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An Unusual yet “Mg”nificent Indication for Hemodialysis

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Abstract

Hypermagnesemia is an uncommon electrolyte abnormality, due to the fact that magnesium toxicity is only seen in the setting of a massive exposure to exogenous magnesium, often in the setting of renal insufficiency. Here, we report a case of severe hypermagnesemia that resulted in complete paralysis that was secondary to Renacidin administration, a rarely used agent used for intra-renal pelvic or intra-vesicular instillation dissolution of struvite stones. The patient also had concurrent acute kidney injury (AKI). The patient’s magnesium was as high as 16.7 mg/dL, and he initially received hemodialysis followed by continuous venovenous hemodialysis. These therapies resulted in a rapid reduction in magnesium levels and eventual resolution of the muscular weakness. The case discussion highlights several key aspects of magnesium homeostasis, the limited mechanistic understanding of Renacidin-induced hypermagnesemia, and the role of renal replacement therapies in the treatment of hypermagnesemia.

Clinically relevant or symptomatic derangements in magnesium homeostasis are uncommon. Severe hypermagnesemia is almost always due to an excessive exogenous load and usually in the setting of renal insufficiency. Here, we report a case of hypermagnesemia resulting in complete neuromuscular paralysis apparently due to bladder irrigation with Renacidin. Renacidin has a substantial magnesium content, and significant systemic absorption is variably seen. The patient responded well to intermittent hemodialysis (IHD) and continuous venovenous hemodialysis (CVVHD). We review the epidemiology of hypermagnesemia, describe what is known about Renacidin, and review the rationale for dialysis as a therapy for hypermagnesemia.

Case Report

A 34-year-old man with an extensive medical history, notable for paraplegia due to traumatic spinal cord injury and recurrent struvite nephrolithiasis requiring percutaneous nephrostomy tubes, was electively admitted to the Hospital of the University of Pennsylvania for a left-sided ureteroscopy and lithotripsy. During the procedure, he underwent replacement of a Double J stent in the left ureter. Upon completion of the surgery, he was successfully extubated and transferred from the post-anesthesia care unit to the urology service. His bladder was then irrigated with Renacidin at 60 ml/hour for approximately 28 hours to assist with dissolution of residual fragments.

Two days following surgery, the patient was found unresponsive and apneic. The rapid response team was called and he was emergently intubated and transferred to the surgical intensive care unit (SICU). Table 1 summarizes his laboratory data. Of note were the new development of AKI with the creatinine rising from 1.1 mg/dL to 3.1 mg/dL and an extremely elevated magnesium level at 11.4 mg/dL. Urgent nephrology consultation was requested.

The patient's temperature was 98°F, pulse was 61 beats per minute, blood pressure was 138/47 mmHg, and oxygen saturation was 100% on a ventilator. The urine output could not be accurately determined due to the bladder irrigation. Examination revealed an obese male who appeared chronically ill. There was no pupillary response to light. Neck examination was notable for a well-healed tracheostomy scar, and an endotracheal tube was in place. He had an absent gag reflex with deep suctioning even though several hours had passed since the last dose of any sedatives, paralytics, or psychoactive agents. Pulmonary auscultation was limited to the anterior chest, and bilateral breath sounds were present. The abdominal examination was unremarkable. There was 1+ pitting edema present in both lower extremities. All extremities were flaccid, and deep tendon reflexes could not be elicited.

Furosemide (120 mg) was administered intravenously to increase renal magnesium excretion; there was no appreciable increase in his urine output. Intravenous calcium gluconate (1 g) was also administered in an attempt to temporarily reverse the neurotoxicity from hypermagnesemia. The serum magnesium level continued to increase (16.7 mg/dL), and a nontunneled dialysis catheter was placed in the right internal jugular vein. IHD was initiated with a blood flow rate of 400 ml/minute and a dialysate flow rate of 600 ml/minute containing a magnesium concentration of 0.9 mg/dL (0.75 mEq/L). The serum magnesium level fell from 16.7 mg/dL at the start of IHD to 6.9 mg/dL immediately after its completion 3 hours later. This was followed by CVVHD with a high dialysate flow rate (5000 ml/hour) using a dialysate magnesium concentration of 1.8 mg/dL (1.5 mEq/L). Figure 1 shows the temporal magnesium and creatinine trends for the first six hospital days.

The patient began to show signs of spontaneous breathing and increased muscle tone within 12 hours of CVVHD at which time his magnesium level was 6.0 mg/dL. CVVHD was continued until hospital day 4, at which point the magnesium level was stable at 3.3 mg/dL and the patient had recovered baseline neuromuscular function. His subsequent ICU stay was complicated by acute respiratory distress syndrome requiring prolonged mechanical ventilation. Ultimately, his AKI resolved and he was discharged approximately 1 month after admission. Two weeks after discharge, his serum creatinine and magnesium levels were 0.9 mg/dL and 1.9 mg/dL, respectively.

Discussion

Urologic chemolysis has been variably employed as a treatment option for renal calculi for many decades (1,2). Renacidin (United Guardian), also known as hemiacidrin, contains citric acid, magnesium carbonate, and glucono-delta-lactone, and has been reported to be clinically effective for the dissolution of struvite calculi (3–7). The clinical efficacy of this

agent is based on its ability to lower pH surrounding the stone and by forming soluble complexes with calcium and phosphate present in the stone (8).

Renacidin contains 0.82 g/dL of magnesium, and if administered at the same rate that our patient received, it would result in the exogenous administration of approximately 12 g of elemental magnesium within a 24-hour period. By comparison, a typical 4-g intravenous rider of magnesium sulfate contains approximately 10% elemental magnesium.

Hypermagnesemia complicating Renacidin use should not be surprising, but has not been reported in the literature for approximately 20 years (9–13), perhaps due its infrequent use and intermittent availability on the market. To our knowledge, these are the highest magnesium levels reported in the literature as a consequence of Renacidin use. This is also the first report describing the use of dialysis in the treatment of hypermagnesemia related to Renacidin exposure.

Hypermagnesemia occurs most commonly in the setting of reduced glomerular filtration rate due to chronic kidney disease (CKD), often end stage (14,15). Assuming an average amount of dietary magnesium intake, hypermagnesemia in hemodialysis patients tends to be mild and asymptomatic with levels typically around 2.5–3.5 mg/dL. Hypermagnesemia can occur in patients with normal renal function with the administration of very large doses (e.g., the parenteral magnesium therapy for obstetric indications). Epidemiologic details and historical context surrounding these various causes have been reviewed elsewhere (16). Table 2 provides an overview of reported cases of hypermagnesemia with an emphasis on cases related to Renacidin (9–13,17–21). Renacidin has similarly been reported to cause hypermagnesemia in the absence of reduced renal function at baseline. A 34-year-old woman with normal renal function developed hypermagnesemia to 12.5 mg/dL during Renacidin therapy (13). Although her creatinine at baseline was 0.2 mg/dL, it did increase to 0.5 mg/dL at the time of her respiratory arrest.

Mechanistic investigations of Renacidin-induced hypermagnesemia have been carried out in dogs in the 1950s and came to the general but obvious conclusion that hypermagnesemia would occur when the infusion rate exceeded renal clearance rate for magnesium (22). Initial reports of infusion into the renal pelvis speculated that magnesium absorption could occur across damaged urothelium (from struvite stones) as well as passively via the renal parenchyma. This latter mechanism is further enhanced by an increased hydrostatic intra-ureteral pressure as a result of the infusion (12). While struvite stones do contain magnesium (they are composed of a mixture of magnesium ammonium phosphate and calcium carbonate), the contribution of struvite dissolution to development of hypermagnesemia is likely insignificant compared to the infusion itself.

Lastly, even if baseline renal function is normal (as it likely was in our case), Renacidin-induced hypermagnesemia may be exacerbated by kidney injury directly related to the infusion itself. The mechanism of this potential nephrotoxicity is thought to be from papillary necrosis, possibly due to the low pH (4.0) of the solution (23,24). Whether there are direct effects of hypermagnesemia or hypermagnesuria on renal function similar to phosphate nephropathy following bowel prep for colonoscopy (25) is unclear and unreported. Magnesium is known to be a vasodilator (26), so it is unlikely that there are

harmful effects on renal vascular tone such as those seen with hypercalcemia. Therefore, although AKI certainly increases the risk of hypermagnesemia in patients receiving Renacidin, the role of Renacidin in causing AKI is not firmly established.

In this report, successful restoration of a normal magnesium level was achieved through a combination of IHD and CVVHD. The physiological basis for this strategy was to rapidly reduce magnesium levels by relying on IHD for its high flows and efficient diffusive clearance of magnesium. As much as 70% of magnesium in plasma is normally found in the ionized form with another 5–10% is complexed with anions such as bicarbonate or citrate (27); both of these pools are dialyzable. The remaining 20–25% of magnesium in plasma is protein bound and is not dialyzable. In the setting of marked hypermagnesemia, a higher dialyzable fraction may well be present but data do not exist on this point. Most (99%) of the body's magnesium is outside the plasma space in bone and intracellular compartments. In the setting of substantial magnesium excess, these pools may contribute to “rebound” hypermagnesemia following extracorporeal treatment. Although there is a lone report describing this phenomenon after IHD in the setting of magnesium toxicity (17), it is unclear if this entity widely occurs.

Given these theoretical concerns and the persistence of hypermagnesemia in our patient after IHD, further magnesium removal via CVVHD was performed. There are few quantitative assessments of magnesium flux on CRRT. A single study involving six trauma patients suggested that approximately 598 mg (23.9 mmol) of elemental magnesium can be removed per day. However, this was calculated in the absence of hypermagnesemia, which is a critical determinant of magnesium removal rate (28). As reflected in Table 2, there are widely varying practice patterns on the use of dialysis for severe hypermagnesemia, perhaps reflecting the observation that symptom severity may not always correlate with magnesium levels.

The cause of hypermagnesemia in this case was not immediately apparent. Our initial input as the consulting nephrology service, aside from urgent dialysis, was to jointly review all medication administration with the SICU team with a special emphasis on perioperative infusions that may have contained magnesium. Renacidin is not a standard order in our hospital electronic medical record, and thus, the record of its administration was only discovered by the surgical intern who examined the operative report.

Even though Renacidin is not commonly used, nephrologists and urologists should be aware of its potential toxicity if they plan on using it. Although no formal guidelines exist, monitoring the serum magnesium and serum creatinine at least twice daily would be advisable since very rapid increases are possible, as was likely the case with our patient. We suggest this approach even if the patient has normal renal function prior to administration.

References

1. Kachrilas S, Papatsoris A, Bach C, Bourdumis A. The current role of percutaneous chemolysis in the management of urolithiasis: review and results. *J Urol*. 2013; 111:313–314.
2. Bernardo N, Smith A. Chemolysis of urinary calculi. *Urol Clin N Am*. 2000; 27:355–365.

3. Angermeier K, Stroom S, Yost A. Simplified infusion method for 10% hemiacidrin irrigation of renal pelvis. *Urology*. 1993; 41:243–246. [PubMed: 8442307]
4. Sant GR, Blaivas JG, Meares EM Jr. Hemiacidrin irrigation in the management of struvite calculi: long-term results. *J of Urol*. 1983; 130:1048–1050. [PubMed: 6644880]
5. Wall I, Tiselius HG, Larsson L. Hemiacidrin: a useful component in the treatment of infectious renal stones. *Eur Urol*. 1987; 15:26–30.
6. Massaro FJ, Weiner B, Sant GR, Meares EM Jr. Dissolution of struvite calculi by hemiacidrin solution. *Pharmacotherapy*. 1983; 3:344–348. [PubMed: 6657490]
7. Collins S, Ortiz J, Maruffo F, Hruby GW, Pierorazio PM, Gupta M, et al. Expedited struvite-stone dissolution using a high-flow low-pressure irrigation system. *J Endourol*. 2007; 21:1153–1157. [PubMed: 17949316]
8. Healy KA, Ogan K. Pathophysiology and management of infectious staghorn calculi. *Urol Clin N Am*. 2007; 34:363–374.
9. Thompson IM, Mora RV. Hypermagnesemia associated with hemiacidrin irrigation. *J Urol*. 1984; 132:741–742. [PubMed: 6471222]
10. Wilson C, Azmy AF, Beattie TJ, Murphy AV. Hypermagnesemia and progression of renal failure associated with renacidin therapy. *Clin Nephrol*. 1986; 25:266–267. [PubMed: 3720036]
11. Jenny DB, Goris GB, Urwiller RD, Brian BA. Hypermagnesemia following irrigation of renal pelvis. Cause of respiratory depression. *JAMA*. 1978; 240:1378–1379. [PubMed: 682332]
12. Cato AR, Tulloch AG. Hypermagnesemia in a uremic patient during renal pelvis irrigation with renacidin. *J Urol*. 1974; 111:313–314. [PubMed: 4813568]
13. Fassler CA, Rodriguez RM, Badesch DB, Stone WJ, Marini JJ. Magnesium toxicity as a cause of hypotension and hypoventilation. Occurrence in patients with normal renal function. *Arch Intern Med*. 1985; 145:1604–1606. [PubMed: 4026491]
14. Saha H, Harmoinen A, Pietilä K, Mörsky P, Pasternack A. Measurement of serum ionized versus total levels of magnesium and calcium in hemodialysis patients. *Clin Nephrol*. 1996; 46:326–331. [PubMed: 8953122]
15. Navarro-González J, Mora-Fernández C, García-Pérez J. Reviews: clinical implications of disordered magnesium homeostasis in chronic renal failure and dialysis. *Semin Dial*. 2009; 22:37–44. [PubMed: 19250445]
16. Agus ZS, Wasserstein A, Goldfarb S. Disorders of calcium and magnesium homeostasis. *Am J Med*. 1982; 72:473–488. [PubMed: 7036737]
17. Weng YM, Chen SY, Chen HC, Yu JH, Wang SH. Hypermagnesemia in a constipated female. *J Emerg Med*. 2013; 44:57–60.
18. Yagil Y, Stalnikowicz R, Michaeli J, Mogle P. Near drowning in the Dead Sea: electrolyte imbalances and therapeutic implications. *Arch Intern Med*. 1985; 145:50–53. [PubMed: 3970646]
19. Ellis RJ. Severe hypernatremia from sea water ingestion during near-drowning in a hurricane. *West J Med*. 1997; 167:430–433. [PubMed: 9426487]
20. Qureshi T, Melonakos T. Acute Hypermagnesemia After Laxative Use. *Ann Emerg Med*. 1996; 28:552–555. [PubMed: 8909278]
21. Morisaki H, Yamamoto S, Morita Y, Kotake Y, Ochiai R, Takeda J. Hypermagnesemia-induced cardiopulmonary arrest before induction of anesthesia for emergency cesarean section. *J Clin Anesth*. 2000; 12:224–226. [PubMed: 10869923]
22. Wrong O, Davies HEF. The excretion of acid in renal disease. *Q J Med*. 1959; 110:259–313.
23. Gonzalez R, Whiting B, Canales B. The history of kidney stone dissolution therapy: 50 years of optimism and frustration with renacidin. *J Endourol*. 2012; 26:110–118. [PubMed: 21999455]
24. Fostvedt GA, Barnes RW. Complications during lavage therapy for renal calculi. *J Urol*. 1963; 89:329–331. [PubMed: 13958911]
25. Brunelli S. Association between oral sodium phosphate bowel preparations and kidney injury: a systematic review and meta-analysis. *Am J Kid Dis*. 2009; 53:448–456. [PubMed: 19100671]
26. Houston M. The role of magnesium in hypertension and cardiovascular disease. *J Clin Hypertens*. 2011; 13:843–847.

27. Alhosaini M, Leehey D. Magnesium and dialysis: the neglected cation. *Am J Kidney Dis.* 2015; 66:523–531. [PubMed: 25864370]
28. Klein C, Moser-Veillon P, Schweitzer A, Douglass L, Reynolds H, Patterson K, et al. Magnesium, calcium, zinc, and nitrogen loss in trauma patients during continuous renal replacement therapy. *JPEN J Parenter Enteral Nutr.* 2002; 26:77–92. [PubMed: 11871740]

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Fig. 1.

Values for serum magnesium and creatinine based on hospital day. IHD, intermittent hemodialysis; CVVHD, continuous venovenous hemodialysis.

TABLE 1

Relevant metabolic laboratory data obtained around the time of nephrology consultation

Units	Parameter	Perioperative Day 0	Routine labs Day 2	Arrival in SICU Day 2	Four hours later Day 2
mmol/l	Lactic acid			2.7	
	Sodium	143	138	130	130
	Potassium	3.6	3.1	4.9	5.7
	Chloride	108	113	102	102
	HCO ₃	27	24	26	26
mg/dL	BUN	9	16	28	25
	Creatinine	1.1	2.0	3.1	3.2
	Glucose	90	87	139	130
	Calcium	8.8	6	7.7	7.8
	Magnesium			11.4	16.7
	Phosphate			3.5	

Examples of symptomatic hypermagnesemia. Impaired renal function is not necessary for developing hypermagnesemia in the setting of an exogenous load

TABLE 2

Peak Mg level (mg/dL)	Initial creatinine (mg/dL)	Etiology	Dialysis	Outcome	Reference
7.4	1.9	Magnesium oxide ingestion	Yes	Died (PEA arrest)	17
26.4	Unavailable	Near drowning in the Dead Sea	Yes (peritoneal)	Died (intractable arrhythmia)	18
3.3	1.1	Caribbean Sea water ingestion	No	Recovered	19
21.7	1.8	Epsom salts (intended as laxative)	No	Recovered	20
10.9	1.1	Renacidin (7-year-old child)	Yes	Dialysis dependent	10
15.6	1.9	Renacidin	No	Recovered	11
3.3	9.5	Renacidin	No	Recovered	12
12.4	“Normal”	Renacidin	No	Recovered	9
12.5	0.2	Renacidin	No	Recovered	13
19.9	Unavailable	Magnesium sulfate for pre-eclampsia	No	Recovered	21