Acute Respiratory Failure Induced by Magnesium Replacement

in a 62-Year-Old Woman with Myasthenia Gravis

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Magnesium is known to act at the neuromuscular junction by inhibiting the presynaptic release of acetylcholine and desensitizing the postsynaptic membrane. Because of these effects, magnesium has been postulated to potentiate neuromuscular weakness. We describe the case of a 62-year-old woman with myasthenia gravis and a metastatic thymoma who was admitted to our intensive care unit for management of a myasthenic crisis. The patient's neuromuscular weakness worsened in association with standard intravenous magnesium replacement, and the exacerbated respiratory failure necessitated intubation, mechanical ventilation, and an extended stay in the intensive care unit. The effect of magnesium replacement on myasthenia gravis patients has not been well documented, and we present this case to increase awareness and stimulate research. In addition, we discuss the relevant medical literature. (Tex Heart Inst J 2015;42(5):495-7)

Key words: Magnesium/blood; magnesium sulfate/administration & dosage/adverse effects/therapeutic use; myasthenia gravis/complications/physiopathology; neuromuscular junction/drug effects; pre-eclampsia/complications; respiratory insufficiency/drug effects; risk factors; vital capacity

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Myasthenia gravis, an autoimmune disorder of the neuromuscular junction, can cause severe skeletal-muscle weakness.¹ About 15% to 20% of myasthenia gravis patients experience myasthenic crises, defined as respiratory failures that necessitate mechanical ventilation.² Myasthenic crisis is typically triggered by an infection; however, it can be precipitated by any stressful event or by drugs.³ Patients with myasthenia gravis are typically prescribed pyridostigmine and steroids as maintenance to prevent a crisis, and they are given intravenous immunoglobulin (IVIG) and plasmapheresis as rescue therapies. It is crucial to avoid interventions that might exacerbate the disease process.

We report the case of a patient with myasthenia gravis and metastatic thymoma who was admitted to our institution's intensive care unit (ICU) for management of a myasthenic crisis. Her condition was worsened by the administration of intravenous magnesium (Mg). In addition, we discuss the relevant medical literature.

Case Report

In 2014, a 62-year-old woman with a history of metastatic thymic carcinoma and myasthenia gravis presented at our emergency center with a 2-day history of difficulty in swallowing, shortness of breath, and progressive weakness. She was taking 30 mg of prednisone every morning, 60 mg of pyridostigmine twice/d, and 180 mg of extended-release pyridostigmine at night. Her symptoms suggested a myasthenic crisis, and she was admitted to the ICU. She was given steroids, IVIG, scheduled pyridostigmine, and broad-spectrum antibiotics for suspected pneumonia. On ICU day 2, her serum Mg level was 2.2 mg/dL, and she was given 16 mEq of magnesium sulfate intravenously. That evening, test results of pulmonary function showed substantial decreases in the patient's vital capacity (from 1.1 to 0.6 L) and negative inspiratory force (from -15 to -10). The patient declined intubation and invasive mechanical ventilation. During the morning of ICU day 3, the patient was granted a trial of noninvasive ventilation and was given steroids, IVIG, and a pyridostigmine drip. When the trial ventilation failed to improve her condition, she agreed to intubation and mechanical ventilation. She underwent 3 plasma exchanges and was successfully extubated on ICU day 4. The next morning, her serum Mg level of 2.2 mg/dL prompted another intravenous dose of 16 mEq of magnesium sulfate. The patient reported worsening weakness in her upper extremities, hoarseness, and

difficulty in swallowing. Of note, her vital capacity decreased from 2 to 1.2 L without substantial change in her negative inspiratory force. Her symptoms resolved after a plasma exchange the same morning, and she was not reintubated. Her subsequent therapy included daily electrolyte replacement with specific orders not to treat serum Mg levels higher than 1.6 mg/dL. The pyridostigmine drip was converted to oral doses, and the steroid regimen was tapered. She was transferred from the ICU on day 7 and was discharged from the hospital 3 days later, with follow-up monitoring as an outpatient.

Discussion

Correcting our patient's low serum Mg level led to acute respiratory failure, intubation, invasive mechanical ventilation, and a prolonged ICU stay. Magnesium is used frequently in hospitals and has well-described effects on the neuromuscular junction; however, we found only a few reports of Mg replacement that led to the diagnosis or exacerbation of myasthenia gravis.⁴⁻⁸ In 1954, Del Castillo and Engbaek⁹ stated that Mg's effects on neuromuscular transmission come primarily from its ability to decrease the depolarizing capacity of acetylcholine on the motor endplate. Subsequent investigators concluded that Mg's major action is to compete with calcium at the presynaptic membrane, thereby interfering with acetylcholine release.^{10,11} The detrimental effect of Mg on the neuromuscular junction is therefore both pre- and postsynaptic.

Patients who are admitted to the ICU often have low serum Mg levels.¹² Hypomagnesemia is associated with higher mortality rates and can lead to neuromuscular excitability, abnormalities in calcium metabolism, arrhythmias, altered mental status, and hypokalemia.¹²⁻¹⁴ Magnesium replacement is often necessary in critically ill patients, especially those with preeclampsia. Cohen and associates⁵ reported the case of a myasthenic and preeclamptic patient who sustained postpartum respiratory failure after Mg therapy. The authors concluded that Mg replacement is contraindicated in the myasthenic patient. However, given the higher mortality rate of patients who present with hypomagnesemia, and its role in life-threatening cardiac arrhythmias and other conditions, strictly avoiding Mg replacement in patients with myasthenia gravis might not be feasible. Bashuk and Krendel⁶ reported the development of quadriplegia in a preeclamptic patient during parenteral Mg therapy. Klair and colleagues⁷ reported a case of myasthenia gravis that was unmasked by intravenous Mg replacement in a patient who had presented with chronic dysphagia; the authors recommended avoiding drugs that affect neuromuscular transmission, to reduce the risk of myasthenic crisis. Mueksch and Stevens⁸ reported the protracted hospitalization of a patient who presented in

labor and who sustained respiratory failure associated with Mg replacement.

Magnesium is used therapeutically to prevent seizures in severe preeclampsia, and as therapy for eclampsia and cardiac arrhythmias.^{10,15} Herpolsheimer and associates⁴ found that intravenous Mg infusion in parturient patients with preeclampsia significantly decreased forced vital capacity and negative inspiratory force, both of which indicate generalized muscle weakness. Side effects most typically seen in association with serum Mg concentrations from 2.1 to 4 mEq/L are nausea, flushing, hypotension, bradycardia, and loss of deep tendon reflexes.¹⁶ Serum toxicity can progress to complete heart block and flaccid quadriplegia.¹⁶

Patients with junctional disorder are more sensitive to Mg-induced weakness, so a lower Mg level and a higher threshold for Mg replacement are indicated in those who have been diagnosed with myasthenia gravis.¹⁷ Furthermore, Mg-containing antacids and laxatives, and lactate-containing infusions such as Lactated Ringer's solution, should be avoided or used with caution.^{18,19} Vital capacity and maximal inspiratory force should be monitored every 2 to 4 hours after Mg replacement. When this monitoring is not feasible, then pulse oximetry, blood gas analysis, plethysmography, and transcutaneous carbon dioxide monitoring are alternative methods, albeit less sensitive.^{20,21} Educating patients to avoid pharmacologic precipitants of neuromuscular weakness is also recommended.

We conclude that routine Mg-replacement protocols might be inappropriate in the treatment of patients who have myasthenia gravis and in other patients who have borderline respiratory function.

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