

Exercise-associated hyponatremia: a local case report

運動有關的低血鈉症：一個本地個案報告

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Most of us know the risk of dehydration during endurance exercise under extreme heat. We report a case that occurred in cool weather and when there was an abundant supply of fluid – the so-called exercise-associated hyponatremia. It is a potentially life-threatening condition and has led to at least seven fatal outcomes reported in the literature. (*Hong Kong j.emerg.med.* 2009;16:88-92)

我們大多數都知道在極熱環境下進行耐力運動，會有脫水的風險。我們報告一個號稱「運動有關的低血鈉症」個案，發生於清涼的天氣下及有充裕的飲品供應。這是一個對生命有潛在威脅的情況，文獻中最少已有7個死亡個案的報告。

Keywords: Athletic injuries, exercise, physical endurance, running, water intoxication

關鍵詞：運動員受傷、運動、運動耐力、跑步、水中毒

Case report

At around 14:30 hour on 17th February 2008, a 35-year-old male participant of the Standard Chartered Hong Kong International Marathon was sent to the emergency department of Pamela Youde Nethersole Eastern Hospital by ambulance. The race started at 7:45 hour in the morning. The patient had run about 30 km, which was about three quarters of the 42 km race, in more than five hours. At that point he was forced to give up by the race organiser due to overtime. He took a bus provided by the race organiser to the finishing point and started to complain of dizziness. After taking a rest, he found himself too dizzy to walk and he was then sent to hospital.

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There were about 6000 participants in the race. The atmospheric temperature ranged from 13 to 17°C during the race period. The relative humidity was about 60%. There were drinking stations every 5 km, serving both plain water and sports drink.

At the triage station, the patient was fully alert with a blood pressure of 121/64 mmHg and pulse rate of 71. There was no fever and the oxygen saturation was 100% on room air. After briefly assessed by the attending doctor, he was diagnosed to have exhaustion and was admitted to the observation ward for a rest. The nurse reported no urine output after four hours. He was reassessed with a set of blood investigation and 500 ml intravenous normal saline was given. The blood results showed a sodium level of 119 mmol/L, potassium of 3.6 mmol/L, creatinine of 65 umol/L and creatine kinase of 1135 mmol/L. He was then transferred to the medical ward for further management.

Further history revealed that the patient was in good medical health except taking venlafaxine, a serotonin noradrenaline reuptake inhibitor for depression,

prescribed by his family doctor. He had no marathon running experience but he had attempted 10-km race twice in the past. On the day of the race, he denied excessive drinking before the race but took over 30 cups of plain water during the race. (The organiser only provided 11 water stations along the race tract. He stopped at water stations, took plenty of water and refilled a bottle carried with him). During the race, he had one episode of urination and one bowel opening.

In the medical ward, he remained drowsy for the whole night and could not get up from the bed, so a Paul's tube was offered to monitor urine output. He was put on a slow normal saline drip supplemented with oral sodium chloride tablets. The urine output in the next morning was 2.5 liters cumulatively. Other significant laboratory investigations were as follows: serum osmolarity 250 mOsmol/kg, urine osmolarity 512 mOsmol/kg and urine sodium 101 mmol/L. This picture was suggestive of the syndrome of inappropriate anti-diuretic hormone secretion (SIADH). The patient felt much better on the second day with a sodium level of 139 mmol/L, and was discharged home with a diagnosis of exercise-associated hyponatremia (EAH).

Discussion

Definition

Exercise-associated hyponatremia is defined as a serum sodium level less than 135 mmol/L during or within 24 hours after prolonged vigorous activity. Moderate EAH is defined as a serum sodium level between 130 to 121 mmol/L; and critical EAH is when the serum sodium level is equal to or less than 120 mmol/L.

Clinical features

Mild EAH is usually asymptomatic and usually not detected unless the runner has blood electrolytes measured for other reasons. Otherwise, early signs of EAH can include dizziness, nausea, vomiting and headache, which are very non-specific and simulate exercise-associated exhaustion.

As the degree of EAH progresses, hyponatremic encephalopathy may develop from brain swelling and

result in change in the mental status with confusion or agitation, seizure and even coma. Respiratory distress may also occur as non-cardiogenic pulmonary oedema develops.

Historical aspects

Historically, fluid ingestion was discouraged during endurance exercise. To run a marathon without any fluid replacement is regarded as the ultimate aim of elite runners and a test of their fitness. It was believed that 'at the moment drink is taken, the body has to start dealing with its ingestion, and in so doing some discomfort will almost invariably be felt'.¹

This may partially explained that there was no known case of EAH reported before 1981. It started to attract attention only after Naokes reported the first case series of 4 cases in 1985, which included cases diagnosed in 1981.² In this case series, 3 were participants of 88 km ultra-marathon (twice of an ordinary marathon) and 1 of triathlon. All of them had spent more than 7 hours in the races. All the runners had weight gain or exhibited features of excessive fluid intake. Naokes therefore suggested that 'water intoxication' due to voluntary over-hydration with hypotonic solutions was the possible cause of the hyponatremia. He had also noticed that the fluid excess in the runners was not corrected by increased urinary losses. He suggested that this might relate to the 'sodium and water conserving mechanism' activated by the prolonged exercise.

With increasing cases of EAH being recognised in the past 20 years, including multiple fatal cases among young and fit athletes, two international congresses were carried out in 2005 and 2007 with consensus on the topic being published.^{3,4}

Incidence

There are few studies on the incidence of hyponatremia in marathon available in the literature. In the 2000 Houston Marathon, among 55 runners requiring intravenous fluid replacement onsite, 21 had hyponatremia. It represented 9% among all those who required medical care, and 0.31% among all 6660 entrants; 11 of them had moderate hyponatremia (Na^+ between 120-129 mmol/L) and 2 of them had critical EAH ($\text{Na}^+ < 120$ mmol/L).⁵

In the 2003 Boston Marathon, Kratz et al found that 6% out of 140 collapsed runners were hyponatremic, compared with 5% of the population of marathon runners who had experienced no medical difficulties. But at the same time, 25% of the collapsed runners were hypernatremic ($\text{Na}^+ > 146 \text{ mEq/L}$), compared with 9% among runners with no medical difficulties. The above occurred despite a new recommendation for fluid replacement for marathon runners to drink ad libitum between 400 and 800 ml/h as opposed to the previous "as much as possible" advice.⁶

Only three prospective cohort studies of the incidence of hyponatremia after marathon are available in the literature.

In the 2002 Boston Marathon, Almond et al found that 13% of the 488 runners who had finished the race had hyponatremia. Critical EAH account for 0.6% ($\text{Na}^+ < 120 \text{ mmol/L}$). Water stations were available every mile (1.6 km) in that race.⁷

In the 2002 New Zealand City of Christchurch Marathon, among the 134 marathon finishers studied, there was no case of biochemical or symptomatic hyponatremia. This finding relates to a marathon run under ideal conditions (minimal climatic stress) and in which there were fewer aid stations (every 5 km) than those common in North American marathons (every 1.6 km). Also, aggressive hydration practices were not promoted.⁸ In the 2006 Zurich Marathon, in a cohort of 167 runners, 3% (5 subjects) developed

asymptomatic EAH, and no symptomatic EAH was found (cool and rainy weather, time limit of 5 hours).⁹

Pathophysiology

As recognised by Noakes when he first reported his case series, the cause of EAH is related to excessive intake of fluid resulting in an enormous positive fluid balance and body weight gain.

EAH is primarily a dilutional hyponatremia because it is associated with over-consumption of fluid and weight gain in the athletes, but most of the time the volume of urine production is still far below the maximal excreting capacity of the kidneys. Detail investigation in the athletes has shown that part of the reason is fluid retention due to a suppressed renal excreting capacity and the investigation finding is compatible with SIADH.

Risk factors

There are several risk factors for developing EAH as suggested by different studies. The 2007 EAH consensus summarised the risk factors as listed in Box 1.⁴

Our patient is an inexperienced slow runner, with positive history of excessive drinking. Despite his positive fluid balance, he had initially a low urine output and high urine sodium that was suggestive of SIADH. Apparently the EAH seemed to be resulting from over-hydration only, but he had been taking venlafaxine, a serotonin noradrenalin reuptake

Box 1. Risk factors for exercise-associated hyponatremia (2007 consensus)⁴

- Low body weight
 - Female sex
 - 4 hours of exercise duration
 - Slow running or performance pace
 - Race inexperience
 - Excessive drinking behaviour
 - High availability of drinking fluids
 - Altered renal water excretory capacity (potentially impaired by drugs, such as non-steroidal anti-inflammatory agents, intrinsic renal disease or syndrome of inappropriate antidiuretic hormone secretion)
 - Extremely hot or cold environmental conditions
-

inhibitor which could possibly cause SIADH, the latter being an additional risk factor for EAH. We tried to investigate along this line by calling him back for rechecking. However, at the time of call back he had stopped the drug and his serum and urine sodium and osmolarity were all back to normal.

Among the individuals developing EAH, a sub-group of them have been proven to have relatively low urine output and high urine sodium. These individuals are thought to have physiologically inappropriately high level of anti-diuretic hormone (ADH). The reason for this is not completely understood. Possible explanation could be physical and psychological stress during the race that keeps the ADH level high. Another postulation is drugs, e.g. serotonin reuptake inhibitors, causing altered renal sodium excretion.

Sports drink

Plain water intake is a known risk factor while excessive intake of electrolyte-containing sports drinks, which is still hypotonic, has not been shown to be protective against EAH.⁴

Treatment

The definitive treatment of EAH encephalopathy is immediate onsite administration of intravenous hypertonic saline. Aggressive treatment with hypertonic saline in EAH patients in critical condition is frequently withheld because of the fear of the complication of central pontine myelinolysis. However, evidence has suggested that the fear of the complication is ungrounded and the treatment is, instead, always life saving.⁴

Ayus et al first reported cases of EAH treated with hypertonic saline in 2000. Among 7 cases of hyponatremic encephalopathy presenting with the complication of non-cardiogenic pulmonary oedema, the 6 treated with hypertonic saline survived, and the one without this treatment died. They therefore strongly recommended giving runners presenting with this problem 100 ml of 3% saline over 3 minutes,

which will raise the sodium level by 2 to 3 mmol/L to decrease brain swelling onsite before sending out the patient to hospital.¹⁰

The use of 3% hypertonic saline in the hospital setting is subsequently documented. Successful use onsite has also been documented since 2004. The current recommendation is 100 ml 3% saline up to 2 additional doses at 10 minutes intervals. If the symptoms persist or worsen after transfer to hospital, admission into the intensive care unit should be arranged and appropriate consultation should be made.⁴

Runners with asymptomatic EAH or mild symptoms should be detained to have oral fluid until the onset of urination. Administration of intravenous normal saline or hypotonic fluids, which may worsen the degree of hyponatremia, is contraindicated.

Conclusion

EAH is a condition requiring prompt diagnosis and treatment. A history of excessive fluid intake before, during and/or after the race is an important clue to diagnosis, as positive weight gain. On-site blood analysis for collapsed runners is recommended as an important investigation. For proven cases of critical EAH with neurological symptom, 3% hypertonic saline infusion is the treatment of choice, while isotonic and hypotonic fluid is contraindicated.

Being emergency physicians, we need to gain adequate knowledge in sports medicine emergencies. The common misconception is either assuming all collapsed runners with a crude diagnosis of exhaustion, or assuming hypovolaemia and treats them by isotonic intravenous fluid bolus. These will delay the diagnosis and make the condition worse. As marathon is becoming a popular event among non-athletes, EAH is expected to rise in the future locally and public education should be introduced before the yearly races.

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