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LETTER TO THE EDITOR

Factors influencing magnesium infusions in hematopoietic cell transplants

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To the Editor:

We read with interest the comparison of intravenous (IV) short (mean 2.07 g/h; actual 0.8–6 g/h) vs. prolonged (0.5 g/h) magnesium sulfate infusions in hospitalized autologous and allogeneic hematopoietic cell transplant (HCT) patients [1]. These different rates of magnesium infusion showed no significant improvement in the percentage of days in the therapeutic serum magnesium range of 2–2.7 mg/dL. This was also similarly seen in an outpatient allogeneic HCT population comparing 4 g/h vs. 4 g/2 h with lower magnesium doses (median 2.2 vs. 2.9 g/day, respectively) needed over the shorter infusion duration of 1 h [2].

The short magnesium infusion group had a mean hospital length of stay of 24.4 days with 6.2 days of magnesium repletion totaling 21.4 g received compared to the prolonged magnesium infusion group staying 29 days in the hospital with 7.2 days of magnesium repletion totaling 22.5 g received. The magnesium dosing and treatment threshold for hypomagnesemia was not clearly stated and appears to be under-dosed based upon the power analysis estimating HCT patients would have 60% of days with a therapeutic serum magnesium range of 2–2.7 mg/dL, while observing 28.1% in the short infusion and 32.2% in the prolonged infusion groups. Without knowing what the average serum magnesium concentrations were in the autologous and allogeneic HCT patients, this patient population represents extreme values that skew the reference range leading the authors to use their technical therapeutic range of 1.3–2.7 mg/dL. While 97.3% of the short magnesium infusion group and 97.9% of the prolonged infusion group were within this technical therapeutic range, it would appear that 69.2% of the short infusion group and 65.7% of the prolonged infusion group were outside the normal serum magnesium range of 2–2.7 mg/dL, unknowingly above the 60% threshold chosen for their power analysis. The practice of IV magnesium replacement is largely based upon acute myocardial infarction trials administering an initial magnesium bolus (e.g., 2 g) followed by continuous infusions up to 16 g over 24 h [3–6]. The observed changes in serum magnesium concentrations have ranged from 0.08 to 0.13 mg/dL per gram of IV magnesium administered. Given that the short magnesium infusion group received an estimated 3.5 g and the prolonged infusion group received an estimated 3 g dose, the maximum expected change in serum magnesium concentrations would have been in the range of 0.2 to 0.5 mg/dL after the infusions depending on renal function. It is unclear what possible role electrolyte shortages of IV magnesium may have had during this study time period possibly limiting dosing to be able to achieve a normal serum magnesium concentration. Magnesium has a relatively wide therapeutic index as an electrolyte (e.g., approximately 7 g of IV magnesium is required to change the serum concentration from 2 up to 2.7 mg/dL) and dosing ideally should be weight-based in HCT patients as they clinically require 0.05–0.2 g/kg/day to reach the desired normal range. The provision of patient weights and daily IV magnesium dosages would have allowed for the estimation of change in serum levels.

Interestingly, more patients receiving the prolonged magnesium infusion experienced hypermagnesemia (> 2.7 mg/dL) than the shorter infusion (12% vs. 5%, $p = 0.43$). True hypomagnesemia (< 2 mg/dL) was not specifically reported for either infusion group, only as the technical therapeutic range < 1.3 mg/dL. Interpreting these results is difficult without an assessment of renal function, a noted

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deficiency in both of the publications assessing magnesium infusion rates [1, 2]. The use of other therapies or disease states affecting serum magnesium, namely diuretics (e.g., furosemide) and proton pump inhibitors [7] or diarrhea, were also not reported and are commonly seen in hospitalized HCT patients. Since more prolonged magnesium infusion patients received oral magnesium replacement than the short infusion group (31.7% vs. 21.9%, $p = 0.32$), this may have also affected fecal magnesium losses, as all the oral salts (e.g., oxide, chloride, gluconate) are associated with diarrhea. While parenteral nutrition with magnesium contribution was noted, there was no mention of other dietary intake, enteral nutrition, or oral nutrition supplements that may have also contributed magnesium intake.

The use of a therapeutic outcome, such as cessation of physical or cardiac symptoms or even use of potassium replacement needs [8], instead of serum magnesium concentrations may benefit future prospective trials of IV magnesium to determine the optimal infusion rate. Since this is one of the few published studies comparing IV magnesium infusion rates to date, the missing details may explain why no differences were noted, as well as a type II statistical error.

Authorship Authors had access to the data and participated in writing the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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