



CASE REPORT

Exercise-Associated Hyponatremia in Cystic Fibrosis

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INTRODUCTION

Cystic fibrosis (CF) is a full body, multi-system disease resulting from dysfunctional chloride ion transport across the cell membrane because of a dysfunctional Cystic Fibrosis Membrane Conductance Regulator (CFTR) protein.¹ While pulmonary and pancreatic dysfunction are its classic phenotype, the sweat glands also are affected significantly, and sweat chloride testing remains a gold standard in the diagnosis of CF. Alongside high sweat chloride concentrations, those with CF also experience elevated sweat sodium concentrations and, therefore, the potential to lose meaningful amounts of sodium chloride in their sweat.

Focusing on what has been described as “voluntary dehydration” due to a theorized lower thirst drive within the CF population, non-evidence based recommendations² have been to drink beyond level of thirst and to increase consumption of sodium via salty foods to attenuate body sodium loss and maintain volume within the vascular space.³ Concern with this advice arises with the observation of the well-established body of evidence demonstrating overconsumption of fluids to be the major contributing factor in the development of exercise-associated hyponatremia (EAH), a phenomenon whose incidence increased alongside “drink beyond one’s thirst” advice within the general athletic community.⁴ The following case demonstrates the point at which CF and EAH meet and describes how the current fluid intake recommendations and the lack of evidence-based sodium replacement guidelines in the CF community may function to increase the risk of hyponatremia rather than achieving the intended goal of preventing dehydration.

CASE REPORT

In 2015, a 36-year-old female with CF status-post lung transplantation at age 22, was hiking in the Grand Canyon with a friend. In the nine years since transplantation, her forced

expiratory volume in 1 second (FEV1) averaged 70% and she routinely was active on a daily basis. Temperature during the hike ranged from 60 to 85 degrees Fahrenheit. The descent took 2.5 hours, and they took a 30-minute rest in the shade. The ascent took 1.5 hours. The patient recalled feeling progressively “unwell”. Her self-assessment was that of dehydration since the symptoms of nausea, dizziness, confusion, and weakness were consistent with dehydration she had experienced in the past. She stopped to urinate several times during the hike. The US National Park Service described the route as three miles, round trip with an elevation difference of 1,140 feet between these points on the trail.⁵

After a 10 minute rest, they boarded a shuttle bus where she vomited “copious amounts of clear water into a bag” and required assistance to get off the bus. Her vision deteriorated to where she was “only able to see colors and no discernible shapes”. She did not remember walking to the car, but recalled her friend “depositing” her into the front seat. At this point, she lost consciousness. Her next memory was waking up intubated in a hospital intensive care unit (ICU).

When she lost consciousness, her friend drove her to a local clinic where she communicated with the staff but was combative. From the available medical records, the Glasgow Coma Score (GCS) was 6, and on-site serum sodium was 126 mmol/L. The physician at the clinic ordered 300 mL of intravenous (IV) 3% saline as the patient was prepared for transport by helicopter to an appropriate facility. Upon arrival in the emergency department (ED), her blood pressure was 137/95 mmHg, heart rate was 82 bpm, respiratory rate was 18 bpm, oxygen saturation on room air was 93%, and her GCS had improved to 12. Additional indications of volume status in the medical record included extremities described as “warm and well perfused” and “without edema.” She remained intermittently somnolent and combative, and serum sodium persisted at 126 mmol/L. Computed tomography (CT) of the head suggested diffuse cerebral edema but was otherwise un-interpretable from motion artifact, and magnetic resonance imaging (MRI) was recommended. Due to unchanged mental status and continued hyponatremia, an additional 100 mL of 3% hypertonic saline was given. Repeat serum sodium, 7 - 8 hours after presentation, was 127 mmol/L so a 3% saline IV drip was initiated at 40 mL/hr. She was intubated and sedated due to combativeness and inability to cooperate with the MRI. MRI demonstrated no acute changes.

In the ICU, serum sodium rose to 130 mmol/L after eight hours of 3% saline therapy. GCS was 13 - 14 and the 3% infusion rate was decreased to 10 mL/hr. Over the following 10 hours, serum sodium drifted to 135 mmol/L and hypertonic saline was changed to normal saline. The patient was extubated the next day and, at 22 hours after presentation, serum sodium was 137 mmol/L. She was discharged around 48 hours after presentation. In all, the patient received 820 mL of IV 3% saline during the first 24 hours.

In the ED, this patient’s serum osmolality was 274 mOsm/kg while serum sodium was 126 mmol/L.

After receiving 820 mL of 3% saline, osmolality was 287 mOsm/kg with a sodium of 135 mmol/L. Ten hours after hypertonic saline had been switched to normal saline, osmolality was 291 mOsm/kg with a sodium of 138 mmol/L. Urine studies were not performed and weight changes were not in the available records. Her condition most likely demonstrated a free water intoxication state that corrected with fluid restriction and osmolar load supplementation with a subsequent free water diuresis that led to the improvement in serum sodium.

She did not recall being given more specific recommendations for hydration and sodium intake from the CF community than that she “can’t hydrate enough” and that she needs to eat salty foods. On the day of the hike, she was not concerned about replacing lost sodium, and the emergency department record indicated that she had consumed 3 - 5 liters of fluid prior to and during the hike. The patient confirmed that she consumed more than was typical for her in anticipation of the low humidity and heat. In addition, she described not feeling thirsty during the hike. Her solute intake amounted to a breakfast of eggs and bacon, beef jerky, trail mix, and a few salted peanuts.

DISCUSSION

The standard recommendation for preventing dehydration in patients with CF has been to drink fluids before thirst develops and to continue drinking beyond the level of thirst.² The standard recommendation for sodium replacement has been to increase ingestion of salty foods and to add salt to fluids ingested.³ These recommendations lack emphasis on the importance of balancing fluid and sodium intake for those with CF and may increase the risk of hyponatremia. Exercise-associated hyponatremia is a well-defined condition, known to occur when fluid ingestion is out of balance with water excretion, and can be thought of as existing along a spectrum with pure overconsumption of fluids on one end (more common) and the overconsumption of fluid relative sodium loss on the other (more rare).⁴ Additional factors that are known to contribute in the development of EAH are the persistent secretion of antidiuretic hormone (ADH), the inability to utilize internal stores of exchangeable sodium and, in individuals with pathologically high sweat sodium concentrations, sweat sodium loss.⁴ This patient’s fluid intake was likely excessive along with an osmolar intake that was insufficient. If she had followed the evidence-based recommendation on drinking to thirst that is gaining traction in the non-CF community,⁴ she possibly could have avoided developing hyponatremia altogether.

CF patients should be counseled to consider thirst drive rather than drinking beyond it. Brown et al.⁶ compared cohorts of healthy individuals with normal sweat sodium, healthy individuals with elevated sweat sodium, and CF patients by measuring thirst perception during exercise to 3% dehydration (based on % body weight loss) without drinking. While plasma volume

decreased and serum osmolality increased according to sweat sodium losses, thirst response was identical in all three cohorts at all levels of dehydration. Exercise time to 3% dehydration varied by only eight minutes across cohorts, and total body water loss and sweat rates also were statistically similar. The CF cohort, however, had meaningful lower free water losses. During recovery, the CF cohort consumed 40% less fluid ad libitum, a demonstration of the “involuntary dehydration” principle in CF.² Even so, 40 minutes into recovery, they demonstrated a decrease in serum sodium relative to baseline and were allowed salty foods against protocol. While serum sodium did not drop below 135 mmol/L, they were below baseline two hours into recovery.⁵

CONCLUSION

This case demonstrated that the “involuntary dehydration” behavior in CF may originate in its protective effect against hyponatremia and that the non-specific recommendations for fluid and sodium replacement in the CF community may not be adequate.⁶ This patient reported not feeling thirsty during the hike. EAH likely could have been avoided if she observed her level of thirst and consumed fluid accordingly rather than consuming beyond thirst to avoid dehydration and had more specific sodium replacement guidelines available. In an era where CFTR modulators are available for an increasing number of CF patients,¹ it is imperative that evidence-based guidelines for fluid intake and sodium replacement be developed to address hypovolemia and EAH in this population. With the hope of leading a more normal life, those with CF may be at risk for developing EAH and its potentially devastating effects as they become more active.

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Informed, written permission from the subject of this Case Report is on file with the corresponding author.

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