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Dilutional Hypocalcemia in Association with Dilutional Hyponatremia

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THE risk of hypotonic fluid absorption and dilutional hyponatremia after hysteroscopy has been described.¹⁻³ In the case presented, the presence of Chvostek's sign led to the diagnosis of dilutional hypocalcemia in association with dilutional hyponatremia. We propose that dilutional hypocalcemia often may go unrecognized and that hypocalcemia could contribute to the neurologic and cardiac effects of acute free-water absorption.

Case Report

A healthy 32-yr-old, 75-kg woman was admitted for laparoscopy and hysteroscopy for lysis of a uterine septum. Preoperative laboratory tests were normal.

Anesthesia was induced with propofol (170 mg), and fentanyl (50 µg). Tracheal intubation was facilitated with atracurium (30 mg). Anesthesia was maintained with inspired isoflurane (1-2%) and 50% N₂O in oxygen. No additional muscle relaxant was given, nor were the effects of atracurium reversed after the 2.5 h procedure.

After laparoscopy, hysteroscopy with lysis of uterine septum was performed. During the 105 min hysteroscopy, the uterus was distended with 250 ml of dextran solution (Hyskon, Kahi Pharmaceuticals, Piscataway, NJ) and 11.8 l of 1.5% glycine. After 60 min of hysteroscopy, furosemide (20 mg) was given intravenously for presumed glycine absorption. At the end of the procedure, it was estimated, based on uterine inflow and outflow, that the patient had absorbed 3 l of glycine. Intravenous fluids were 1,400 ml of lactated Ringer's solution. Urine output was 1,000 ml.

As the patient emerged from anesthesia, she was tapped on the check to determine her level of alertness. A brisk Chvostek's sign was noted. End-tidal carbon dioxide was 35 mmHg with the patient's lungs mechanically ventilated. A blood sample was obtained, and extubation was delayed to avoid tetany-induced stridor. The patient was given 75 µg fentanyl for sedation and analgesia as she awakened.

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Serum sodium concentration was 118 meq·l⁻¹, potassium concentration was 4.4 meq·l⁻¹, and ionized calcium concentration was 1.02 mm/l (normal range, 1.14-1.29 mm/l). After 1 g of calcium chloride was administered intravenously, the patient's Chvostek's sign was diminished markedly, and the trachea was extubated uneventfully.

In the recovery room, the patient was given 100 cc of 3% saline solution intravenously over 1 h. Subsequent chemistry results were as follows: sodium concentration, 129 meq·l⁻¹; potassium concentration, 3.4 meq·l⁻¹; chloride concentration, 88 meq·l⁻¹; total carbon dioxide concentration, 29 mm/l; creatinine concentration, 0.7 mg/dl; and calcium concentration, 8.8 mg/dl. A faint Chvostek's sign persisted.

The patient was admitted for overnight observation. Calcium, magnesium, and electrolyte concentrations the following morning were normal, and the patient was discharged without further evaluation.

Discussion

Although the risk of hysteroscopy-induced hyponatremia has been established,¹⁻³ there are few clinical reports describing this phenomenon. In contrast, there are numerous reports on transurethral resection of the prostate (TURP), and study of this syndrome has yielded years of experience with fluid absorption.^{4,5} The TURP syndrome, symptoms of which are nausea, lethargy, neurologic irritability, seizures, coma, bradycardia, blood pressure lability, and congestive heart failure, is thought to result mainly from hyponatremia and hypervolemia.^{4,5} Because of the vast experience with TURP, authors generally refer to the TURP syndrome in describing the potential sequelae of fluid absorption after hysteroscopy.¹⁻³

One little-studied aspect of the TURP syndrome is the effect of acute fluid absorption on extracellular calcium. Despite the essential role of calcium in cardiovascular and neurologic function, only one study has measured calcium concentration in patients undergoing TURP. Malone studied 25 patients and reported a mean intraoperative decrease in serum calcium concentration of 6%.⁶ All patients later received bumetan-

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ide therapy, and the mean serum calcium concentration remained at the depressed intraoperative levels for 24 h postoperatively. Malone did not report individual calcium concentrations, the variance of calcium concentrations, or any case of overt hypocalcemia. He did state that the decrease in serum calcium "occurred before any rise in urinary excretion of calcium and was most marked in those patients who had a significant fall in their plasma sodium levels."⁶ Malone also found that serum magnesium concentrations did not decrease intraoperatively; however, they decreased significantly 12 h postoperatively and were associated with an increase in urinary magnesium excretion.

Aside from Malone's series, there is only anecdotal evidence that hypocalcemia may play a role in the TURP syndrome. Malone's series included one patient who suffered a cardiac arrest with a sodium concentration of 97 mEq/l⁻¹. The patient "responded dramatically to calcium infusion" administered during resuscitation.⁶ Charlton also reported improvement with calcium therapy in a cardiac arrest caused by TURP syndrome.⁷ Pennisi reported a case of brief facial tetany in a patient with a sodium concentration of 98 mEq/l⁻¹ after TURP.⁸ Marx described "tetanic-like twitchings" as symptomatic of TURP syndrome.⁴ In none of these cases was serum calcium measured before calcium therapy was administered.

A brief review of calcium homeostasis can explain the occurrence of dilutional hypocalcemia.⁹ Extracellular calcium, which represents only 0.1% of total body calcium, must retain a normal ionized concentration for normal neurologic and cardiac function. Normocalcemia is maintained by the buffering of extracellular calcium by large intracellular calcium stores. Although 99% of intracellular calcium is bound tightly in bone, 1% is bound loosely to bone and other tissues.

Over a period ranging from several hours to days, parathormone, calcitonin, and vitamin D act on the tightly bound bone calcium to maintain normocalcemia. Acute calcium homeostasis depends on the buffering effect of the small, loosely bound pool of intracellular calcium. After an acute change in serum calcium concentration, normocalcemia is restored largely by diffusion between the loosely bound bone salts and blood flowing through bone. Guyton estimates the half-time for this equilibration to be 70 min.⁹

Therefore, acute changes in extracellular water volume can occur too quickly for buffering to maintain normocalcemia.

The case presented may be the first confirmed case of clinically evident dilutional hypocalcemia. Although the patient's serum ionized calcium was only mildly depressed, the symptomatic level of hypocalcemia is quite variable and depends on the speed of onset of hypocalcemia.¹⁰ In this case, a small but rapid decrease in ionized calcium probably resulted in latent tetany, as evidenced by the presence of Chvostek's sign.

Although Chvostek's sign may be found in normal individuals, this patient's brisk response is characteristic of tetany. Chvostek's response can be elicited by tapping over the facial nerve in either the subzygomatic (Chvostek II) or preauricular (Chvostek I) area.¹¹ The incidence of Chvostek's response appears to peak in adolescence and decline through adulthood.^{11*} In one series, Chvostek II response was found in 36% of normal subjects, and Chvostek I was found in 8%.¹² The Chvostek II response was consistently the stronger response. The authors graded the response by muscles involved: 1+, labial twitch; 2+, lip and ala nasi; 3+, lip, nose, and orbicularis oculi; and 4+, all ipsilateral facial muscles. Although 3+ responses were found in normal children, in adults, the response was limited to 1+ or 2+. These results are consistent with other authors' findings.^{11*}

The patient in the case presented had a 3+ response to the less sensitive Chvostek I test. This response would not be expected in a normal adult. After calcium therapy, the patient's response decreased to 1+. Based on the patient's exaggerated Chvostek response, hypocalcemia, and response to calcium therapy, the diagnosis of hypocalcemic tetany seems reasonable. In the anesthetized patient, additional confirmation of tetany can be obtained by testing for Trousseau's sign, which is more specific for tetany than Chvostek's sign.* Because a manual blood pressure cuff was not immediately available and carpedal spasm can take 3–5 min to develop,* evidence of Trousseau's sign was deemed unnecessary for patient management and was not sought.

Although the patient's hypocalcemia probably was related to acute fluid absorption, other causes should be considered. Rapid infusion of albumin or citrated blood, parathyroidectomy, critical illness, and alkalosis are the most common causes of perioperative hypocalcemia.¹³ Of these, only alkalosis could be pertinent in this case. Alkalosis seems unlikely, though, because

* McSweeney AJ: Some observations on tests for tetany. *Illinois Med J* 112:61–64, 1957.

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of the patient's normal end-tidal carbon dioxide reading and normal postoperative serum bicarbonate concentration. Endocrine disorders could be considered a factor in a patient's development of hypocalcemia; however, initial calcium homeostasis depends mainly on the buffering of extracellular calcium by calcium stores in bone and other tissue.⁹ This buffering occurs independently of parathormone activity. In addition, after initial calcium therapy, the patient maintained a normal serum calcium concentration postoperatively without further intervention, suggesting normal endocrine function. Hypomagnesemia can be ruled out, because the patient had a normal serum magnesium concentration postoperatively without receiving magnesium therapy.

Furosemide therapy also must be considered a potential cause of hypocalcemia. Although furosemide causes calciuria, hypocalcemia is an unusual complication of furosemide therapy.¹⁴ Based on the available data, a significant drop in serum calcium concentration would be extremely unlikely 50 min after a 20 mg dose of furosemide.¹⁵ Malone's data also suggests that furosemide was not the cause of hypocalcemia in this patient.⁶ In Malone's patients, serum calcium concentration decreased because of water absorption that occurred before diuretic therapy was initiated or any rise in urinary calcium concentration was noted.

Although incidence of dilutional hypocalcemia is unknown, dilutional hypocalcemia could be more common than is recognized generally, because the calcium ion concentration, unlike the sodium ion concentration, rarely is measured in patients after acute free water absorption. In addition, hypocalcemia could be an unrecognized cofactor in the development of signs of the TURP syndrome. Neurologic irritability, lethargy, seizures, hypotension, and cardiac depression generally are attributed to hyponatremia and hypervolemia, but could be caused in part by hypocalcemia. Further research is necessary to determine the clinical

significance of dilutional hypocalcemia as well as the relative effect on ionized and total serum calcium concentration. For now, it is reasonable to measure the serum ionized calcium ion concentration in patients with neurologic or cardiovascular impairment in the presence of dilutional hyponatremia.

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