pearson       | 1                | 0.213*          |
| correlation   | (n=99)           |                 |
| p value       | 0.034*           |                 |

*Correlation is significant at the 0.05 level (2-tailed).

**Serum magnesium distribution among subjects**

On day 1 mean serum magnesium was found to be 1.7±0.5, on day 3 mean serum magnesium was 1.86±0.44 and on day 6, mean serum magnesium was 1.95±0.57. There was significant difference (increase) in mean serum magnesium on day 3 and day 6 compared to day 1. In the study there was significant positive correlation observed between serum creatinine and serum magnesium on day 1. That is, with increase in serum creatinine there was increase in serum magnesium and vice versa. In current study there was nonsignificant positive correlation observed between serum creatinine and serum magnesium on day 3, i.e. with increase in serum creatinine there was increase in serum magnesium and vice versa. The present study reported a nonsignificant
negative correlation between serum creatinine and serum magnesium on day 6, i.e. with increase in serum creatinine there was decrease in serum magnesium and vice versa.

On day 1, among those who did not recover, 29.4% had normal magnesium, 52.9% had hypomagnesaemia and 17.6% had hypermagnesaemia. Among those who recovered, 45.5% had normal magnesium, 53% had hypomagnesaemia and 1.5% had hypermagnesaemia. There was significant association between magnesium levels and outcome. On day 3, among those who did not recover, 50% had normal magnesium, 38.2% had Hypomagnesaemia and 11.8% had hypermagnesaemia. Among those who recovered, 63.6% had Normal magnesium, 21.2% had hypomagnesaemia, 25.8% had normal magnesium, 38.2% had Hypomagnesaemia and 11.8% had hypermagnesaemia. There was significant association between magnesium levels and outcome.

There was significant correlation between serum magnesium levels and outcome. On day 3, among those who did not recover, 26.5% had normal magnesium, 38.2% had Hypomagnesaemia and 10.6% had hypermagnesaemia. Among those who recovered, 47% had normal magnesium, 21.2% had Hypomagnesaemia and 31.8% had hypermagnesaemia. There was significant association between magnesium levels and outcome on day 6 as well.

The results of present study revealed that there was significant increase in mean serum magnesium on day 3 and day 6 in those with recovery compared to day 1 magnesium levels. There was difference between day 1 and day 3 magnesium, day 1 and day 6 magnesium and day 3 vs. day 6 magnesium. There was significant difference in serum magnesium levels in non recovery group as well. However there was significant decrease in magnesium on day 6 compared to day 3 values.

Table 2: Correlation between serum creatinine and serum magnesium on day 3.

| Variables          | Serum creatinine | Serum magnesium |
|--------------------|------------------|-----------------|
| Pearson correlation| 1                | 0.188           |
| P value (n=99)     |                  | 0.062           |

Table 3: Correlation between serum creatinine and serum magnesium on day 6.

| Variables          | Serum creatinine | Serum magnesium |
|--------------------|------------------|-----------------|
| Pearson correlation| 1                | -0.064          |
| P value (n=99)     |                  | 0.530           |

Table 4: Distribution of parameters in the study.

| Variable                  | Mean | Median | Mode | SD  | Range | Minimum | Maximum |
|---------------------------|------|--------|------|-----|-------|---------|---------|
| Age                       | 43.1 | 44     | 45   | 13  | 49    | 21      | 70      |
| Hb (gm/dl)                | 13.0 | 13.35  | 14.20| 1.99| 10.58 | 6.02    | 16.60   |
| TLC (/cumm)               | 14.5 | 15.20  | 10.40| 5.96| 28.90 | 2.20    | 31.10   |
| Basal creatinine (mg/dl)  | 4.6  | 3.95   | 2.40 | 2.67| 12.90 | 0.80    | 13.70   |
| Day 1 Serum creatinine (mg/dl) | 4.8 | 4.20   | 2.40 | 2.71| 12.90 | 0.80    | 13.70   |
| Serum magnesium (mg/dl)   | 1.7  | 1.60   | 2.00 | 0.458| 2.700 | 0.80    | 3.50    |
| Day 2, Serum creatinine (mg/dl) | 4.5 | 3.50   | 2.40 | 2.989| 13.50 | 0.90    | 14.4    |
| Serum magnesium (mg/dl)   | 1.9  | 1.80   | 1.80 | 0.487| 3.00  | 1.00    | 4.0     |
| Day 3, Serum creatinine (mg/dl) | 4.1 | 2.55   | 1.90 | 3.482| 15.00 | 0       | 15.0    |
| Serum magnesium (mg/dl)   | 2.0  | 2.00   | 2.20 | 0.571| 4.20  | 1.0     | 5.2     |
| Urine output (24hr)       | 472.5| 480    | 100  | 296 | 1460  | 40      | 1500    |

Table 5: Association between magnesium levels on day 1 and recovery.

| Recovery day 1          | No Count | %  | Yes Count | %  |
|-------------------------|----------|----|-----------|----|
| Normal                  | 10       | 29.4| 30        | 45.5|
| Hypomagnesaemia         | 18       | 52.9| 35        | 53.0|
| Hypermagnesaemia        | 6        | 17.6| 1         | 1.5 |

χ²=9.78, df=2, p=0.007

Table 6: Association between magnesium levels on day 3 and recovery.

| Recovery day 3          | No Count | %  | Yes Count | %  |
|-------------------------|----------|----|-----------|----|
| Normal                  | 17       | 50.0| 42        | 63.6|
| Hypomagnesaemia         | 13       | 38.2| 17        | 25.8|
| Hypermagnesaemia        | 4        | 11.8| 7         | 10.6|

χ²=1.899, df=2, p=0.387
Table 7: Association between magnesium levels on day 6 and recovery.

| Recovery day 6 | No | Yes |
|----------------|----|-----|
|                | Count | %  | Count | %  |
| Normal         | 9    | 26.5 | 31    | 47.0 |
| Hypomagnesaemia| 22   | 64.7 | 14    | 21.2 |
| Hypermagnesaemia| 3   | 8.8  | 21    | 31.8 |

$x^2=19.093$, df=2, p<0.001

DISCUSSION

Hypomagnesemia is one of the most common electrolyte disturbance found in hospitalized patients especially in the critically ill patients. Prevalence of hypomagnesemia varies from 11 to 65% in different studies. In a study done by Larissa et al, the prevalence of hypomagnesemia was 63%.

Several studies have explained the association between hypomagnesemia and impaired AKI recovery. Magnesium relaxes smooth muscle by competing with calcium transport in cell membrane. Cyclosporine and angiotensin II-induced contraction in mesangial cells was inhibited by magnesium. Hypomagnesaemia alters the glomerular filtration rate (GFR) and the renal blood flow (RBF) and increases renal injury caused by post-ischemic insult. The aim of this study was to assess the prevalence of magnesium levels in acute kidney injury patients and to evaluate the role of magnesium in non-recovery of acute kidney injury.

Out of 120 cases, 20 cases were excluded out of which 4 were due to obstructive uropathy, 6 were suffering from multi-organ dysfunction syndrome and 10 were diabetic. 66 patients recovered from AKI and 34 did not recover. Out of 34 patients were treated with haemodialysis. Mean hospital stay was 7±2 days, majority of the patients were males (n=70, 70%). Most of the patients belonged to the age group 41 years and above (n=49, 49.0%). Symptomatic and protocol treatment was given in 100 patients and they recovered.

On day 1 mean serum magnesium was 1.7±0.5, on day 3 mean serum magnesium was 1.86±0.44 and on day 6, mean serum magnesium was 1.95±0.57. There was significant difference (increase) in mean serum magnesium on day 3 and day 6 compared to day 1 (p<0.001).

The current study revealed that there was significant positive correlation (Pearson correlation for serum creatinine=1 and serum magnesium=0.213) on day 1 (p=0.003). A nonsignificant positive correlation (Pearson correlation for serum creatinine=1 and serum magnesium=-0.188) on day 3 (p=0.062) and there was non-significant negative correlation observed (Pearson correlation for serum creatinine=1 and serum magnesium=-0.064) on day 6 (p=0.53).

Table 8: Serum magnesium in patients with recovery from AKI and non recovery from AKI.

|                | N  | Mean | SD  | ANOVA p value | Day 1 Vs. Day 3 | Day 1 Vs. Day 6 | Day 3 Vs. Day 6 |
|----------------|----|------|-----|---------------|-----------------|-----------------|-----------------|
| Recovered      |    |      |     |               |                 |                 |                 |
| Day 1 Magnesium| 66 | 1.65 | 0.36| p=0.000, Highly significant | p<0.001, Highly significant | p<0.001, Highly significant | p<0.001, Highly significant |
| Day 3 Magnesium| 66 | 1.88 | 0.45|               |                 |                 |                 |
| Day 6 Magnesium| 66 | 2.10 | 0.60|               |                 |                 |                 |
| Not Recovered  |    |      |     |               |                 |                 |                 |
| Day 1 Magnesium| 34 | 1.83 | 0.60| p=0.000, Highly significant | p=0.883, Not significant | p=0.142, Not significant | p=0.009, Highly significant |
| Day 2 Magnesium| 34 | 1.84 | 0.44|               |                 |                 |                 |
| Day 3 Magnesium| 34 | 1.66 | 0.38|               |                 |                 |                 |

On day 1, day 3, day 6, 53%, 30% and 36% had hypomagnesemia respectively. On day 1, out of 53 hypomagnesemia patients, 35 (66%) recovered and 18 (33.9%) did not recover. Out of 40 normomagnesemia patients 30 (75%) recovered and 10 (25%) did not recover. The p values of these observations were 0.007 which is statistically significant. On day 3, out of 30 hypomagnesemia patients, 17 (56.6%) recovered and 13 (43.3%) did not recover. Out of 59 normomagnesemia patients, 42 (71.1%) recovered and 17 (28.8%) did not recover. Out of 11 hypermagnesemia patients 4 non recovered. The p value of these observations is 0.387 which is non-significant. On day 6, out of 36 hypomagnesemia patients, 14 (38.8%) recovered and 22 (61.1%) did not recover. Out of 40 normomagnesemia patients 31 (77.5%) recovered and 9 (22.5%) did not recover. Out of 24 hypermagnesemia patients 21 recovered and 3 did not recover. The p value of these observations is 0.001 which is significant. These observations suggest that patients who were recovered

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from acute kidney injury were more in normal magnesium and hypermagnesium levels compared with hypomagnesemia on day 1, 3 and day 6. In the study there was significant increase in mean serum magnesium on day 3 and day 6 in those with recovery compared to day 1 magnesium levels. There was significant difference between day 1 and day 3 magnesium, day 1 and day 6 magnesium and day 3 versus day 6 magnesium with p<0.001.

Figure 1: Serum magnesium in those with recovery from AKI and non recovery from AKI.

A study done by Satish et al on 50 patients of ARF at St. John’s hospital showed 31 patients developed hypomagnesaemia during recovery phase of ARF, concluded treating hypomagnesaemia and associated electrolyte abnormalities ameliorated the symptoms. A study done by Alves et al, on 232 ICU patients, the prevalence hypomagnesaemia was high (63%). The presence of hypomagnesaemia is higher in patients whose renal function did not recover when compared with patients whose renal function recovered (p=0.003). Hypomagnesaemia is an independent risk factor for delayed recovery of renal function in critically ill AKI patients.

Limitation

Sample size was small and single centre study and there is lack of correlation between causes of acute kidney injury and severity of hypomagnesemia.

CONCLUSION

This study showed prevalence of hypomagnesemia was significantly higher in AKI patients and normal magnesium and hypermagnesium on day 1, 3 and day 6 was associated with recovery than non-recovery. Hypomagnesemia was associated more with non-recovery then recovery group. This study highlights the need of a large scale study to determine the association between magnesium levels and recovery of AKI and also whether serum magnesium monitoring and infusion helps AKI patients.

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