Persistent Hyponatremia Ameliorated by Discontinuation of Hypertonic Saline Administration

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ABSTRACT

Background/Aims: This is a case report of a patient with hyponatremia who was given hypertonic saline chronically to correct his low serum sodium concentration.

Methods: Intravenous hypertonic saline administration was given in an attempt to correct hyponatremia. When hyponatremia persisted, tapering of hypertonic saline was instituted.

Results: Intravenous hypertonic saline administration in this patient resulted in the excretion of the saline load, which in turn limited renal free water excretion. Limitation in free water excretion resulted in further reduction in his serum sodium concentration or worsening of his hyponatremia, during hypertonic therapy. The patient's serum sodium concentration increased concomitantly with tapering of hypertonic saline, in the absence of other therapeutic or clinical changes.

Conclusion: Hyponatremia is a water disorder. Thus, treatment of hyponatremia includes water restriction and/or measures to increase water excretion by the kidneys. The administration of sodium either orally or intravenously results in an increased sodium delivery to the loop of Henle and an increased renal tubular reabsorption of water, which may lead to worsening of hyponatremia.

INTRODUCTION

Hyponatremia is one of the most prevalent electrolyte disorders among hospitalized patients.[1-5] Its treatment involves increasing the patient's serum sodium concentration only to the extent necessary to ensure the patient has normal respiration and mental status. This approach almost never requires that the sodium level be corrected entirely to normal.[2,5] In the syndrome of inappropriate antidiuretic hormone secretion, hypertonic saline (3% saline) with or without a loop diuretic may be administered in an attempt to raise the serum sodium concentration at an initial rate of 0.5 mmol/L per hour until symptoms resolve.[6-9] Regardless of the rate chosen, the treatment should be ceased once the patient's symptoms resolve or a safe level of serum sodium (generally

greater than 120 mmol/L) is achieved.[2,3,5] This seldom necessitates administering more than 1 liter of 3% saline, and often requires as little as a few hundred milliliters. Such therapy must be accompanied by water restriction and possibly administration of demeclocycline or lithium to decrease the maximal renal concentrating ability. Some authorities, however, have suggested using continuous infusion of hypertonic saline to treat patients with hyponatremia, and this practice is followed by some neurosurgeons.[10]

It is well known that the administration of a nonreabsorbable hypertonic solute, such as mannitol, can cause hyponatremia, especially in patients with renal insufficiency.[11,12] We are unaware of any previously reported cases in which the administration of hypertonic saline prevented amelioration of hyponatremia. However, theoretically this is possible since the administration of hypertonic saline is associated with a monotonically increasing nonplateauing relationship between increased sodium delivery to the loop of Henle and increasing renal tubular reabsorption of water.[12] Such renal responses will decrease urinary free water excretory capacity and could conceivably result in the development of hyponatremia in patients with an abnormal pituitary-renal axis.

We report the case of a patient with acute postoperative hyponatremia, treated with prolonged hypertonic saline infusion, which resulted in persistent and worsening hyponatremia.

CASE REPORT

A 49-year-old white male underwent his fourth transbasal subfrontal craniotomy and tumor resection under general anesthesia for resection of recurrent chordoma. Postoperatively, the patient was started on decadron 10 mg intravenously every 6 hours, famotidine 20 mg intravenously twice a day, phenytoin 100 mg intravenously three times a day, ceftriaxone 1 gm intravenously daily, morphine sulfate 1 to 2 mg intravenously as needed, trimethobenzamide hydrochloride (Tigan) 20 mg intramuscular every 6 hours as needed for nausea and vomiting, and acetaminophen 650 mg orally every 6 hours as needed. He received an intravenous infusion of normal saline with potassium chloride 20 mmol/L at a rate of 100 mL per hour. Serum chemistries showed a sodium concentration of 129 mmol/L, potassium 4.7 mmol/L, chloride 100 mmol/L, bicarbonate 21 mmol/L, BUN 5 mmol/L, and creatinine 61.9 μmol/L. The acute asymptomatic hyponatremia was thought to be secondary to the osmotically active mannitol that was administered. Intravenous infusion of 3% saline was started at 30 mL per hour in addition to normal saline with potassium chloride 20 mmol/L at 100 mL per hour. Over the next 24 hours, his urine output was 4300 mL with a specific gravity of 1.010 to 1.015. On postoperative day 2, his serum sodium was 130 to 133 mmol/L. Until a renal consult was obtained, he continued to receive normal saline with 20 mmol/L potassium chloride, from 50 to 100 mL per hour, whenever his serum sodium was above 130 mmol/L or 3% saline from 30 to 40 mL per hour continuously over 24 hour periods whenever the serum sodium was below 130 mmol/L. Oral fluid restriction to less than 800 mL per day was instituted. The patient was thought to be euvolemic.

His hospital course was highlighted by pseudomonas meningitis on postoperative day 11, which was treated with antibiotics; a left lower extremity deep venous thrombosis diagnosed on postoperative day 22 was initially treated with heparin and later warfarin; and a focal seizure on postoperative day 23, secondary to a subacute left parietal infarct. Additional medications received during

the hospitalization included famotidine, nizatidine, propoxyphene napsylate and acetaminophen (Darvocet), oxycodone and acetaminophen (Percocet), and demeclocycline.

The renal service was consulted on postoperative day 31 for persistent hyponatremia despite continuous hypertonic saline administration. On the day of the consult, the patient was orthostatic on physical examination, with a blood pressure of 112/68 mmHg, and a pulse of 84/min in the supine position, and a blood pressure of 85/68 mmHg and a pulse of 112/min in the standing position. He had a normal mental status and no edema. He was receiving intravenous infusion of 3% saline at 50 mL per hour, oral fluid restriction to less than 800 mL per day, demeclocycline 300 mg orally every 6 hours, and furosemide 10 mg intravenously twice a day, in addition to intravenous ceftazidime, ciprofloxacin, and decadron. His urinary sodium concentration was 89 mmol/L and his urine volume on that day was 2050 mL. Thyroid function tests were checked and were normal. We recommended tapering the rate of infusion of 3% saline by 10 mL an hour per day, which was eventually stopped on postoperative day 35. His serum sodium concentration gradually increased from 132 mmol/L to 135 mmol/L over this period.

DISCUSSION

Persistent hyponatremia due to a saline diuresis was suspected in view of the administration of hypertonic saline to the patient. This was confirmed by the high urinary sodium concentration and excretion rate. Sodium and osmolar balances and their progressive decrease (calculated assuming urine osmolalities of 350, 700, and 1050 mosm/kg for specific gravities of 1.010, 1.020, and 1.030, respectively were closely approximated when urine volume was accurately documented (Days 28 to 35).[13]

The urine volume (V) can be divided into 2 theoretical components, one containing all of the urinary solute in a solution that is iso-osmotic to plasma (osmolar clearance, C_{osm}), and one consisting of free water that has been generated (free water clearance, C_{H2O}) or reabsorbed (free water reabsorption, T^c_{H2O}) in order to attain the final urine osmolality (U_{osm}).[14-16]

Equation 1:

Thus, urine volume

$$V = C_{osm} + C_{H2O}$$

C_{osm} represents the volume of plasma cleared of the solute it contains by urinary excretion and can be calculated from the general formula for clearance:

Equation 2:

$$C_{osm} = (U_{osm})\, V \div P_{osm}$$

Using these equations, C_{H2O} and T^c_{H2O} can be calculated. From equation 1,

$$C_{H2O} = V - C_{osm}$$

substituting equation 2 and factoring for V, resulting in

Equation 3:

$$C_{H2O} = V\,(1 - (U_{osm} \div P_{osm}))$$

In contrast to the C_{H2O}, which is equal to the free water excreted per unit time, the T^c_{H2O} is equal to the volume of free water reabsorbed per unit time.

Therefore $T^c_{H2O} = -C_{H2O}$ and so $V = C_{osm} - T^c_{H2O.}$

Equation 4:

$$T^c_{H2O} = V\,((U_{osm} \div P_{osm}) - 1)$$

and

Equation 5:

$$U_{osm} = P_{osm}\,(1 - (C_{H2O} \div V))$$

Hypertonic saline administration to normal subjects resulted in a linear relationship of T^c_{H2O} plotted against the logarithm of increasing C_{osm} or increasing urinary sodium excretion (U_{Na} V). In contrast, the administration of increased amounts of mannitol resulted in a plateau in the rise of T^c_{H2O}.[12] These changes were consistent, even in the same subject, when sequentially switched between mannitol and hypertonic saline diureses. Mannitol, by lower-

ing the sodium concentration in the tubular fluid entering the loop, imposes a limitation on sodium transport from the ascending limb into the renal medulla, and may be responsible for the observed limitation of the increase in T^c_{H2O}. In addition, mannitol is not reabsorbed in the nephron.

During hypertonic saline diuresis, as both the rate of delivery of sodium and the sodium concentration of the fluid entering the loop of Henle are increased, progressively more sodium is reabsorbed and transported into the medulla. This is reflected in the increasing T^c_{H2O} without evidence of a maximum value. Thus, the tubular fluid sodium concentration appears to be a critical determinant of the rate of renal tubular sodium transport, and hence of the T^c_{H2O}. In contrast, C_{H2O} (factored for glomerular filtration rate) approached a limit in patients with complete central diabetes insipidus undergoing hypertonic saline diuresis.[17]

With tapering of hypertonic saline over days 31 to 36, as the patient's T^c_{H2O} decreased, his serum sodium concentration initially increased and then remained stable. An increase in U_{osm} with a concomitant decrease in P_{osm} (Equation 3) would result in increased tubular reabsorption of water, causing persistence and worsening of hyponatremia secondary to continuous infusion of hypertonic saline. The ability of the kidneys to excrete water efficiently is compromised as the urinary flow rate increases during saline diuresis and U_{osm} approaches P_{osm} (Equation 5). We were unable to calculate the electrolyte free water clearance in this patient, as the urinary potassium concentration was not available.[18,19]

In summary, continuous administration of hypertonic saline in this patient resulted in the excretion of the saline load, which limited renal free water excretion, resulting in worsening of the patient's water intoxication. Treatment of chronic hyponatremia in euvolemic patients without a sodium metabolism disorder should be directed towards increasing plasma osmolality over the short term by giving hypertonic (3%) saline acutely, and over the long term by diminution of water ingestion and renal concentrating ability. In assessing the development of hyponatremia, the renal response must be fundamentally considered, as well as the volume status of the patient and the tonicity of the administered fluids.[4] In this case, the administration of large amounts of hypertonic sodium solutions, in the setting of euvolemia and probable high levels of circulating antidiuretic hormone, led to an appropriate saline diuresis, but an inappropriate renal response, culminating in increased renal tubular water reabsorption. This process has recently been termed renal "desalination" and has been shown to result in the development of postoperative hyponatremia in patients treated with isotonic saline replacement fluids.[4] We extend this finding to the case of patients treated with continuous hypertonic saline solutions.

Long-term infusion of hypertonic saline in patients with hyponatremia may not be an appropriate treatment option. This case reinforces the concept that hyponatremia is a disorder of water and not of sodium metabolism.

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