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LARGE-VOLUME HYPERTONIC SALINE THERAPY IN ENDURANCE ATHLETE WITH EXERCISE-ASSOCIATED HYPONATREMIC ENCEPHALOPATHY

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☐ **Abstract—Background: Small-volume boluses of intravenous hypertonic saline are the recommended therapy for exercise-associated hyponatremic encephalopathy (EAHE). Failure to properly diagnose and treat EAHE has been associated with significant morbidity and death. To prevent this, current consensus statement guidelines recommend up to three 100-mL boluses of 3% NaCl spaced at 10-min intervals to correct symptoms. Due to lack of evidence, however, guidelines are vague regarding the maximal volume that can be safely administered in a given time period beyond these initial boluses. Objectives: This case report will review the underlying pathophysiology, clinical presentation, diagnosis, and management of EAHE in a patient refractory to initial treatment. Case Report: We report a case of EAHE in an experienced marathon runner requiring large-volume infusion (950 mL) of 3% NaCl therapy for resolution of symptoms without any adverse events. Conclusion: Although further research is needed, this case may provide helpful information for acute care and sports medicine physicians who encounter patients with EAHE refractory to initial therapy. Published by Elsevier Inc.**

☐ **Keywords—exercise-associated hyponatremia (EAH); exercise-associated hyponatremic encephalopathy (EAHE); hypertonic saline; syndrome of inappropriate anti-diuretic hormone secretion (SIADH); sports medicine; marathon**

INTRODUCTION

Exercise-associated hyponatremia (EAH) is defined by serum sodium concentration below the normal reference range of the laboratory performing the test, typically < 135 mmol/L, during or up to 24 h after prolonged physical activity (1). EAH is a dilutional hyponatremia secondary to an increase in total body water relative to the amount of total body exchangeable sodium. It is primarily caused by the consumption of fluids in excess of urinary and sweat loss, creating a hypervolemic hyponatremia.

In marathon runners, the incidence of EAH may be as high as 13% (2). More commonly seen in inexperienced long distance athletes (e.g., first-time marathon runner), female gender, and with excessive fluid consumption, early signs and symptoms include bloating, nausea, vomiting, and headache (3). Although this hyponatremia is often mild and corrects without significant intervention, the development of neurologic sequelae suggests exercise-associated hyponatremic encephalopathy (EAHE). These symptoms stem from cerebral edema and resulting encephalopathy, and include altered mental status, seizures, coma, and death. Failure to rapidly diagnose and properly treat EAHE has resulted in death in otherwise young, healthy individuals (3). A military review article in 2002 brought further attention to the risk of EAH from over-hydration by reporting the deaths of three soldiers who consumed more than 5 L of water over a period of a few hours while exercising (4).

Prevention of EAH focuses on reducing excess fluid retention by consuming fluids according to thirst, and monitoring body weight to avoid weight gain during

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exercise, both of which may be difficult during endurance events. Due to deaths attributed to the improper management of EAHE, the 2nd International Exercise-Associated Hyponatremia Consensus Conference recommends that treatment focus on prompt diagnosis and immediate administration of intravenous hypertonic saline (5). This entails immediate onsite infusion of 100 mL of 3% NaCl, with up to two additional 100-mL 3% NaCl bolus infusions at 10-min intervals if there is no clinical improvement (5). However, if patients fail to respond adequately to these initial boluses, further treatment guidelines and recommendations are absent.

CASE REPORT

A 51-year-old man presented to the Emergency Department (ED) via Emergency Medical Services after running the Chicago Marathon. Upon completion in 4 h and 10 min, he traveled to a predetermined location to wait for his wife, who was also participating in the marathon that day. Finishing approximately 1 h after the patient, his wife found him at their meeting point significantly confused. She promptly brought him to a medical tent for evaluation, where a serum sodium of 119 mmol/L was ascertained on an on-site, hospital-grade, blood gas analyzer. The patient was transferred to the ED for further medical management after his mental status did not improve after a 100-cc intravenous bolus of 3% NaCl.

Race-day weather was typical for early fall in Illinois, with a high of 27°C/81°F and low humidity. On presentation to the ED, the patient's wife reported a past medical history significant only for hyperlipidemia, with a single cholesterol-lowering agent of unknown name. Additionally, she stated that her husband was a veteran athlete, having successfully completed 22 marathons without complication, and that he had completed the marathon that day at a pace consistent with previous races. Initial vital signs were as follows: rectal temperature 37.4°C (99.3°F), blood pressure 112/65 mm Hg, heart rate 85 beats/min, and respiratory rate in the 40s, with oxygen saturation 99% on room air. On initial examination, the patent had spontaneously open eyes fixed superiorly, he moaned incomprehensible sounds, withdrew from painful stimulus, and had suppressible rhythmic movement of both upper extremities.

Using a protocol endorsed by the 2nd International Exercise-Associated Hyponatremia Consensus Conference, the patient was promptly administered 100-cc intravenous boluses of 3% NaCl every 10 min for EAHE (5). When the patient continued to show clinical signs of EAHE despite 300 mL of 3% NaCl, the decision was made to continue hypertonic saline therapy. From this point forward, the volume administered ranged from 50 to 100 mL per bolus, and the timing between boluses ranged between 10 and 36 min, with frequent interval assessments.

Over the 2 h after the first bolus in the field, the patient received an additional 550 mL of 3% NaCl, for a total of 650 mL. A chest X-ray study demonstrated mild prominence of the central pulmonary vasculature and Kerley B lines in the lung periphery, suggestive of mild pulmonary edema, consistent with hypervolemia. Further diagnostic evaluation, including non-contrast computed tomography scan of the brain and electrocardiogram, were unrevealing. Laboratory testing demonstrated a leukocytosis to 14.5, sodium 121, potassium 3.5, chloride 85, bicarbonate 20, blood urea nitrogen 12, creatinine 1.02, creatine phosphokinase 1707, troponin 0.19, lactic acid 5.9, and an arterial blood gas of pH 7.63, $PaCO_2$ 16, PaO_2 143, FiO_2 22. The patient remained afebrile throughout his stay in the ED with no significant changes in his vital signs, except for a lowering of his respiratory rate. The patient became increasingly agitated and was found to have urinary retention, which was relieved by catheter placement. Although there were brief episodes when the patient seemed to be improving, his mental status would then relapse to his initial presentation.

Given the persistent mental status changes in the presence of a hypervolemic patient with hyponatremia, hypertonic saline boluses with interval neurologic assessments were continued as treatment for EAHE despite reaching volumes greater than previously reported in the medical literature. Seven hours after the first bolus in the field, the patient returned to his baseline mental status. Over this period of time, the patient was administered 950 mL of 3% NaCl, 850 mL in the ED. The patient was observed in the medical intensive care unit overnight and was subsequently discharged home the following day with complete return to baseline function. A telephone follow-up at 4 months showed the patient to be at baseline neurologic function without any medical conditions as a result of his episode of EAHE.

DISCUSSION

We report the largest known volume of hypertonic saline used for successful treatment of EAHE in the ED setting. Hypertonic saline therapy was first used successfully in the field at the 2004 Boston Marathon, and was first administered as a bolus at the Two Oceans Marathon in Cape Town, South Africa in 2005 (6,7). The rapid correction of severe and prolonged hyponatremia is thought to cause damaging fluid shifts between the intracellular and extracellular space, resulting in myelin disruption in the pons and other areas of the brain (8,9). As EAH is an acute hyponatremia, these same fluid shifts have not occurred; no cases of osmotic demyelination syndrome (ODS) or central pontine myelinolysis have been reported