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CONCEPTS

Exercise-Associated Hyponatremia: Overzealous Fluid Consumption

Ian R. Rogers, MB, BS, FACEM; Tamara Hew-Butler, DPM, PhD

From Sir Charles Gairdner Hospital, Nedlands, Western Australia (Dr. Rogers); and Department of Kinesiology, Arizona State University, Tempe, AZ (Dr. Hew-Butler).

Exercise-associated hyponatremia is hyponatremia occurring during or up to 24 hours after prolonged exertion. In its more severe form, it manifests as cerebral and pulmonary edema. There have now been multiple reports of its occurring in a wilderness setting. It can now be considered the most important medical problem of endurance exercise. The Second International Exercise-Associated Hyponatremia Consensus Conference gives an up-to-date account of the nature and management of this disease. This article reviews key information from this conference and its statement. There is clear evidence that the primary cause of exercise-associated hyponatremia is fluid consumption in excess of that required to replace insensible losses. This is usually further complicated by the presence of inappropriate arginine vasopressin secretion, which decreases the ability to renally excrete the excess fluid consumed. Women, those of low body weight, and those taking nonsteroidal anti-inflammatory drugs are particularly at risk. When able to be biochemically diagnosed, severe exercise-associated hyponatremia is treated with hypertonic saline. In a wilderness setting, the key preventative intervention is moderate fluid consumption based on perceived need (''ad libitum'') and not on a rigid rule.

(Editor's Note: This paper was written at my request in an effort to increase awareness of this important clinical entity among members of the wilderness community, many of whom are involved in activities that place them at risk of its development. I thank the authors for their diligent efforts.)

Key words: exercise associated hyponatremia, fluid balance, endurance exercise, arginine vasopressin

Introduction

Having first been reported a little more than 2 decades ago,[1,2] exercise-associated hyponatremia (EAH) has now come to be recognized as arguably the most important, serious medical problem in endurance sports participants.[3] Much research has followed these initial reports. For some time there was debate about its etiology between 2 firmly entrenched camps, supporting either the water intoxication[1] or the salt loss hypotheses.[4] More recently there has been an increasing consensus about the definition, manifestations, etiology, treatment, and prevention strategies for EAH.

EAH Consensus Statement

The consensus on EAH is represented in its most up-to-date form by the Consensus Statement of the Second International Exercise-Associated Hyponatremia Consensus Development Conference, published last year in the *Clinical Journal of Sports Medicine*,[3] to which readers are directed for a more comprehensive review of EAH in general. The meeting, held in New Zealand in late 2007, brought together 18 researchers and experts in EAH from multiple disciplines and multiple countries to review all the existing data on EAH and update its 2005 statement.[5] Their stated aim with regard to EAH was to develop a document that could help to ''curtail the morbidity and mortality associated with the disorder.'' Notably the meeting was free of commercial sponsorship and used a recognized consensus conference protocol.

EAH is formally defined as hyponatremia (less than the laboratory reference range) occurring during or up to 24 hours after prolonged exertion (generally considered to be >4 hours' duration). The EAH consensus statement gives us a clear and updated view as to the manifestations, pathophysiology, risk factors, treatment, and prevention of EAH. It also highlights those areas

Corresponding author: Professor Ian Rogers, Postgraduate Medical Education, Sir Charles Gairdner Hospital, Hospital Ave, Nedlands, Western Australia 6009 (e-mail: ian.rogers@health.wa.gov.au).

that remain controversial and research questions that remain to be answered. Much of this knowledge can be applied to the wilderness setting.

Relevance to the wilderness setting

The direct relevance of a statement on EAH to our preferred wilderness environment may not seem obvious. The largest studies to date on EAH have been conducted in the setting of mass participation sporting events, such as endurance triathlons[6,7] and conventional marathons.[8,9] However EAH has been reported in hikers,[10] trekkers,[11,12] climbers,[13] and cold climate endurance athletes.[14] It is likely that these reports understate the incidence of EAH given the difficulties of conducting large prospective studies in wilderness settings.

Manifestations

The most serious manifestations of EAH are primarily neurologic. Generally, symptoms are not obvious until the [Na^+] falls below 130 mmol/L or there has been at least a 7% fall from the patient's baseline [Na^+],[15] although large interindividual variation exists.[16,17] However, the absolute serum [Na^+] is less important than the patient's clinical status. The most serious symptoms and signs of EAH are reflective of pulmonary and cerebral manifestations of fluid overload and include noncardiogenic pulmonary edema[18] and cerebral edema with encephalopathy. Early symptoms include nausea, vomiting, and headache, and later signs include confusion, disorientation, seizures, coma, and the crepitations of pulmonary edema. In the wilderness setting, plausible differentials can include heat stroke, hypothermia, hypernatremia, and high-altitude cerebral edema.

Etiology and pathophysiology

In the majority of published cases, the primary etiologic factor in EAH is fluid consumption in excess of fluid losses.[3] In the resting state, maximal urine excretory rates are typically 800 to 1000 mL/hr, so prolonged fluid consumption above this rate can lead to dilutional hyponatremia.[19,20] During exercise, however, sweating becomes the primary mode of water and sodium loss. Thus, athletes exercising at low intensities will require less fluid than when exercising at higher exercise intensities due to the decreased rate of metabolic heat production, leading to a smaller rise in body core temperature and a commensurate lower heat dissipation requirement. The exercising situation is further complicated by the stimulation of nonosmotic arginine vasopressin (AVP) secretion, which is the body's main antidiuretic hormone, during prolonged endurance events.[21,22] AVP is now recognized as an exacerbating factor in most cases of EAH as a variant of the syndrome of inappropriate AVP secretion (otherwise known as syndrome of inappropriate antidiuretic hormone secretion [SIADH]).[23] AVP has a very short half-life, so research in this area has proved difficult. Nevertheless, what would be regarded as a normal AVP level at rest is physiologically inappropriate in the presence of hyponatremia or hypervolaemia.[24,25] Many of the recognized stimuli to AVP secretion, such as exertion, nausea, vomiting, exertional hypovolemia, pain, and thermal stress, can occur in the wilderness. So the complex interplay between excessive fluid consumption and elevated AVP levels may lead to EAH with high or even more moderate levels of fluid intake and may in part explain the individual variability in the predisposition to EAH. In contrast to the strong evidence for excessive fluid consumption and elevated AVP levels in the development of EAH, no strong evidence currently exists for loss of sodium as the primary cause. However, one case of recurrent EAH in a lawn bowler carrying the cystic fibrosis gene mutation Delta F508 has recently been reported[26] with a sweat sodium value of 103 mmol/L, which represents the *exception* rather than the rule.

Risk factors

The profile of a ''typical'' athlete developing EAH is a slow, low–body weight, female taking nonsteroidal antiinflammatory drugs (NSAIDs). However, experienced and well-trained male athletes are not immune to developing this fluid balance disorder if sustained fluid intake exceed the capacity for fluid output.[27] The combination of exuberant fluid intake beyond thirst in combination with antidiuresis (from nonosmotic AVP secretion[21] with or without the potentiating effects of antidiuresis from the ingestion of NSAIDs[28,29]) can create conditions ideal for the development of EAH in both novice and experienced athletes in and out of the wilderness setting. It is noteworthy that both selective and nonselective cyclooxygenase inhibition by NSAIDs can inhibit free water clearance during exercise, suggesting that cyclooxygenase-2 inhibition at the kidney is important in the maintenance of renal function during physical activity.[30] Therefore, it is strongly advised that athletes refrain from ingesting NSAID medications while participating in sustained physical activity in the wilderness setting. Further identified risk factors of particular relevance to the wilderness setting include prolonged exercise duration and extremes of temperature.[10] These associations have been documented in research scenarios, but their presence