

CASE REPORT

Hypocalcemia and hyperkalemia during magnesium infusion therapy in a pre-eclamptic patient

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Introduction

Magnesium sulfate has been used for a long time in the obstetric population for management of premature labor, preeclampsia and eclampsia. High levels of serum magnesium (4.8–8.4 mg/dL) [1] are targeted to exert its therapeutic effect in preeclampsia and eclampsia. While generally safe, a review of literature reveals infrequent occurrences of hypocalcemia or hyperkalemia secondary to high magnesium levels [2]. We report a patient who developed both electrolyte abnormalities due to hypermagnesemia and discuss potential mechanisms explaining the same.

Case Report

A 21-year-old African American female, G2P1 was hospitalized to the intensive care unit for the management of severe preeclampsia during her 17th week of gestation. Her past medical history was relevant for preeclampsia in her previous pregnancy. However, she lacked a diagnosis of chronic hypertension, chronic renal disease or proteinuria. She presented with symptoms of headache, palpitations, abdominal pain, nausea and vomiting of 1 week duration. Upon initial evaluation, she was noted to have

Key Clinical Message

We present a case of prominent hypocalcemia and hyperkalemia attributed to magnesium infusion in a preeclamptic patient. Iatrogenic hypermagnesemia is an underrecognized cause of hypocalcemia and hyperkalemia. Our report illustrates the effects of magnesium therapy on serum calcium and potassium, necessitating close electrolytes monitoring when used.

Keywords

Hyperkalemia, Hypermagnesemia, Hypocalcemia.

severe hypertension, BP 173/114 mm Hg. Rest of the vital signs were: pulse 98 bpm, temperature 36.5°C and oxygen saturation of 99% in room air. Physical examination revealed mild, diffuse abdominal tenderness to palpation and mild, symmetric peripheral edema. Remainder of the systemic examination was normal. Laboratory investigations were significant for marked proteinuria, bland urine sediment examination, slight elevation of hepatic enzymes, elevated serum uric acid and a normal renal function, as depicted in Table 1. Her admission blood gas showed a nonanion gap metabolic acidosis with mild respiratory alkalosis (PH: 7.37, HCO₃: 15 meq/L, PCO₂: 27 mm/Hg and PaO₂: 106 mm/Hg, Anion gap: 8).

An obstetric ultrasound was done revealing holoprosencephaly, enlarged anterior placenta with extremely elevated βHCG levels (2285500 mIU/mL), suggesting partial molar pregnancy.

A diagnosis of early severe preeclampsia was made and the patient was managed with antihypertensive therapy, she was given three doses of intravenous (IV) Hydralazine (total 25 mg), one dose of IV Labetalol 20 mg and then was started on Nicardipine infusion with a mean arterial pressure goal of 120 mm/Hg. She was also given multiple doses of Furosemide as shown in Table 2 to manage her volume status. One dose of sodium polystyrene sulfonate

Table 1. Initial lab studies.

Lab	Result	Normal reference
TSH (uIU/mL)	0.62	0.45–4.70 uIU/mL
ALT (U/L)	55	9–51 U/L
AST (U/L)	79	13–40 U/L
Alkaline phosphatase (U/L)	84	34–122 U/L
Total Bilirubin (mg/dL)	0.8	0.1–1.1 mg/dL
Total protein (g/dL)	4.1	6.3–8.2 g/dL
Uric Acid (mg/dL)	8.2	2.9–6.0 mg/dL
Albumin (g/dL)	2	3.5–5.0 g/dL
Urine protein (g/day)	7	0.020–0.080 g/day
Creatinine (mg/dL)	0.8	0.50–1.04 mg/dL
WBC $\times 10^3$ (μ L)	7.8	4.3–11.1/ μ L
RBC $\times 10^6$ (μ L)	3.95	3.93–5.25/ μ L
Hgb (g/dL)	11.3	11.6–15.0 g/dL
Platelets $\times 10^3$ (μ L)	225	166–358/ μ L
ANA	Negative	–
Prothrombin time (seconds)	11.2	12.0–14.7 sec
Partial thromboplastin time (seconds)	33	23–38 sec

(Kayexalate) suspension (15 g) to manage her mild hyperkalemia. Infusion of magnesium sulfate in Lactate Ringer (40 g/500 mL) was started at a rate of 25 mL/h for seizure prophylaxis, the infusion was continued for the first 3 days of hospitalization with close neurologic and electrolytes monitoring. An urgent delivery of the fetus was indicated due to severe preeclampsia and fetal ultrasound findings incompatible with life, so a cesarean section was performed as per patient's preference. Chromosomal examination of the fetal tissue led to a diagnosis of fetal triploidy.

After delivery, the patient's blood pressure started to improve gradually over the following few days. However, she was noted to have significant changes in serum calcium and potassium levels during that period, corresponding to high serum magnesium levels, as depicted in Figure 1 and Table 2.

Work up for etiology of hyperkalemia included Plasma Aldosterone Concentration (PAC) (19.2 ng/dL), Plasma Renin activity (PRA) (9.6 ng/mL/h) and a Trans-Tubular Potassium Gradient (TTKG) of 4.6. There was no evidence of hemolysis, acute decline in renal function or administration of medications known to affect serum potassium levels such as NSAIDs, beta blockers, heparin, etc. Additionally, the patient was tested negative for HIV, Hepatitis serologies, and serum ANA. Also her serum TSH level was normal. After excluding other causes of hyperkalemia, a diagnosis of hypermagnesemia-induced hyperkalemia was made. The serum potassium level started to decline after the discontinuation of magnesium

Table 2. Changes during magnesium infusion.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 8	Day 9
Time	22:00	09:20	12:30	12:30	17:55	00:05	06:05
Mg ⁺	2.6	6.6	7	7.6	7.6	7.6	7.6
K ⁺	4.8	5.3	5.4	5.2	5.1	4.8	4.8
Ca ²⁺	7.9	7.2	6.7	5.7	5.9	6.2	5.9
Creatinine	0.8	0.82	0.9	0.89	0.9	1	1.11
GFR (MDRD formula)	118	114	103	104	103	91	81
BUN	18	17	17	18	18	20	17
Na ⁺	130	132	132	128	127	124	132
Total intake (oral+IV)	2106	6773	4657	1827	1827	1827	3039
Urine Output (mL/day)	1153	1485	2085	4016	4016	4016	2625
Blood Pressure	140-180/ 110-115	141-162/90-112	141-162/90-112	130-158/85-100	130-150/85-110	130-170/ 90-110	155-170/ 90-110
Furosemide	2 doses of 10 mg IV	2 doses of 20 mg IV	2 doses of 20 mg IV	2 doses of 20 mg IV	2 doses of 20 mg IV	2 doses of 20 mg IV	2 doses of 20 mg IV
						recorded	recorded
						1450	2750
						136	133
						Not	Not
						3	6
						04:00	04:00
						16:45	16:45
						1.6	1.6
						3.4	3.9
						7.2	7.6
						0.53	0.6
						189	164

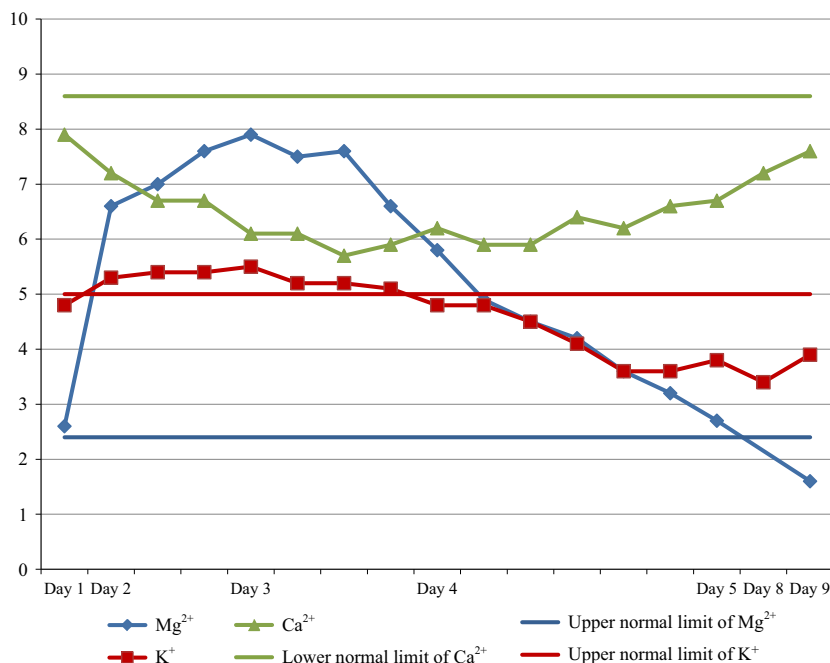


Figure 1. Changes in electrolytes with Hypermagnesemia.

infusion on day 3 of hospitalization. Patient was noted to have slight hypokalemia after normalization of serum magnesium levels, which was attributed to administration of IV Furosemide (utilized for management of volume overload and hypertension). As also depicted in Figure 1 and Table 2; the calcium level started to decline, corresponding to increasing magnesium levels. Serum parathyroid hormone (PTH) was obtained and was 86 pg/mL (normal). Serum calcium normalized after normalization of serum magnesium levels.

Discussion

A number of reports in the medical literature describe the association between magnesium and other electrolytes mainly calcium and potassium. While it is well known that hypomagnesemia can cause resistant hypokalemia if not corrected [3], there is little information that explains the relationship between hypermagnesemia and hyperkalemia. In the literature, we found three case reports describing persistent hyperkalemia during magnesium infusion in the setting of preeclampsia treatment [4, 5]. Our patient had persistent hyperkalemia despite medical therapy, and the fact that her urine potassium excretion was low (TTKG 4.6) indicates that a renal defect plays a major role in her sustained hyperkalemia.

The exact mechanism by which magnesium affects renal potassium handling is still unclear. It has been previously postulated that a hyporeninemic hypoaldosteronic

state in the setting of hypermagnesemia in preeclamptic patients could be contributory to impaired renal potassium excretion [5]. This is derived from the observation of effects of magnesium infusion on PRA and PAC in two pregnant women with preeclampsia [6]. In this report, PRA was inappropriately low for the pregnant state and PAC was low despite the presence of hyperkalemia. However, as described above, in our patient the renin levels were actually high with normal aldosterone levels, suggesting that an alternative mechanism might explain this relationship.

Ichihara A. et al. [7] studied the effect of magnesium infusion in normal subjects and similar to our observation, showed that magnesium infusion (postinfusion serum magnesium level 2.32 meq/L) increased renin levels and paradoxically suppressed aldosterone levels. The effect on PRA was mitigated by administration of indomethacin and that on PAC was abolished by administration of diltiazem. The authors thus concluded that the increase in PRA resulted from increased renal prostaglandins and the suppression of PAC was a result of intracellular calcium mobilization [7]. At the level of serum magnesium achieved and in normal healthy volunteers, serum potassium levels did not change, indicating that hyperkalemia likely occurs at much higher serum magnesium levels, this observation potentially explains the mild increase in serum potassium in our case, which might be potentially ameliorated further by the use of Furosemide and sodium polystyrene sulfonate. Conversely, some other changes in

renal potassium excretion inherent to preeclamptic population could be contributory to the occurrence of hyperkalemia.

Other hypothesis includes the direct effect of magnesium infusion in suppressing the potassium excretion by the kidneys [8–10]. It has been reported that intracellular magnesium modulates the ROMK channel by direct inhibition, playing a major role in potassium wasting under conditions of low magnesium and potassium levels [11–13]. The opposite could be postulated to be the cause for reduced potassium excretion in face of hypermagnesemia. It has been described that magnesium infusion increases sodium and chloride excretion but decreases potassium excretion via an unknown mechanism [8, 9]. It has been suggested that in the presence of increased intracellular magnesium, an increase in ATP:ADP ratio could occur and this may exert an inhibitory effect on ATP sensitive, ROMK channels, which play an important role in renal potassium secretion [6]. It is also important to mention here that significant hyperkalemia in the setting of magnesium infusion hasn't been reported in nonpregnant women with normal renal function [14, 15]; despite the fact that the effect on sodium and chloride was evident in one of the two cases reported by Cheryl et al. [15], and the case reported by Zwanger et al. [14]. Therefore, some of the factors contributing to the effect of magnesium on the renal potassium handling might be related to pregnancy.

Few reports of hypocalcemia associated with magnesium infusion in pregnancy document the relationship between magnesium and calcium [2, 16–18]. It has been shown that hypermagnesemia increases the urinary calcium excretion [19–22]. Furthermore, magnesium can suppress PTH secretion at the parathyroid gland level [18]. In our patient the PTH levels were appropriately high and that may support that hypermagnesemia blunts the peripheral effect of PTH as described by Cholst et al. [20]. Cholst et al. noted a biphasic relationship between magnesium infusion and PTH levels; the beginning of the infusion was associated with a marked decline in PTH levels without any change in calcium, followed by an increase in PTH levels and decrease calcium levels later on. The high PTH and low calcium levels in our patient might be representative of the later phase described above.

Other potential mechanisms contributing to the drop in calcium level is that magnesium might compete at the calcium sensing receptor on the basolateral surface of loop of Henle [17, 22]. Molecular studies have shown that the calcium-sensing receptor is also sensitive to magnesium, although a much higher threshold is required at a ratio of 10:3 [23–25]. This might explain the effect of magnesium on calcium at high doses when utilized for

the treatment of preeclampsia. Urinary calcium excretion was not measured to support our hypothesis and Vitamin D deficiency was not excluded as a cause of hypocalcemia in our patient, but the fact that calcium levels normalized once magnesium levels returned to normal supports the association, though.

Conclusion

We report the development of hypocalcemia and hyperkalemia attributable to magnesium infusion in a preeclamptic patient. Iatrogenic hypermagnesemia should be considered in the differential diagnoses of hypocalcemia and hyperkalemia whenever magnesium infusions are used, especially for obstetric indications. Stopping the magnesium infusion will likely reverse the electrolytes changes, if the renal function is intact, but sometimes temporary stabilizing measures for management of hypocalcemia and hyperkalemia may be required. Therefore, we suggest close monitoring of electrolytes while administering magnesium infusion.

Conflict of Interest

None declared.

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