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Severe hyponatremia induced with mannitol in a patient with Bartter's syndrome

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Introduction

We recently anesthetized a patient with Bartter's syndrome for clipping of an aneurysm of the right midcerebral artery. The patient developed severe hyponatremia after administration of mannitol. The cause of hyponatremia and problems relating to the management of anesthesia are discussed.

Case report

The patient was a 45-year-old man, weighing 50 kg, with Bartter's syndrome, who had been treated with indomethacin, a prostaglandin synthetase inhibitor, and potassium supplement for the past 10 years. He was under adequate control with this regimen, having normal serum potassium levels and slight metabolic alkalosis. He presented with sudden onset of a severe headache and was admitted to our hospital for emergency craniotomy for subarachnoid hemorrhage. Preoperative blood gas analysis revealed a pH of 7.495, Pao_2 of 86.5 mmHg, $Paco_2$ of 40.8 mmHg, HCO_3 of 31.4 mEq·l^{-1}, and BE of 8.4 mEq·l^{-1}. Serum Na^+, K^+, and Cl^- levels were 139 mEq·l^{-1}, 2.7 mEq·l^{-1} and 95 mEq·l^{-1}, respectively. Plasma aldosterone and plasma renin activity were 250 pg·ml^{-1} (10.9–62.7) and 17.0 ng·ml^{-1}·hr^{-1} (0.5–2.0), respectively. Blood pressure was 140/80 mmHg and pulse rate was 110 beats per min.

Oral medication was discontinued. He was premedicated with atropine 0.5 mg and meperidine 35 mg i.m. Prior to the operation, 1000 ml of lactated Ringer's solution containing 40 mEq·l^{-1} of KCl was infused. Before induction of anesthesia, an arterial catheter was inserted in the radial artery for blood pressure monitoring and arterial blood sampling. Urinary output and Spo_2 (Sao_2 measured by pulse oxymetry) were monitored. Anesthesia was induced with fentanyl 100 μg and thiopental 150 mg, and pancuronium 4 mg was administered as a muscle relaxant to facilitate intubation. Anesthesia was maintained with 67% nitrous oxide, 33% oxygen, and 0.2%–1.0% isoflurane, supplemented with fentanyl and pancuronium. Before starting the operation, 250 ml of 20% mannitol (1 g/kg) was given over 20 min. Thirty minutes after mannitol infusion, urine output reached more than 1000 ml and blood pressure decreased to 80/45 mmHg. At this point, serum Na^+, K^+, and Cl^- levels were 113 mEq·l^{-1}, 2.9 mEq·l^{-1} and 79 mEq·l^{-1}, respectively. Blood gas analysis revealed a pH of 7.547, Pao_2 of 164.8 mmHg, $Paco_2$ of 32.9 mmHg, HCO_3^- of 30.6 mEq·l^{-1} and a BE of 7.6 mEq·l^{-1}, consistent with mixed respiratory and metabolic alkalosis. To trent this condition, 0.9% NaCl solution and lactated Ringer's solution, 500 ml each, supplemented with KCl 20 mEq were infused over a period of 60 min. After this infusion, the blood pressure increased to 110/70 mmHg, and the patient remained stable. The tidal volume was reduced to improve respiratory alkalosis. Diuretics were given and urinary output reached 2000 ml in 4 h. Hyponatremia, hypokalemia, and hypochloremia did not improve. The time required for this operation was 4 h and 30 min. The estimated blood loss was 300 ml and the urine output reached 2750 ml. Serum Na^+, K^+, and Cl^- were 125 mEq·l^{-1}, 3.3 mEq·l^{-1} and 86 mEq·l^{-1}, respectively, at the end of the operation, and were in the normal range postoperatively. The patient was extubated and treated in the intensive care unit for 7 days. His postoperative course was uneventful.

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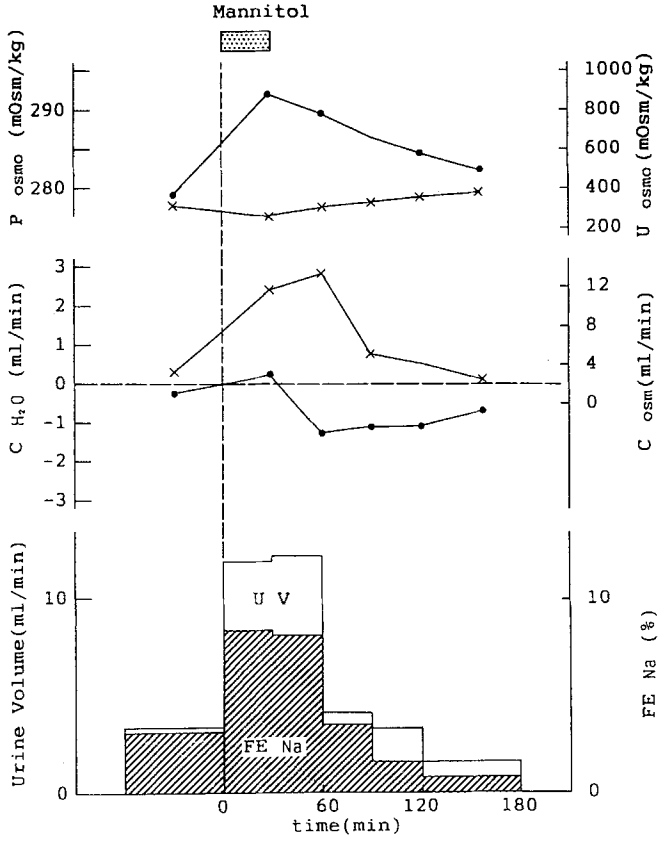
One month after surgery, a mannitol tolerance test (MTT) was performed with the patient's informed consent. His breakfast and usual drugs were withheld on the day of the procedure. After inserting a radial artery catheter for blood sampling and a Foley catheter for urinary sampling, he was given 250 ml of 20% mannitol over 30 min. Urine and arterial blood were collected every 30 min, and Na^+, K^+, Cl^-, vasopressin, renin, creatinine, osmotic pressure, and alcohol dehydrogenase (ADH) were measured in both serum and urine.

After the administration of mannitol, his urine output reached about 1100 ml in 30 min and his serum Na^+ level was decreased by about 15 mEq·l^{-1}, similar to the change observed after mannitol infusion during the operation. Hyponatremia continued for about 3 h. We calculated the fractional excretion of Na^+ and K^+, plasma and urine osmolality, free water clearance, osmolar clearance, plasma renin activity, and plasma aldosterone concentration from the data obtained from the MTT. The results are summarized in Fig. 1. The figure shows that plasma osmolality was markedly increased, but urine osmolality was not increased with the administration of mannitol. The fractional excretion of Na^+ and K^+ were both increased, whereas serum K^+ was not decreased.

Discussion

Bartter's syndrome is characterized by hypokalemic, hypochloremic alkalosis, normal blood pressure, elevated plasma renin and aldosterone levels, and hyperplasia of the renal juxtaglomerular apparatus [1–4]. This syndrome is rare, and there have been only two reports concerning the anesthetic management of patients with this syndrome [5,6]. In the patients with Bartter's syndrome, anesthesia induces renal insufficiency, hypokalemia, metabolic alkalosis, or unresponsiveness of vascular smooth muscle to angiotensin II and norepinephrine.

For healthy patients, administration of mannitol 1–2 g/kg produces an increase in osmolality with significant decrease in serum Na^+ and HCO_3^-. Serum K^+ is either increased or decreased after the administration of mannitol 1–2 g·kg^{-1} [7,8]. However, the extent of the decrease in serum Na^+ typically seen in normal



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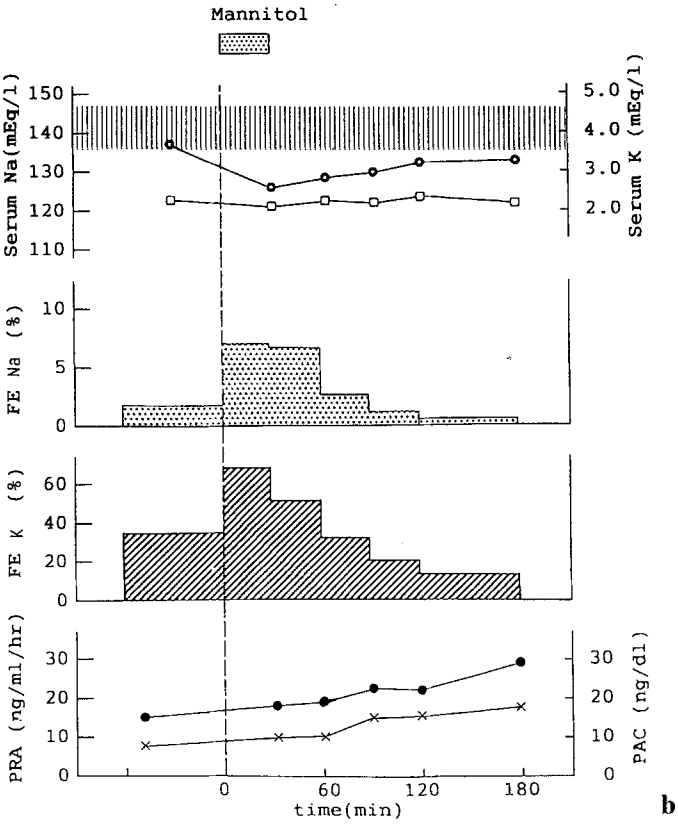

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Fig. 1a,b. Results of the mannitol tolerance test. FE Na, fractional excretion of Na; FE K, fractional excretion of K; P Osm, plasma osmolality; U Osm, urine osmolality; C H_2O, free water clearance; C Osm, osmolar clearance; PRA, plasma renin activity; PAC, plasma aldosterone concentration

patients after mannitol 1 $g \cdot kg^{-1}$ is about 8 $mEq \cdot l^{-1}$, and these changes are transient [7]. In this patient, we observed an unexpectedly abrupt decrease in serum Na^+ by 25 $mEq \cdot l^{-1}$ which lasted approximately 4 h during the course of the operation.

We offer three possible explanations for the hyponatremia seen in this patient after mannitol infusion. First, the elevated serum osmotic pressure produced by mannitol caused water molecules to shift from the intracellular to the extracellular space, leading to hyponatremia. Second, if this patient's ability to reabsorb Na^+ through Henle's tubules was decreased, the resulting increased Na^+ excretion also would have aggravated the hyponatremia. Third, despite the increase in both Na^+ and K^+ excretion rate due to mannitol, it is possible that intracellular K^+ shifted to the extracellular space because concentration of serum K^+ remained unchanged. This movement of K^+ out of the cells might have been accompanied by a shift of Na^+ ions into the intracellular space, lowering the serum Na^+ concentration.

As a remedial measure the following procedures may be used: (1) adequate replenishment of extracellular fluid, (2) administration of spironolactone, and (3) maintenduce of normal serum potassium. Of course, normal acid-base status should be established prior to induction.

A transient hyponatremia may occur in a patient undergoing craniotomy which can be explained by the "cerebral salt wasting syndrome" or SIADH concept [9,10]. Our case of hyponatremia can be differentiated from this syndrome because hyponatremia occurred before the operation was performed.

From the results of the postoperative MTT in this patient, we conclude that the defects in the reabsorption of Na^+ through Henle's tubules and preexisting hypokalemia were the principle causes of the hyponatremia seen in our patient.

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