Hiponatremia asociada al ejercicio en deporte de resistencia: revisión con recomendaciones prácticas

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Resumen

La participación en actividades de resistencia se ha popularizado y está en continuo crecimiento. La hidratación adecuada es importante para el rendimiento y para evitar complicaciones médicas. El consumo excesivo de líquidos, en combinación con una secreción inadecuada de la hormona arginina vasopresina puede llevar a una hiponatremia asociada al ejercicio (EAH). Estos dos factores son los principales responsables del desarrollo de la EAH, lo que resulta en retención de agua y hiponatremia dilucional. La EAH se define como concentración sérica < 135 mol/L durante o hasta 24 horas tras el ejercicio. Los atletas pueden presentar síntomas como náuseas, vómitos o incremento de peso. En casos severos o con ejercicio asociado al encefalopatía hiponatremica (EAHE) pueden presentarse cuadros graves como cefaleas, alteración del nivel de conciencia, convulsiones e incluso coma, lo que representa una emergencia médica. El tratamiento estándar es la administración de una solución salina hipertónica intravenosa. Otros factores de riesgo incluyen ejercicio de más de 4 horas, altas temperaturas, falta de experiencia en el evento, entrenamiento inadecuado, consumo de líquidos libre o ritmo de carrera inadecuado. La prevención implica un enfoque de hidratación apropiado y educación del personal cualificado.

Palabras clave:
- Hipertónica salina solución.
- Edema cerebral.
- Fluidos.
- Ultramaratón.
- Ciclismo.
- Natación.
- Triatlón.

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**Introduction**

Participation in endurance sports has seen an important rise over the last twenty years, especially in activities such as running, but also in cross country skiing, triathlons, and cycling.

Medical problems can be observed in endurance sports, but most are minor in nature, however serious medical problems also occur, such as cardiovascular issues, exertional heat illness, hypothermia, accidental falls or exercise associated hyponatremia (EAH).

EAH is defined as a serum sodium concentration \([\text{Na}^-]\) below standard laboratory measurements of < 135 mmol/L either during or up to 24 hours after exercise. The main mechanisms leading to EAH are overconsumption of fluids and inappropriate secretion of the hormone arginine vasopressin (AVP). The result is a positive fluid balance leading to a dilutional hyponatremia and EAH. Symptoms can range from mild to severe and life threatening. Mild symptoms are often non-specific and can generally be treated with fluid restriction or oral hypertonic saline. Severe EAH or exercise associated hyponatremia encephalopathy (EAHE) with cerebral oedema is a life-threatening condition and prompt treatment with intravenous hypertonic saline is necessary to avoid unfavourable outcomes and fatalities. Prevention, early recognition and appropriate treatment of EAH is important to reduce the burden of this illness.

We summarized the pertinent literature related to EAH in this educational review and give an overview of the definition, pathophysiology, history, incidence, risk factors, clinical signs and symptoms, diagnosis, treatment and prevention of EAH. Further we are giving practical advice and recommendations for athletes participating at endurance events, as well as for the medical staff caring for those athletes.

**Definition**

EAH is defined as a serum sodium concentration \([\text{Na}^-]\) below standard laboratory measurements of < 135 mmol/L either during or up to 24 hours after exercise. EAH can be classified as mild (\([\text{Na}^-]\) of 130-134 mmol/L), moderate (\([\text{Na}^-]\) of 125-129 mmol/L), or severe (\([\text{Na}^-]\) < 125 mmol/L). Clinically it may be asymptomatic or symptomatic with mild, moderate or severe clinical features. Clinical symptoms may not correspond to the severity in drop in serum sodium concentration but with the speed in which this decline occurs. Severe symptomatic EAH or EAHE can present as life-threatening medical emergency and prompt recognition and treatment is necessary to avoid fatalities. Severe cases can also lead to EAH with pulmonary oedema.

**Pathophysiology**

There are several factors involved in the pathophysiology of EAH (Figure 1). The main underlying mechanisms are overconsumption of fluids and inappropriate secretion of the hormone arginine vasopressin (AVP). Drinking beyond thirst and/or overconsumption of fluids beyond fluid losses during exercise (such as sweat, urine or insensible fluid losses) lead to a dilutional hyponatremia, resulting in a relative excess of body water in relation to the total content of exchangeable body sodium.

![Figure 1. Pathophysiological mechanisms leading to exercise associated hyponatremia.](image-url)

The two larger circles represent the main underlying cause. AVP=arginine vasopressin, ANP=atrial natriuretic peptide, BNP=brain natriuretic peptide, GI=gastro-intestinal.

Most symptomatic cases have been observed with overconsumption of fluids and weight gain or inadequate weight loss, but symptomatic EAH has also been described with dehydration, although this is rare. The other main mechanisms is the inappropriate secretion of AVP or anti diuretic hormone (ADH). AVP is the main hormone regulating the water and fluid balance within the human body. The secretion of AVP is regulated through changes in plasma osmolality but can also be stimulated via non-osmotic stimuli such as stress, pain, nausea, vomiting, hypoglycaemia, heat, non-steroidal anti-inflammatory (NSAID) and IL6. These non-osmotic stimuli, often encountered in ultra-endurance events, lead to an inappropriate secretion of AVP and can further exacerbate fluid retention, and worsening symptoms of EAH.

There are a number of other contributing factors, which exacerbate the development of EAH, such as the rapid absorption of fluids from the gastro-intestinal tract after exercise cessation, through an increase in splanchnic blood flow. Other factors that are less well investigated include the inability to mobilize the non-osmotic form of sodium which is bound to bone, skin and cartilage and the activation of the renin angiotensin aldosterone system with decrease in renal filtration and reduction in water excretion and sodium losses through sweat and urine through elevated levels of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP).

EAHE is a severe form of EAH with neurological affection due increased intracranial pressure from cerebral oedema. This form is due to a low serum sodium concentration in the cerebral blood flow when extra cellular water follows an osmotic gradient into the intracellular compartment causing swelling or oedema. This can also occur in the lungs, leading to pulmonary oedema.
Historical perspective

EAH was first described in 1981 by Tim Noakes during the Comrades Marathon in South Africa. The first scientific publication in 1985 described four cases of endurance athletes with severe hyponatraemia. Shortly afterwards further reports of EAH were published. Since then, a growing number of reports about EAH exists, including cases of fatalities. Interestingly, up to 1969, athletes were advised not to consume fluids during exercise and to avoid drinking altogether and no cases of EAH were reported. This advice subsequently changed and between 1987-2007 the American College of Sports Medicine (ACSM) and the US Military advised to drink as much as tolerated during exercise, supported by the drink industry. This may have led to a rise in cases of EAH. The current advice is to drink to thirst, which not only provides an effective preventative strategy for EAH but also has positive effects on performance.

Incidence according to type of sports

EAH develops during exercise, with less than 1% of athletes having low pre-race sodium concentrations. The incidence of EAH varies among sports with the highest numbers being reported in rowers, during a four week training camp. In running the incidence seems to increase with an increase in exercise duration. For example, no reports are available in half-marathon distance runners whereas in marathon running, reports range from 0 to 22% with an average incidence of around 8%. In ultra-endurance distances the average incidence in races below 100 km is <1%, in 100 km races < 3% and races with 100 miles distances this grows to over 20% with some races reporting incidences of up to 51%. In multi-stage ultra-distance events the incidence goes up to 42%, however all of those athletes were asymptomatic.

Similarly, for triathlon, the incidence of EAH increases with increasing race distance. The incidence in Ironman triathlons has been reported to be around 20% whereas in Triple Iron ultra-triathlon distance this goes up to 26%. In long-distance open-water swimming, 36% of women and 8% of men showed biochemical signs of EAH. In road cycling and mountain biking, the incidence is generally lower ranging from no reported cases to 12%, but severe cases of EAH and EAHE can occur. Incidence among rugby players has been reported to be 33% after a rugby match.

Fatalities are rare but have been reported in runners, triathletes, canoeists, hikers, American football players, soldiers and the police.

Table 1. Risk factors for the development of exercise associated hyponatremia.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overconsumption of fluids</td>
<td></td>
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<tr>
<td>Exercise duration over 4 hours</td>
<td></td>
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<tr>
<td>Event inexperience</td>
<td></td>
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<tr>
<td>Inadequate training</td>
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<tr>
<td>High or low body mass index (BMI)</td>
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<tr>
<td>Female sex</td>
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<tr>
<td>Use of non-steroidal anti-inflammatory drugs (NSAID)</td>
<td></td>
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<tr>
<td>Thermal stressing environment (extreme heat, cold, humidity)</td>
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</tr>
<tr>
<td>Geographical location where race is held</td>
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</table>

Clinical signs and symptoms

In the early stages of EAH, symptoms are fairly non-specific and are summarized in Table 2. A high index of suspicion of EAH should be

Table 2. Symptoms of mild symptomatic cases of exercise-associated hyponatremia (EAH) and treatment.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Restrict oral fluid intake until free-flowing urination</td>
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<tr>
<td>Vomiting</td>
<td>If athlete is alert and able to tolerate oral fluids provide oral hypertonic fluids</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Oral hypertonic fluids may include 3% NaCl (100ml) or other hypertonic solutions with high sodium concentrations (e.g. concentrated bouillon)</td>
</tr>
<tr>
<td>Weakness</td>
<td>If athlete is unable to tolerate oral fluids or symptoms are not improving or are progressing use intravenous bolus of 100 mL 3% NaCl (hypertonic saline) as per severe cases of EAH</td>
</tr>
<tr>
<td>Light headiness</td>
<td></td>
</tr>
<tr>
<td>Adynamia</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
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<tr>
<td>Puffiness</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
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<tr>
<td>Muscle cramps</td>
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<tr>
<td>Tremor</td>
<td></td>
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<tr>
<td>Oliguria</td>
<td></td>
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<tr>
<td>Bloatedness</td>
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<tr>
<td>Increase in body weight</td>
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</tbody>
</table>

in the heat but also in extreme cold. Heat seems to be a risk factor with more cases reported in extreme environmental conditions. Interestingly enough, the geographic location seems to have an influence on EAH incidence, as races in Northern America, Asia or Oceania cases of EAH are less likely and rare.

Risk factors

The development of EAH is multifactorial and several risk factors have been described (Table 1). However, the main risk factor is overhydration and may be caused by consuming fluids at rates above the recommended levels. The first case of EAH was documented in a woman but apparent sex differences with an increased incidence in women is not statistically significant. Women may be more at risk however due to an increased fluid intake compared to men. Extreme temperature range seems to be a risk factor, especially in thermal stressing environments especially
Table 3. Symptoms and treatment of severe cases of exercise-associated hyponatraemia (EAH) and exercise associated hyponatraemic encephalopathy (EAHE). ABC (Airway, Breathing, Circulation).

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>− Fatigue</td>
<td>− Emergency assessment (ABC)</td>
</tr>
<tr>
<td>− Confusion</td>
<td>− Onsite serum sodium concentration [Na+] measurement if available</td>
</tr>
<tr>
<td>− Agitation</td>
<td>− If measurement unavailable treat empirically</td>
</tr>
<tr>
<td>− Lethargy</td>
<td>− Intravenous access (i.v.)</td>
</tr>
<tr>
<td>− Altered mental state</td>
<td>− L.v. bolus of 100 mL 3% NaCl (hypertonic saline), every 10 min at least twice or until clinical improvement</td>
</tr>
<tr>
<td>− Disorientation</td>
<td>− Alternatively, other comparable solution containing sodium can be used (e.g. 10 mL of 20% NaCl)</td>
</tr>
<tr>
<td></td>
<td>− Arrange emergency transport to nearest medical facility</td>
</tr>
</tbody>
</table>

warranted especially if there is a history of overhydration. Care must also be taken not to miss other medical conditions that may present in a similar way. Onsite [Na+] measurement can aid in the correct diagnosis but this is not always available or possible. If symptoms progress or in cases of EAHE or rapid decrease in serum sodium levels symptoms may include confusion, agitation, altered mental state, dyspnoea or phantom running (Table 3). This may progress to seizure activities or coma, which constitutes a medical emergency and prompt recognition and treatment is warranted. Deaths have also been reported from EAH.

Diagnosis

The correct diagnosis is made biochemically with serum sodium concentrations of < 135 mmol/L. However, on-site sodium measurements during competitions are not always available or feasible in remote environments. Empirical treatment is recommended in the absence of biochemical results.

Treatment

Treatment strategies depend on clinical symptoms. Asymptomatic athletes generally do not require any active form of treatment but advice about proper fluid consumption is advisable (e.g. drink to thirst). Fluids can be restricted until onset of urination or oral hypertonic saline solutions may be given in order to reduce the risk of progression to symptomatic EAH.

Table 4. Practical advice on exercise associated hyponatraemia (EAH) for athletes and coaches. NSAID (non-steroidal anti-inflammatory drugs).

- Drink to thirst
- Overconsumption of fluids is the main risk factor
- Sports drinks cannot prevent EAH when overconsumption takes place
- Salt tablets do not offer protection so use with caution
- Do not use NSAID in training or competition
- Be well prepared for competition
- Acclimatize when competing in hot environments
- Educational material is available on trusted websites
- EAH can kill and knowledge about this condition and recognition is vital for everyone involved in endurance sports
- Alert and teach other athletes and coaches about EAH

Treatment strategies for mild symptomatic cases of EAH are summarized in Table 2. If patients are not improving or are unable to tolerate oral fluids, intravenous administration of fluids is recommended, as in severe cases of EAH or EAHE (Table 3). If onsite [Na+] measurement is not available, empirically lifesaving treatment with intravenous hypertonic saline solution should be given as this empirical treatment is unlikely to cause any harm even if the presumed diagnosis is wrong. Emergency transfer to the nearest hospital should be arranged, especially if recovery is slow or delayed.

Prevention

As the main mechanism for the development of EAH is the overconsumption of fluids the most effective preventative measure is an adequate fluid intake. This can be achieved through drinking to thirst. It is important to know that sports drinks are hypertonic when compared to plasma and overconsumption can also lead to EAH and do not offer any protection. In the past the sports industry heavily promoted the consumption of sports drinks and overzealous fluid consumption. Care needs to be taken when replacing sodium losses with salt tablets, although offering theoretical benefits and possibly slowing down the development or progression of EAH, salt tablets can increase thirst and thus lead to overconsumption of fluids thus aiding in the development of EAH. An important aspect of prevention is education and information about EAH is available on trusted websites in English and Spanish (www.ultrasportsscience.org).

Advice for athletes

It is important for athletes and coaches to be aware of proper hydration strategies during ultra-endurance events and that the current guidance of drinking to thirst are followed, which effectively can prevent the development of EAH without decrements in performance. The consumption of sports drinks is widely used among ultra-endurance athletes. An important aspect of prevention is education and information about EAH is available on trusted websites in English and Spanish (www.ultrasportsscience.org).

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as sports drinks are hypertonic and when overconsuming can lead to EAH. This also applies to the ingestion of salt tablets that may slow down the development of EAH, but the high salt content can increase thirst which again leads to overhydration and EAH. Athletes also need to be aware of certain medications, especially NSAIDs, that can aid the development of EAH. EAH is a serious medical condition and deaths have been reported so being aware of this condition, its symptoms and signs and risk factors is important for athletes. When talking to other athletes sharing the knowledge about this is paramount. This will be important in reducing the medical complications arising from EAH and help reducing the incidence of EAH.

Advice for medical personnel

Medical personnel should be aware of EAH, its symptoms, pathogenesis and treatment (Table 5). It may be difficult to recognise EAH in its early stages, but prompt recognition and appropriate treatment can reduce the disease burden. When planning for medical care it is therefore important to have all the necessary medical equipment (intravenous giving set, hypertonic saline solution etc.) within the medical facilities and depending on competition onsite blood analysers. Pre-race planning should include evacuation procedures and knowledge and contact details of the nearest hospitals. An information leaflet about EAH accompanying the patient to the hospital with pertinent treatment may be helpful as receiving staff at these facilities may not be aware of EAH and its treatment. Liberal fluid availability at some races has promoted the development of EAH, so careful planning when organising a race is important. Educating other health care professionals or giving advice on proper hydration on race websites can also be an important factor in reducing the incidence of EAH. Leaflets, online teaching resources and congresses are available to train and update medical staff.

Table 5. Practical advice of exercise associated hyponatraemia (EAH) for medical personnel.

- EAH can kill
- Knowledge about EAH and recognition of clinical signs is paramount for the medical team involved in endurance sports
- Consider availability of equipment for on-site serum sodium (Na⁺) measurement during competition
- Consider providing pre-race briefing about proper hydration (drink to thirst) and advice on EAH to athletes and coaches
- Consider adequate fluid availability at event
- Pre-race planning of evacuation procedures and nearest medical facilities
- Consider preparing information leaflets on EAH for receiving medical team when transferring patient, as they may not be familiar with this condition
- Online learning resources and congress are available for further advice
- Hypertonic saline should be part of the mandatory medical equipment of health care professional providing care at endurance events

Conclusion

Endurance activities are popular, and participation is growing. Proper hydration is important for performance and avoiding medical problems. Overconsumption of fluids is the main mechanism, in combination with inadequate secretion of the hormone arginine vasopressin, in the development of exercise associated hyponatraemia (EAH). Most cases of EAH are mild but serious complications and deaths have occurred. Intraavenous administration of hypertonic saline solution can be lifesaving in severe cases. Prevention focuses on adopting a hydration strategy where fluids are consumed by drinking to thirst. Educating athletes, coaches and medical personnel about EAH is important.

Conflict of interest

The authors declare no conflict of interest.

Bibliography

Exercise associated hyponatremia in endurance sports: a review with practical recommendations


