Hypomagnesemia in Intracerebral Hemorrhage

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BACKGROUND: **Magnesium (Mg) is an essential element for the body's normal physiological functioning. It has a major role in modulating vascular smooth muscle tone and peripheral arterial resistance. A low serum Mg level on admission (HMg_0) has been associated with more severe presentation in patients with subarachnoid hemorrhage. However, data on HMg_0 specifically in relation to intracerebral hemorrhage (ICH) are scarce. We sought to determine the incidence and clinical significance of HMg_0 in patients with ICH.**

METHODS: **We reviewed the records of consecutive patients with ICH over a 2-year period. Data collected included initial Mg levels (Mg_0), clinical and radiologic characteristics on presentation, and discharge outcomes. Regression analysis was performed to look for any association of low Mg_0 with admission blood pressure (BP) and Glasgow Coma Scale (GCS) scores. We also examined the correlation of HMg_0 with clinical/radiologic features, admission severity (based on the ICH score), and poor outcome on discharge.**

RESULTS: **In all, 33.6% presented with HMg_0. Mg0 levels were negatively associated with systolic BP presentation ($P < 0.0001$) and positively associated with the initial GCS scores ($P = 0.01$). Multivariate logistic regression showed an association between HMg_0 and severity at presentation ($P = 0.03$), but not with poor outcome on discharge ($P = 0.26$).**

CONCLUSIONS: **HMg_0 occurs in one third of patients with ICH and is associated with more severe presentation and intraventricular hemorrhage. Mg levels on admission correlate inversely with systolic BP and directly with GCS scores at presentation. HMg_0 does not influence outcomes at discharge.**

INTRODUCTION

Magnesium (Mg), the fourth most abundant cation in the human body, is an essential element in normal physiological functioning.[1] It plays a critical role in modulating vascular smooth muscle tone, which dominates peripheral vascular resistance and blood flow dynamics.[2] Admission hypomagnesemia (HMg_o) has been found in up to 38% of patients with subarachnoid hemorrhage (SAH), and is associated with higher World Federation of Neurosurgical Societies severity scores.[3] The incidence and significance of HMg_o in patients with intracerebral hemorrhage (ICH) are, however, unknown. ICH comprises 10%–15% of all strokes and is associated with high mortality.[4] The aim of this study was to assess the incidence of HMg_o in patients with ICH, and its relationship to clinical/radiologic features, severity at presentation, and discharge outcomes.

PATIENTS AND METHODS

Institutional review board approval was obtained for this study. We reviewed the medical records of consecutive patients with

Key words
- Blood pressure
- Hypomagnesemia
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- Magnesium
- Outcomes
- Severity

Abbreviations and Acronyms
BP: Blood pressure
GCS: Glasgow Coma Scale
HMg_0: Hypomagnesemia on admission
ICH: Intracerebral hemorrhage
IVH: Intraventricular hemorrhage
Mg_0: Serum magnesium on admission
SAH: Subarachnoid hemorrhage

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nontraumatic ICH treated at a tertiary care academic medical center between January 2011 and December 2013. We used the International Classification of Diseases, Ninth Revision, diagnosis code for ICH (431) to compile a list of patients for our analysis. Patients with ICH related to trauma, tumor, aneurysm, or arteriovenous malformation, and those who underwent emergency craniotomy for hematoma evacuation, were excluded. At our institution, all patients with ICH are managed in accordance with the American Heart Association/American Stroke Association Guidelines.[5]

We recorded the following data: initial blood pressure (BP) reading and Glasgow Coma Scale (GCS) scores from ambulance or emergency department records, serum Mg levels in the first set of laboratory tests (Mg_o), ICH volume, location, intraventricular hemorrhage (IVH), and patient age and sex. $HMg_o$was defined as Mg_o level $\leq$1.7 mg/dL (0.7 mmol/L). We used the ICH score to estimate ICH severity at presentation. The ICH score is a clinical grading scale that allows risk stratification on presentation with ICH.[6] It is valid for prediction of early mortality and long-term functional outcome.[7] An ICH score $\geq$3 was considered severe. Hematoma volume was measured on the initial computed tomography scan of the head using the ABC/2 method.[8] Outcomes on hospital discharge were recorded as scores on the modified Rankin scale, a stroke outcome scale with scores ranging from 0 (no symptoms at all) to 6 (dead).

We used Minitab 17 (Minitab Inc., State College, Pennsylvania) software for the statistical analysis. Variables were categorized as continuous (age, systolic BP, GCS, ICH volume), ordinal (ICH and mRS scores), and categorical (IVH, infratentorial ICH, hypomagnesemia). We first performed logistic regression analysis including Mg_o as a continuous variable, assessing its relationship with admission systolic BP and GCS scores. Student's t test was used to assess the association of Mg_o and HMg_o with continuous and ordinal variables. We dichotomized severity on admission and outcomes into categorical variables as follows: severe presentation was defined as ICH score $\geq$3, and poor outcome as mRS $\geq$4. Fisher's exact test or the χ^2 test (when appropriate) was used to relate HMg_o to clinical severity and to poor outcome. We then conducted a multivariate analysis of HMg_o with poor outcome as the categorical variable, adjusting for age, ICH volume, ICH location, IVH, and GCS. A P value of 0.05 or less was considered significant in all analyses.

RESULTS

Our cohort consisted of 128 patients with spontaneous ICH. Mean age was 70.7 $\pm$ 13.6 years, and 60.9% were men. All patients had serum Mg levels assessed as part of the emergency department laboratory tests within 6 hours of symptom onset. The average serum Mg_o level was 1.8 $\pm$ 0.24 mg/dL. Forty-three patients (33.6%) presented with hypomagnesemia. Table 1 presents the analysis of variables in relation to HMg_o in more detail. Logistic regression analysis showed an inverse linear relationship between Mg_o levels and presenting systolic BP ($P < 0.001$), and a direct correlation with admission GCS scores ($P = 0.014$). In addition, HMg_o was associated with more severe presentation, evident by higher average ICH scores (odds ratio, 2.51; 95% CI, 1.15–5.38; $P = 0.03$). No relationship was noted between HMg_o and poor discharge outcomes in univariate or multivariate analysis, after adjusting for the effects of other variables. There was an association between hypomagnesemia on admission and IVH ($P = 0.015$).

DISCUSSION

This study is the first to assess the incidence and the clinical significance of HMg_o in patients with ICH. Approximately 1 in 3 patients with ICH presented with hypomagnesemia. A significant linear correlation was noted between decreasing Mg_o levels and increasing systolic BP at presentation.

As many as 90% of patients with ICH present with increased BP.[9] The relationship between hypomagnesemia and hypertension has been demonstrated in animal models. The mechanism of hypertension is thought to be due to activation of phosphatidylinositol 3-kinase by low extracellular Mg concentrations, which ultimately leads to increased arterial tone and resistance.[10] Although there are some reports that poor intake or chronically low serum Mg levels may be associated with hypertension, there is little evidence that hypomagnesemia causes acute increase in BP.[11] No study to date has explored the existence of this relationship. The exact mechanism behind the

Table 1. Comparison of Characteristics Between Hypomagnesemic and Normomagnesemic Patients with Intracerebral Hemorrhage

Characteristic	HMg_0 (n = 43)	NMg_0 (n = 85)	Odds Ratio (95% Confidence Interval)	*P*
Mean age, years $\pm$ SD	71.5 $\pm$ 11.3	70.3 $\pm$ 14.6	–	0.63
Mean SBP, mm Hg $\pm$ SD	197.2 $\pm$ 19.5	173.9 $\pm$ 23.0	–	< 0.0001
Mean ICH volume, mL $\pm$ SD	43.5 $\pm$ 61.9	31.1 $\pm$ 40	–	0.9
Median GCS	11	14	–	0.01
IVH	58.1%	25.3%	2.5 (1.2–5.40)	0.015
Infratentorial ICH	18.6%	10.6%	1.9 (0.69–5.42)	0.27
ICH score $\geq$3	46.5%	25.9%	2.5 (1.15–5.40)	0.03
mRS score $\geq$4	65.1%	54.1%	1.6 (0.74–3.38)	0.26

HMg_0, hypomagnesemic on admission; NMg_0, normomagnesemic on admission; SD, standard deviation; SBP, systolic blood pressure; ICH, intracerebral hemorrhage; GCS, Glasgow Coma Scale; IVH, intraventricular hemorrhage; mRS, modified Rankin scale.