Acute Hyponatremia in Ultra-Endurance Athletes

STEPHEN SURGENOR, MD, RUTH E. UPHOLD, MD

The case of a 57-year-old male athlete who developed acute hyponatremia during participation in a 100 mile ultra-marathon is discussed. The initial presentation was one of rapid neurological deterioration and transient cardiovascular instability. Current theories on how hyponatremia develops in athletes are discussed. Treatment modalities, such as the use of hypertonic saline and the management of increased intracranial pressure, are addressed. With increasing interest in ultra-endurance events, the incidence of acute hyponatremia may increase. It is important that emergency physicians recognize this phenomenon and be familiar with the principles of acute intervention. (Am J Emerg Med 1994;12:441-444. Copyright © 1994 by W.B. Saunders Company)

During the past several years, an association has been reported in the literature between hyponatremia and participation in triathlons, ultra-marathons, and in a single marathon.[1-9] This common electrolyte disorder is generally associated with a low mortality; however, hyponatremia can cause significant neurological sequelae and even death in some cases.[10,11] At least 10 of the reported cases of hyponatremia within the population of ultra-endurance athletes have been life threatening.[1,3,5-9] The case of an athlete who developed acute symptomatic hyponatremia during participation in a 100 mile ultra-marathon is presented, and the available data on incidence and pathophysiology is reviewed to provide insight into the treatment of hyponatremia in this distinct population.

CASE REPORT

The patient is a 57-year-old male, who was described by his son as an avid runner who averaged 75 to 100 miles per week. By his son's report, he had complained of decreased urinary output at mile 30 of a 100-mile ultra-marathon race, despite the consumption of 2 gal of Kool Aid (Kraft General Foods, Inc, White Plains, NY). He also ingested 6 to 8 Advil 200 mg tablets during the race but dropped out after 55 miles because of painful blisters on his feet. He ingested an additional 2 to 3 pints of Kool Aid after the race, and then complained of dizziness. He was noted to have slurred, unintelligible speech. Emergency medical technicians (EMTs) were called after the patient collapsed and became unresponsive.

EMTs arrived to find the patient responding only to painful stimuli by withdrawing. Initial vital signs included a pulse of 80 beats/min, blood pressure of 136/80 mm Hg, and spontaneous respiratory rate of 22 breaths/min. Bystanders reported that the patient may have had a seizure.

On arrival at the emergency department (ED) vital signs included a pulse of 69 beats/min, blood pressure of 146/86 mm Hg, respiratory rate of 14 breaths/min, and a temperature of 36.6°C. He was unable to respond verbally, but he was moving all four extremities. He was agitated but had no lateralizing neurological signs. His pupils were equal and reactive to light. Mucous membranes were moist, and skin turgor was normal. His oxygen saturation and glucose levels were within normal limits.

The patient was sedated with 4 mg of intravenous midazolam, nasally intubated, and underwent computerized tomographic (CT) scan to evaluate acute mental status change. The CT scan was negative for hemorrhage, midline shift, edema, or mass effect. Initial laboratory results were available as the patient was returned to the ED. Significant findings included sodium, 119 mEq/L; chloride, 89 mEq/L; potassium, 3.6 mEq/L; bicarbonate, 13 mEq/L; and serum osmolality, 248. Arterial blood gas was pH = 7.43 with Pco_2 of 34 mm Hg and Po_2 of 120 mm Hg, on Fio_2 of 100%.

Two hours after presentation to ED and 1 hour after the CT scan, the patient was noted to have new onset anisocoria with the right pupil larger than the left. Both pupils were reactive to light. He developed sinus bradycardia with a heart rate of 37 beats/minute and a blood pressure of 39 mm Hg. One milligram of atropine was administered intravenously, and the heart rate and blood pressure promptly returned to previous levels. The patient became combative and was then paralyzed with 20 mg metubine intravenously.

Three percent normal saline was immediately started at a rate of 100 mL/h. Because of the development of anisocoria and cardiovascular instability, the patient was hyperventilated to a goal Pco_2 of 25 mm Hg and was diuresed with furosemide and mannitol. A second CT scan was obtained and was noted to be unchanged. Further laboratory data became available, including a urine sodium of 39 mEq/L, urine chloride of 29 mEq/L, and urine potassium of 32 mEq/L.

Three hours after admission, the serum sodium reached a nadir of 111 mEq/L. By 12 hours after admission, the patient had received 300 mL of lactated Ringer's solution, 600 mL of normal saline, 500 mL of 20% mannitol, and 600 mL of 3% normal saline, with a corresponding urine output equal to 2,990 mL. The serum sodium levels increased to 121 after the first 12 hours. This corresponds to an average correction rate for serum sodium of 1.1 mEq/L/h from the nadir. The patient was noted to have pupils of equal size and reactivity, and he began to spontaneously open his eyes and move all extremities. The 3% saline drip was discontinued.

The patient was extubated without difficulty and subsequently discharged on hospital day three. There was complete return of neurological and mental function, with no apparent sequelae.

INCIDENCE

Hyponatremia is a common electrolyte disorder.[10,11] Acute symptomatic hyponatremia, however, is quite uncommon and is most often seen in three distinct populations: (1) psychogenic polydipsia; (2) inpatients with impaired water excretion who are treated intravenously with hypotonic fluids; and (3) inpatients who systemically absorb electrolyte-free irrigating solutions during prostate surgery.[13] We propose that ultra-endurance athletes represent a fourth population of individuals who may develop acute hyponatremia.

From the Department of Surgery, University of Vermont, and the Division of Emergency Medicine, Medical Center Hospital of Vermont, Burlington, VT.

Manuscript received October 19, 1993; revision accepted December, 1993.

Address reprint requests to Dr Uphold, Chairman, Division of Emergency Medicine, Medical Center Hospital of Vermont, Burlington, VT 05401.

0735-6757/94/1204-0011$5.00/0

An ultra-endurance event has no strict definition but at least exceeds a marathon in energy expenditure and duration. A marathon run is 42 km (26 miles). An ultra-marathon is a run over 50 miles.[15] An ultra-endurance event has been described as a triathlon extending 4 hours by Hiller[2] or an event lasting 7 hours or more by Noakes et al.[6]

It seems that athletes who are described as being in excellent health before racing develop acute symptomatic hyponatremia during ultra-endurance events. There are studies that provide insight into the incidence of hyponatremia in this population. One set of studies reports serum sodium values in asymptomatic volunteers engaged in athletic events. Hiller et al found none of the volunteers in a 1.5 km swim, 40 km bicycle, and 10 km run triathlon to have post-race hyponatremia, defined as serum sodium level of less than 135 mEq/L.[3] However, in two longer events, Hiller et al reported that the incidence of hyponatremia increased dramatically. Twenty-seven percent of athletes in a triathlon composed of a 1.9 km swim, 90.2 km bicycle race, and a 21.1 km run, and 29% of athletes engaged in a 3.8 km swim, 180 km bicycle race, and a 42.2 km run triathlon were found to be hyponatremic. These data suggest a trend of increasing frequency of hyponatremia as the length of the event increases. This trend is supported by the report of only one case of symptomatic hyponatremia in the literature associated with participation in a 26 mile marathon.

A second set of studies investigated the incidence of symptomatic hyponatremia among those athletes seeking medical assistance after an event. Hiller et al report 62% of the participants who required medical attention after one of the previously mentioned triathlons were hyponatremic, defined as less than 135 mEq/L.[3] Noakes et al studied athletes who collapsed during a 90 km ultra-marathon and reported that 9% had a post-race serum sodium level of less than 130 mEq/L.[6] A study conducted by Irving et al identified that 3% of collapsed runners in a 90 km ultra-marathon had serum sodiums less than 130 mEq/L.[9]

The incidence of symptomatic hyponatremia among ultra-endurance athletes is presently not well characterized. It is evident that these athletes are at some increased level of risk for developing this complication. In 1980, 3,000 finishers were reported in ultra-marathons, and in 1992, more than 10,000 finishers were reported. The number of ultra-marathon athletes in the United States is currently estimated to be approximately 5,000, and they participate in 250 events in the nation each year. As participation in these events increases, the number of cases of symptomatic hyponatremia will likely increase as well.

PATHOPHYSIOLOGY

Hyponatremia may be defined as a decrease in serum sodium concentration resulting from one or a combination of the following: (1) reduction of total body sodium; (2) increase in the total body water; (3) reduction of the total body potassium; or (4) increase in the nonaqueous components of the serum.[11] The etiology of acute symptomatic hyponatremia associated with ultra-endurance exercise has not been established, but several mechanisms have been proposed.

One mechanism that has been suggested is that a significant total body sodium loss via extensive sweating occurs during the event, which leads to a hypovolemic hyponatremia.[1] A second proposed mechanism is that the exercising athlete consumes excessive volumes of hypotonic fluids (Table 1) during the event, and this fluid is retained within the vascular space, resulting in a hypervolemic hyponatremia.[4,7,9] A third possible mechanism is a marked exercise-related reduction in blood flow to the gastrointestinal system.[15] As a result, minimal amounts of consumed fluids are actually absorbed. Hyponatremia then occurs after completion of the event, when return of mesenteric blood flow leads to massive absorption of the fluid within the gastrointestinal lumen. This proposed mechanism also causes hypervolemic hyponatremia.

Irving et al[9] provide data to support the theory that inappropriate renal function during the race leads to fluid retention in the vascular space causing a hypervolemic hyponatremia. They compared data on eight collapsed athletes with post-race hyponatremia after running a 90 km ultra-marathon with data on 18 athletes without hyponatremia who participated in other ultra-marathons of similar magnitude. They noted that sodium losses were not significantly different in the hyponatremic athletes implying that sweat losses are not causative. They also found that hyponatremic athletes had fluid overload despite no significant difference in fluid intake between the two groups. Therefore they conclude that inappropriate renal function is the probable cause of the hyponatremia. Interestingly, the renal function of the athletes after the race was normal, suggesting that the renal insufficiency is reversible and resolves after completion of exercise.

Several mechanisms are suggested to explain transient and inappropriate renal function.[9] The first is that the intense exercise causes catecholamine-mediated renal vasoconstriction, decreasing the glomerular filtration rate. Glomerular filtration rate may also be affected by the use of nonsteroidal anti-inflammatory agents (NSAIDs), particularly in people who are dependent on prostaglandin synthesis to maintain renal perfusion. Additionally, NSAIDs, by their inhibition of prostaglandin synthesis, potentiate the renal effect of vasopressin.[17] A reduction in plasma volume and/or the stress of the event may stimulate thirst and vasopressin release contributing to free-water retention.

The cause of exercise-induced hyponatremia in ultra-endurance athletes is not presently known. Reduction of total body sodium through sweating, or increase in total body water secondary to ingestion of hypotonic fluids, do not seem to be significant mechanisms. A massive uptake of fluids after the completion of the race is also not the total explanation because the renal system should be able to han-

TABLE 1 Electrolyte Composition

	Blood (mEq/L)	Gatorade (mEq/L)	Orange Juice (mEq/L)	Sweat (mEq/L)
Sodium	135-145	21	1	10-100
Potassium	3.5-5.0	2	43	4-10
Osmolality	280-295	339	500	30-230

dle such loads without difficulty. Therefore, inappropriate renal function and increased antidiuretic hormone (ADH) release are likely mechanisms, but this has not been clearly shown.

The patient presented complained of decreasing urine output one third of the way into the race. There are no objective data available from before or during the race to help substantiate this complaint. The urine and serum studies obtained in the ED show an abnormally high amount of urine sodium in light of the serum hyponatremia, suggesting that there was inappropriate ADH release and/or renal dysfunction.

Although the etiology of hyponatremia in these ultra-endurance athletes is not known, there is a clear understanding of how hyponatremia can cause the clinical presentation of neurological and mental status deterioration. This may be understood by reviewing the physiology of osmotic pressure. In the body, the extracellular and intracellular fluids are in a dynamic osmotic equilibrium across the selectively permeable cell membrane. As hyponatremia develops, a reduction in the extracellular osmolality creates a gradient across the cell membrane. The predicted result of this gradient would be net influx of water into the cell. However, the amount of cerebral edema expected to occur based only on this osmotic gradient may not be actually observed. The cells of the brain are capable of modifying the effects of decreased cellular osmolality through two mechanisms. The first is the loss of intracellular osmotically active substances, such as potassium and organic osmolytes, into the extracellular space.[13,18] This maintains the osmotic equilibrium across the cell membrane. The second defense mechanism is the loss of interstitial fluid around the cells of the brain parenchyma into the cerebral spinal fluid, which allows more potential space for any cellular edema that occurs.[19]

When hyponatremia develops at a slow rate, brain tissues may use these "defense mechanisms" to maintain osmotic equilibrium; therefore, the impact of the decreased serum osmolality is minimized, and patients may be mildly symptomatic, if at all. However, hyponatremia that develops at a rate that exceeds the adaptive mechanisms of the brain may cause clinically significant cerebral edema.[13] Because the cranial vault is a closed compartment, cerebral edema leads to an increase in the intracranial pressure. An increase in brain tissue volume by only 10% causes herniation of the brain stem that is incompatible with life.[13]

MANAGEMENT

This presentation of new and rapid mental status and neurological deterioration in a previously healthy athlete may be caused by a variety of etiologies. The initial differential diagnosis included trauma, hemorrhage, infection, hyperthermia, drugs, electrolyte abnormality, and psychiatric illness.

The clinical characteristics of the case presented are similar to other cases of hyponatremia described in the literature. Initial signs and symptoms often include disorientation, fatigue, nausea, dizziness, slurred speech, confusion, and inappropriate behavior. Findings on physical examination included stupor, coma, hyper-reflexia, muscle fasciculations, papilledema, anisocoria, dilated and poorly responsive pupils, and grand mal seizures.

The initial management begins with a rapid assessment of airway, breathing, circulation, mental status, and neurological examination. Continuous monitoring of vital signs is recommended. A rapid glucose test and blood oxygen saturation provide valuable information on easily reversible causes. Other laboratory studies to be obtained include complete blood cell count (CBC), electrolytes, blood urea nitrogen/creatinine, and arterial blood gas. We sedated and intubated our patient for protection of the airway as his mental status decreased. An emergency head CT scan is indicated to investigate the possibility of cerebral edema, hemorrhage, or underlying structural lesion. After the patient's condition has been stabilized initially, a more thorough secondary evaluation should be completed, and changes in cardiovascular, neurological and mental status must be monitored.

Any available history is essential to direct the management of the patient. In this case, we quickly ruled out trauma and chronic health problems and learned about the patient's participation in the ultra-marathon immediately proceeding the onset of his symptoms. We learned that his deterioration was rapid and that he had been well before the race.

With the head CT scan results negative for mass effect, hemorrhage, midline shift, and edema, the most significant finding was the serum sodium concentration, which was 119 mEq/L. We concluded that the symptoms and signs on initial presentation to the ED were the direct sequela of acute hyponatremia.

The onset of anisocoria, bradycardia, and combativeness suggested that the patient's intracranial pressure was elevated, with incipient herniation. To manage this problem, the patient was further sedated with midazolam and paralyzed with metubine. Mechanical hyperventilation and elevation of the head of the bed was instituted. Furosemide and mannitol-induced diuresis was initiated. A second CT scan was obtained to look again for herniation and edema. These results were also negative. The cardiovascular instability may have been secondary to hyponatremic encephalopathy but not to herniation. After the second CT scan ruled out cerebral edema, no further mannitol was given. The initial sodium of 119 mEq/L dropped to 111 mEq/L despite hypertonic saline and lasix. This may have been secondary to inappropriate ADH- and/or mannitol-induced osmotic hyponatremia.

The management of hyponatremia must carefully consider the risks and benefits of the treatment. There is a potential complication of treatment known as osmotic demyelination syndrome (ODS). ODS has been associated with serum sodium correction rates greater than 20 mEq/L/d.[13] Sterns identifies those patients at greater risk of developing ODS to be (1) those who have been hyponatremic for more than 48 hours or (2) those who have serum sodium levels less than 105 mEq/L.[13] Hyponatremia seen in ultra-endurance athletes has a rapid onset, less than 24 hours; therefore, ODS is unlikely to occur as a sequela of treatment. However, it is essential to rule out chronic hyponatremia by history or other means if available.

Because of the severe and deteriorating clinical picture in our patient, we began correction of the hyponatremia with hypertonic (3%) saline. Sterns concludes that a correction rate of 1 to 2 mEq/L/h using 3% normal saline is the maxi-

mum that may be used without risk of ODS.[13] Generally, a safe way to proceed is to give 3% normal saline at 100 mL/h and check serum sodium hourly. As the clinical picture improves or the sodium increases to 120 mEq/L, this aggressive therapy may be slowed, and a change to hydration with normal saline begun.

SUMMARY

There are several reported isolated cases of acute symptomatic hyponatremia associated with participation in ultra-marathons and ultra-triathlons. One case has been reported in a marathon finisher. There seems to be a relationship between the increasing magnitude of the event and risk of hyponatremia. Additionally, a significant percentage of athletes who request medical assistance after participation in these events may have hyponatremia.

Based on these findings, we recommend that any ultra-endurance athlete who presents for medical assistance after an ultra-endurance event with weakness, malaise, gastrointestinal complaints, or central nervous system signs and symptoms should be evaluated for hyponatremia. Because inadequate renal function may be a contributing mechanism, we also recommend obtaining studies to evaluate renal function.

Hyponatremia in conjunction with signs and symptoms of increased intracranial pressure warrants aggressive therapy. The risk of ODS must be considered seriously, but in the face of a deteriorating clinical picture, initiation of hypertonic saline therapy is indicated. A maximum correction rate of 1 to 2 mEq/L should be attained using serial measurement of serum sodium. As the clinical picture improves, the hypertonic therapy may be discontinued and normal saline initiated.

Hyponatremia may be one of the greatest risks to the health of participants in very prolonged athletic events. Although estimates to date of the incidence of hyponatremia among ultra-endurance athletes are limited, physicians attending EDs in proximity of such events should be aware that hyponatremia is a recognized complication of this sport.

The authors thank Dr Maj Eisinger for her thoughtful review of the report.

REFERENCES

1. Frizzell RJ, Lang GH, Lowance DC, et al: Hyponatremia and ultra-marathon running. JAMA 1986;255:772-774
2. Hiller WDB: Dehydration and hyponatremia during triathlons. Med Sci Sports Exercise 1989;21:S219-S221
3. Hiller WDB, O'Toole ML, Fortress EE, et al: Medical and physiological considerations in triathlons. Am J Sports Med 1987;15:164-167
4. Hiller WDB, O'Toole ML, Laird RH: Hyponatremia and ultra-mechanisms. JAMA 1986;256:213 (abstr)
5. Noakes TD, Norman RJ, Buck RH, et al: Water intoxication: A possible complication during endurance exercise. Med Sci Sports Exercise 1985;17:370-375
6. Noakes TD, Norman RJ, Buck RH, et al: The incidence of hyponatremia during prolonged ultra-endurance exercise. Med Sci Sports Exercise 1990;22:165-170
7. Nelson PB, Robinson AG, Kapoor W, et al: Hyponatremia in a marathoner. Physic Sports Med 1988;16:78-87
8. Young M, Sciurba F, Rinaldo J: Delirium and pulmonary edema after completing a marathon. Am Rev Respir Dis 1987; 136:737-739
9. Irving RA, Noakes TD, Buck RH, et al: Evaluation of renal function and fluid homeostasis during recovery from exercise-induced hyponatremia. J Appl Physiol 1991;70(1):342-348
10. Cluitmans FH, Meinders AE: Management of severe hyponatremia: Rapid or slow correction? Am J Med 1990;88(2): 161-166
11. Swales JD: Management of hyponatremia. Br J Anesth 1991;67(2):146-153
12. Sterns RH: The Treatment of hyponatremia: First do not harm. Am J Med 1990;88:557-560
13. Sterns RH: The Management of hyponatremic emergencies. Crit Care Clin 1991;7:127-142
14. Hiller WDB, O'Toole ML, Massimino F, et al: Plasma and glucose changes during the Hawaiian Ironman Triathlon. Med Sci Sports Exercise 1985;17:219 (abstr)
15. Knochel JP: Catastrophic medical events with exhaustive exercise: "White collar rhabdomyolysis." Kidney Int 1990;38: 709-719
16. Whelton A, Hamilton CW: Nonsteroidal anti-inflammatory drugs: Effects on kidney function. J Clin Pharmacol 1991;31(7): 588-598
17. Cline DM, Stoff JS: Renal symptoms associated with nonsteroidal anti-inflammatory drugs. N Engl J Med 1984;310:563-572
18. Thurston JH, Sherman WR, Manhart RG, et al: Myo-Inositol: A newly identified nonintrogenous osmoregulatory molecule in mammalian brain. Ped Res 1989;26:482-485
19. Berl T: Treating lypotremia: Damned if we do and damned if we don't. Kidney Int 1990;37:1006-1018