Hypermagnesemia: Elderly Over-the-counter Drug Users at Risk

The article by Fung et al[1] published in the August 1995 issue of the ARCHIVES probably created public panic unnecessarily. The 69-year-old woman with hypermagnesemia most likely had abnormal renal function when she consumed the bottles of magnesium-containing antacids. From the case report, the estimated creatinine clearance,[2] calculated from age, sex, and serum creatinine levels, was 0.47 mL/s (28.3 mL/min) (normal range, 0.76-1.19 mL/s [45.7-71.4 mL/min]), suggesting that this patient did indeed have impaired renal function. A patient with normal kidney function secretes magnesium rapidly through the kidneys. In a normal state, the kidney filters approximately 2.5 g of magnesium and reclaims 95%, excreting some 100 mg/d in the urine to maintain homeostasis. Approximately 25% to 30% is reclaimed in the proximal tube through a passive transport system that depends on sodium reabsorption and tubular fluid flow. Usually, as serum magnesium concentration increases, there is a linear increase in urinary magnesium excretion, paralleling that of insulin.[3] With normal kidney function, hypermagnesemia or magnesium intoxication usually does not develop,[4] even during high intravenous magnesium infusion.[5,6] In the ISIS-4 study,[6] about 20 000 patients received 17 g/d of intravenous magnesium without intoxication.

Age per se is not a risk factor for development of hypermagnesemia as written in the article by Fung et al. The magnesium intake of the elderly tends to be low, and their susceptibility to magnesium deficiency is intensified by diminished intestinal absorption and increased urinary output of magnesium.[7,8] Elderly persons, who are subject to disorders that impair absorption and renal function, and who may be taking magnesium-wasting medications, are likely to be particularly vulnerable to magnesium deficiency.[9] Without renal function parameters and magnesium levels, it is unfair to compare other case reports as the authors did in their Table 2.[1] From this table, it is impossible to blame magnesium by itself as the cause of patients' signs and symptoms.

Unfortunately, the name of the article is misleading and might adversely affect the treatment of the elderly population and those who need magnesium supplementation. This case report describes the occurrence of magnesium intoxication due to impaired renal function and magnesium overdose, and not a normal phenomenon seen with magnesium supplementation. Therefore, a better title of the article might have been: "Elderly Patients With Impaired Renal Function and Anticholinergic/Narcotic Medications Should Be Aware of the Possibility of Magnesium Intoxication by an Overdose of Magnesium-Containing Antacids."

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On behalf of Blaine Company, Inc, I would like to respond to the article, "Hypermagnesemia: Elderly Over-the-counter Drug Users at Risk" by Fung et al[1] in the ARCHIVES.

The authors used the work of Whang and Ryder[2] in an incomplete and misleading way. Whang and Ryder reported, "Serum magnesium abnormalities were identified in 546 of the 1033 specimens (hypomagnesemia [<0.74 mmol/L], 487; hypermagnesemia [>0.99 mmol/L], 59."

Fung et al fail to include the data in parentheses, which state that 89% of the 546 "abnormal levels" are hypomagnesemic and only 11% are hypermagnesemic. I think that deleting data from a report to support one's point of view is inappropriate to say the least.

Fung et al report on a patient who consumed bottles of antacid (who had been admitted and discharged the previous month for the same condition): "in her second comatose day . . . a routine laboratory screen that had been ordered earlier in the day by a medical resident revealed a serum magnesium level of 6.65 mmol/L (16.2 mg/dL). . . ."

According to *Webster's College Dictionary*, routine is "customary, regular, habitual." The magnesium screen was not routine or it would have been ordered immedi-

ately, not on the second comatose day by an unnamed resident, whom I applaud for his knowledge and alertness.

This, I think, is the point that needs to be emphasized. Fung et al believe, along with Whang and Ryder, Altura et al,[3] Seelig et al,[4] and thousands of others that the knowledge of magnesium abnormality, especially hypomagnesemia, has been seriously overlooked and neglected and that it is past time for including magnesium in the "routine" blood chemistry profile panel. Since the symptoms of hypomagnesemia also are coma and death, I wonder: How many deaths could be attributed to this side of the abnormal condition and conditions exacerbated by hypomagnesemia?

It is medical reporting like this that leads to sensational journalism such as the headlines, "Magnesium-based Antacids Can Be Lethal" (*Cincinnati Enquirer*. August 30, 1995:A2) and "Magnesium Poisoning From OTCs: Threat to Elderly?" (*Pharmacy Today*. January 15, 1996).

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In reply

We read with interest the letters from Shechter and Blaine commenting on our recent publication of a case of magnesium intoxication due to antacid misuse. These letters raise interesting points, but they miss the major message in our report.

Undoubtedly, clinically significant hypermagnesemia is infrequent in people with normal renal function. The purpose of our report was to raise awareness among medical professionals that hypermagnesemia can develop if patients misuse magnesium-containing products when they are taking certain concomitant medications and/or have coexisting gastrointestinal disease. We must stress that labeled and legitimate use of these products is both safe and effective. However, some consumers misuse magnesium-containing products[1,2] and misuse of laxatives and antacids is not uncommon.[3-5] Further, in addition to electrolyte imbalance, misuse of many of these products may cause dehydration, metabolic alkalosis, or milk alkali syndrome.

We agree that hypomagnesemia may develop from poor diet or decreased gastrointestinal absorption, and we acknowledge that Whang and Ryder[6] reported both hypomagnesemia and hypermagnesemia in routine laboratory screening. However, particularly in elderly patients, self-medication with magnesium supplements can be dangerous if not directed by a health care professional when renal function and concomitant medical factors are unknown. In fact, we reported a MEDWATCH case, an 83-year-old woman who self-medicated with magnesium "supplementation" for an unknown period of time and developed hyporeflexia, muscle flaccidity, bradycardia, and hypotension and died with a toxic serum magnesium level. Nevertheless, as we emphasized in our article, the Food and Drug Administration spontaneous reporting system (our Table 2) may provide a signal for drug-related events but is not constructed to provide a definitive cause and effect relationship.

Shechter incorrectly estimated our patient's creatinine clearance. Based on a more recent edition of the quoted text, calculation of the estimated normal range of creatinine clearance for a woman 60 to 69 years of age is 0.75 to 1.25 mL/s (45-75 mL/min).[7] However, underlying assumptions for application of this equation are lack of obesity, euvolemia, and stable renal function. On admission, our patient was obese and had prerenal azotemia (serum urea nitrogen, 14.3 mmol/L [40 mg/dL]; creatinine, 150 μmol/L [1.7 mg/dL]). At discharge and several months before admission, her creatinine level was normal (71 μmol/L [0.8 mg/dL]). Thus, our patient's clinical status on admission precluded an accurate estimation of her creatinine clearance by this method.

References were given to support the safety of intravenous magnesium, an issue not raised by our article. However, we disagree with Shechter's conclusion that the ISIS-4 study[8] did not show hypermagnesemia. This study was designed to answer whether use of intravenous magnesium after myocardial infarction affects mortality, not magnesium intoxication. Neither serum magnesium levels nor renal function parameters were provided, and the authors stated that symptoms of hypermagnesemia were not actively sought. Nevertheless, bradycardia was recorded to be significantly more common among those given intravenous magnesium, and 89 patients given magnesium developed flushing and burning compared with 12 patients in the control group.

As for the title of our publication, many alternatives may have been superior to our title. However, we believe that Shechter's proposed title would not have been one of these because it is neither brief, succinct, nor relevant to the major point in our publication.

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