Acute Decrease in Serum Magnesium Level after Ischemic Stroke May Not Predict Decrease in Neurologic Function

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Background: Higher serum levels of magnesium (Mg(2+)) may contribute to improved outcome following ischemic stroke, and this may be related to vessel recanalization. Patients with low or normal serum magnesium levels during the acute phase of ischemic stroke may be more susceptible to neurologic deterioration (ND) and worse outcomes. *Methods:* All patients who presented to our center within 48 hours of acute ischemic stroke (July 2008 to December 2010) were retrospectively identified. Patient demographics, laboratory values, and multiple outcome measures, including ND, were compared across admission serum Mg(2+) groups and change in Mg(2+) from baseline to 24-hour groups. *Results:* Three hundred thirteen patients met inclusion criteria (mean age: 64.8 years, 42.2% female, 64.0% black). Mg(2+) groups at baseline were not predictive of poor functional outcome, death, or discharge disposition. Patients whose serum Mg(2+) decreased during the first 24 hours of admission were also not at greater odds of ND or poor outcome measures compared with patients with unchanging or increasing Mg(2+) levels. *Conclusions:* Our results suggest that patients who have low Mg(2+) at baseline or a reduction in Mg(2+) 24 hours after admission are not at a higher risk of experiencing ND or poor short-term outcome. Ongoing prospective interventional trials will determine if hyperacute aggressive magnesium replacement affords neuroprotection in stroke. **Key Words:** Stroke—ischemia—magnesium—neurologic deterioration—neuroprotection.

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Background

Magnesium (Mg(2+)) ions are known to block glutamatergic *N*-methyl-D-aspartate receptors in the central nervous system during instances of glutamate neurotoxicity[1] such as acute ischemic stroke.[2] Low Mg(2+) at the time of stroke may accelerate penumbral compromise and result in more severe stroke presentations[3] or early neurologic deterioration (ND) if not replaced with magnesium therapy.[4] Few studies have evaluated the impact of baseline Mg(2+) on stroke outcome.[3,5,6] The role of serum Mg(2+) or magnesium replacement in ischemic recovery, however, remains controversial and deserves further inquiry.[3,5] Clinical trials have demonstrated the safety of magnesium sulfate ($MgSO_4$) infusion in ischemic stroke patients[7] and suggested that $MgSO_4$ administration offers a therapeutic advantage.[8] Although magnesium infusion within 12 hours of stroke did not confer a survival or morbidity benefit in the Intravenous Magnesium Efficacy in Acute Stroke trial,[9] the ongoing Field Administration of Stroke Therapy–Magnesium trial is investigating the benefit of ultra-early intravenous (IV) magnesium administration.[10] In the present study, we examine the relationship between serum Mg(2+) at presentation and change in serum Mg(2+) at 24 hours with stroke severity and short-term functional outcome in patients with acute ischemic stroke.

Methods

Patients

We conducted a retrospective analysis of acute ischemic stroke admitted to our center between July 1, 2008, and December 31, 2010. Eligible patients were identified retrospectively from a prospectively collected stroke registry as previously described.[11] Admitted patients who did not have serum Mg(2+) assessed within 12 hours of presentation, experienced the index stroke after being admitted for a reason other than stroke, admitted more than 48 hours after stroke symptoms onset, or had an unknown time of stroke onset were excluded.

Variable Definitions

Baseline demographics, clinical and laboratory values, and stroke etiology according to the Trial of org 10172 in acute stroke treatment[12] were collected. Admission serum Mg(2+) level was defined as quantified serum Mg(2+) from a venous blood sample drawn within 12 hours of emergency department arrival. Serum Mg(2+) was also collected at 24 hours. In our clinical setting, serum Mg(2+) of 2.0 mg/dL or less is considered low. We further classified patients into dichotomous groups comparing patients whose Mg(2+) was lower at 24 hours than at admission. Outcomes were compared among patients with low Mg(2+) and patients with normal-to-high Mg(2+). Outcomes were further assessed according to whether their Mg(2+) was lower at 24 hours than admission. Outcomes included length of hospital stay, ND (defined as an increase in National Institutes of Health Stroke Scale [NIHSS] score of 2 points or more in a 24-hour period),[13] short-term neurologic impairment as measured by the discharge NIHSS score, short-term functional disability as measured by discharge modified Rankin Scale score,[14,15] unfavorable discharge disposition (ie, disposition that to a place other than home or inpatient rehabilitation), and all-cause in-hospital mortality.

A secondary analysis of patients with Mg(2+) replacement (≥1 g of IV magnesium sulfate) was conducted where we divided the patients into 4 subgroups: (1) patients who did not receive Mg(2+) replacement whose admission serum Mg(2+) was more than 2 mg/dL; (2) patients who did receive Mg(2+) replacement whose admission serum Mg(2+) was more than 2 mg/dL; (3) patients who did not receive Mg(2+) replacement whose admission serum Mg(2+) was 2 mg/dL or less; (4) patients who did receive Mg(2+) replacement whose admission serum Mg(2+) was 2 mg/dL or less. These 4 groups were used to assess the change in NIHSS measured at baseline, 24 hours, and at discharge.

Statistics

Continuous variables were reported as mean ± standard deviation when the distribution was normal and as median with range for non-normal distributions. Differences in frequencies of categorical variables were assessed by Pearson chi-square test or, if assumptions were not met, by Fisher exact test. Differences in distributions of continuous variables were assessed using Student *t* test for normally distributed variables and the Wilcoxon rank sum test for non-normally distributed variables. Random-effects mixed models were used to assess change in NIHSS over time for the 4 Mg(2+)/magnesium replacement groups, adjusting for IV tissue plasminogen activator use. Logistic regression models were used to assess low versus normal Mg(2+) and Mg(2+) lower at 24 hours versus Mg(2+) better at 24 hours and the association with poor functional outcome, unfavorable discharge disposition, and death. An alpha of .05 was considered significant. No adjustments for multiple comparisons were made because this was an exploratory analysis.[16] This study was approved by our institutional review board.

Results

Study Population

Of the 596 consecutive patients admitted to our center with acute ischemic stroke, 111 patients were excluded because serum Mg(2+) levels were not checked within 12 hours of emergency department arrival, 42 excluded because of stroke experienced after admission, 29 because these patients did not arrive at our emergency department until more than 48 hours after stroke symptoms onset, and 162 because of unknown time of stroke onset. These are