

Severe Hypocalcemia Caused by Absorption of Sorbitol-Mannitol Solution during Hysteroscopy

Hysteroscopic procedure can be complicated by intravascular absorption of irrigating fluid. The clinical features of this complication are similar to transurethral resection of the prostate (TURP) syndrome. There have been few reports on hypocalcemia during endoscopic surgery and clinical implications of hypocalcemia in TURP syndrome have been underestimated. We report a case of TURP syndrome association with a decreased ionized calcium concentration of 0.53 mM/L after the absorption of a large amount of sorbitol-mannitol solution during hysteroscopy. The hypotension which occurred in TURP syndrome did not respond to vasopressor and inotropic agent but responded to the administration of calcium. This case was also accompanied by hyponatremia, hyperglycemia and lactic acidosis through the metabolism of sorbitol.

Key Words : Hypocalcemia; Hyponatremia; Hysteroscopy; Sorbitol-mannitol

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INTRODUCTION

Hysteroscopic procedure has been widely used more recently due to the possibility of an accurate diagnosis and resection of the lesions. However, hysteroscopy is not a completely safe procedure because of some significant complications. Hyponatremia has been reported to be associated with transurethral resection of the prostate (TURP) syndrome due to the absorption of irrigating fluid during endoscopic surgery, whereas hypocalcemia has not. Hypocalcemia reduced contractile force in cardiac muscle and vascular smooth muscle. In our case, hypotension that occurred due to severe hypocalcemia improved after administration of calcium. It has been reported that hyperglycemia and lactic acidosis rarely occur due to the absorption of sorbitol. Thus, we report herein a case of TURP syndrome that was accompanied by severe hypocalcemia, hyponatremia, hyperglycemia and lactic acidosis due to the absorption of a large amount of sorbitol-mannitol solution during hysteroscopy.

CASE REPORT

A healthy 51-yr-old, 60 kg woman with an endometrial mass was scheduled for a hysteroscopic endometrial biopsy and resection under general anesthesia. Apart from a history of exploratory laparotomy that was performed 35 yr ago, her medical history was unremarkable. The preoperative laboratory tests were normal; the patient was premedicated with

midazolam and atropine. Anesthesia was induced with thiopental, midazolam and fentanyl. The tracheal intubation was facilitated with rocuronium. The anesthesia was maintained with 50% N₂O in oxygen, fentanyl, enflurane and rocuronium. The patient was placed in the lithotomy position with a slight Trendelenberg tilting. During hysteroscopy, the uterus was distended with Urosol[®] (a mixture of 2.7% sorbitol and 0.54% mannitol, CJ Pharma, Seoul, Korea) at a height of 135 cm above the operating table. Forty minutes after the initiation of hysteroscopy, the amount of the absorbed Urosol[®] was estimated to be approximately 7 L, based on the uterine inflow and outflow. Radial artery cannulation was performed for continuous monitoring of blood pressure, and for serial blood gas analysis (Table 1). The serum sodium level was <100 mEq/L when measured using a blood gas/electrolyte analyzer in the operating room (GEM Premier 3000, Instrumentation Laboratory, Lexington, MA, U.S.A.), but it was 89 mEq/L when measured again at the central laboratory. The ionized calcium level was 0.53 mM/L. A diagnosis of TURP syndrome was made on the basis of severe hyponatremia. The patient received a total of 100 mg of furosemide in divided doses. One hour after the start of surgery, arterial blood gas analysis showed a severe acidosis (pH 7.19; pCO₂, 39 mmHg; HCO₃⁻, 17 mM/L; and base excess, -12.6 mM/L). Although 80 mL of 8.4% sodium bicarbonate was administered over 90 min, the pH value persisted at a value of ≤ 7.35. Since the blood pressure also decreased to 62/40 mmHg at 105 min after the start of surgery, 10 mg of ephedrine was intravenously administered and dopamine was infused at a

Table 1. Progression of serum chemistries after sorbitol-mannitol irrigation during hysteroscopy

	Preop	40 min	1 hr	1.5 hr	2 hr	2.5 hr	3 hr	3.5 hr	PACU
Sodium	143	<100 =89	<100	<100	<100 =99	100	102	103	105
Calcium ionized		0.53	0.53	0.58	0.72	0.82	0.81	0.83	0.92
Calcium total	9.0								
Lactate		1.7	2.1	3.2	3.8	5.1	6.3	7.1	
Glucose	93	47	68	101	150	274	304	337	248
pH		7.35	7.19	7.32	7.27	7.33	7.30	7.23	7.39
PaO ₂		281	118	141	87	127	105	315	99
PaCO ₂		32	39	45	39	42	39	42	35
BE		-8.3	-12.6	-7.4	-8.4	-3.7	-7.2	-7.2	-6.8

Sodium (mEq/L), ionized calcium (mM/L), total calcium (mg/dL), lactate (mM/L), Glucose (mg/dL), PaO₂ (mmHg), PaCO₂ (mmHg), BE (mM/L). PACU, postanesthesia care unit.

rate of 10 $\mu\text{g/kg/min}$, but the blood pressure did not rise. However, after administration of 40 mL of 3% calcium chloride, the blood pressure increased to preoperative value. The ionized calcium level increased to 0.83 mM/L but a prolonged QT interval on ECG was noted. Two hours after the start of surgery, the PaO₂ level gradually decreased to 87 mmHg when FiO₂ was at 0.75, and the SaO₂ level decreased to 95%. Adhesiolysis of intrauterine synechia was failed due to bleeding from the opened vessel. Two hours and 30 min after the start of surgery, the hysteroscopic procedure was stopped and transabdominal hysterectomy was performed instead. Because the repeated measurements of serum sodium persisted at the level of <100 mEq/L, 2% saline was infused at a rate of 2 mL/kg/hr and thereafter normal saline was infused after the serum sodium level became 103 mEq/L. During surgery, 1,500 mL of normal saline, 160 mL of packed red blood cells and 150 mL of hetastarch were infused. Additionally, since the blood glucose gradually increased to ≥ 300 mg% (Table 1), 5 units of regular insulin were intravenously administered. The lactate level increased to 7.1 mM/L when surgery was completed.

At the completion of surgery, the patient regained full consciousness. Postoperatively, chest radiography and arterial blood gas analysis did not exhibit findings of pulmonary edema. The patient was admitted to intensive care unit for close observation. Normal saline was infused with the maintenance of a central venous pressure at 4 to 6 mmHg in intensive care unit. The ionized calcium returned to normal 6 hr later and serum sodium level returned to normal 24 hr later. The patient recovered uneventfully and was discharged from the hospital.

DISCUSSION

The TURP syndrome is induced by the vascular absorption of irrigating fluids, which can sometimes occur during

hysteroscopy (1, 2) and arthroscopy (3). Hyponatremia induced during hysteroscopy is referred to as female TURP syndrome (4) and its clinical features vary depending on the amount and nature of the irrigating fluid. Since the hydrostatic pressure required to distend the uterus is higher, the resection is more time-consuming and the exposed raw surface is greater than TURP, so the irrigating fluid is more likely to be absorbed during hysteroscopy than TURP (5). In the present patient, adhesiolysis of uterine synechia opened the uterine vein. Hydrostatic pressure increased when the irrigating fluid bag was placed 75 cm higher than the recommended height of 60 cm above the operating table (6), thus leading to rapid absorption of a large amount of irrigating fluid. It is conceivable that rapid absorption of irrigating fluid may induce TURP syndrome. Even though the majority of the clinical symptoms develop due to hyponatremia and hypervolemia in TURP syndrome, hypocalcemia is also important to contribute to the cardiovascular symptoms. Calcium is essential in the maintenance of myocardial functions and vascular tones but there have been few reports of this aspect in TURP syndrome. Hahn (7) found that after intravenous infusion of 1,000 mL of glycine over 20 min in 7 healthy male volunteers and 10 prostatectomy patients, the serum sodium and ionized calcium concentrations diluted to the same extent. Chassard et al. (8) observed that 40 and 60 min after 875, 1,475, and 2,075 mL of 1.5% glycine were intravenously infused in pigs, the ionized calcium level significantly decreased. Malone et al. (9) found that among patients undergoing transurethral prostatectomy using glycine, those with fall of more than 10 mM/L sodium also had a decreased serum calcium level. However, hypocalcemia can result from the complexes of calcium and oxalic acid, another metabolic product of glycine (10). Based on the aforementioned results, although the mechanism of hypocalcemia has not yet been elucidated, hypocalcemia in the present patient may occur through the dilution caused by sorbitol-mannitol absorption. After a review of the literatures related to this case, we consider that hypocalcemia may be associated with severe hyponatremia after the absorption of large amounts of irrigating fluid during endoscopic surgery. In acute decrease in serum calcium concentration, as a first line of defense, buffer function of exchangeable calcium in bones by blood flow through the bones added about one half of any deficit calcium in about 70 min (11). However, in present patient, absorption of 7 L of irrigating fluid over 40 min caused an acute increase in extracellular fluid volume and decrease in blood pressure that reduce blood flow to bones. Therefore, insufficient buffer function to keep normocalcemia result in severe hypocalcemia.

Although absorption of irrigating fluid leads to transitory hypervolemia (12), it may result low cardiac output and hypotension (13). Singer et al. (14) reported that in a patient with a sodium concentration of 88 mEq/L after transurethral prostatectomy who showed hypotension (75/45 mmHg), bradycardia, a wedge pressure of 23 mmHg and a cardiac output of

3 L/min, these clinical signs improved after administration of calcium gluconate and isoproterenol under the clinical impression of hypocalcemia. Aside from the above report, there is anecdotal evidences that patients with TURP syndrome in whom cardiac arrest (15) which appeared probably due to hypocalcemia was successfully treated after administration of calcium although their serum calcium levels was not measured. Hahn (7) advocated that intravenous calcium and hypertonic saline should be administered to patients with TURP syndrome who have severe hypotension. In present patient, serum levels of sodium and ionized calcium were serially measured and the hypotension that did not respond to ephedrine and dopamine improved after intravenous calcium chloride, which confirmed the occurrence of hypocalcemia and the therapeutic effect of calcium therapy in patients with TURP syndrome. It is conceivable that severe acidosis, which developed at the early stage of surgery, was probably induced by the dilutional acidosis (16) rather than lactic acidosis because the serum lactate increased later stage of surgery. According to intravenous furosemide (20-100 mg) therapy (6) for dilutional hyponatremia due to hypervolemia in the early stage of TURP syndrome, in present patient, furosemide was administered in an attempt to induce diuresis. However, the serum sodium level persisted at <100 mEq/L. Thus, according to the treatment guideline of 3% saline (1-2 mL/kg/hr) for profound hyponatremia (17), 2% saline was infused at a rate of 2 mL/kg/hr until the serum sodium level became 103 mEq/L.

Sorbitol is metabolized into fructose and glucose in the liver, and 30% of the fructose is converted into lactate and pyruvate (18, 19). When the isolated liver is perfused with fructose, the fructose is turned into glucose, lactate and pyruvate (20, 21). In present patient, 7 L of the 2.7% sorbitol was absorbed over 40 min and it exceeded the maximum safe infusion rate of 0.25 g/kg/hr (18), which subsequently resulted in lactic acidosis and hyperglycemia.

In summary, we report herein a case of severe hypocalcemia which was induced by the absorption of sorbitol-mannitol solution during hysteroscopy. We suggest that ionized calcium concentration should be measured when a hypotension dose not respond to vasopressors or inotropes during endoscopic surgery.

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