Prevention of acute mountain sickness (AMS) with particular emphasis on hydration: a review

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Abstract

Acute mountain sickness (AMS) causes a number of symptoms within the human body, associated with staying at altitudes higher than 2,500 meters above sea level without prior acclimatization. The human body begins to adapt its functioning to the conditions of hypobaric hypoxia in order to maintain homeostasis. Its disturbance can lead to respiratory failure, pulmonary, or cerebral oedema, and, consequently, death. The best method of AMS prevention is slow acclimatization. A high-carbohydrate diet, thermal protection, and pharmacological agents could be listed as additional prevention measures. The development of AMS is influenced by many factors such as ambient temperature, wind speed, altitude, physical preparation of participants, and appropriate protection against adverse effects of these factors. Nevertheless, both dehydration and overhydration may worsen the AMS symptoms. The body’s exposure to altitude and dehydration alone reduces aerobic performance. Appropriate hydration throughout a climb is necessary due to both intense physical exercise and a hypoxic environment.

Keywords: acute mountain sickness, prevention, hydration
Introduction and Methods

Acute mountain sickness (AMS) causes a number of symptoms within the human body, associated with staying at high altitudes without prior acclimatization [1]. Individuals who have climbed to relatively high altitudes in a short time are at a high risk of developing AMS. A high-altitude environment is defined as areas over 1,500 m above sea level. Peaks located from 3,500 m to 5,500 m above sea level are considered to be very high altitudes. Areas located more than 5500 m above sea level are referred to as extreme altitudes and require the most complex preparation [2].

This article is based on the information derived from 30 articles on AMS and the effects of high altitude on the human body with particular emphasis on the impact of hydration on exercise in high-mountain conditions. The articles included both reviews and original experimental papers posted on PubMed and Google Scholar. The analysed articles were published in 2009 – 2022.

Results and Discussion

The risk of developing AMS is increased during mountain climbing in areas located over 2,500 m above sea level. AMS occurs when the climbing pace exceeds the body's ability to adapt to high altitudes. As altitude increases, the ambient pressure decreases, along with the partial pressures of respiratory gases. That includes the partial pressure of oxygen in the unit of inhaled air (while the percentage of oxygen in the respiratory gas mixture is constant). This results in a decrease in the efficiency of gas exchange occurring in the lungs due to diffusion, and, consequently, the value of blood oxygenation (saturation). Less oxygen reaching the body tissues induces hypoxia. The aforementioned mechanism is called hypobaric hypoxia. To adapt to the new environmental conditions and the resulting hypoxia, the human body triggers a hyperventilatory response. As a result, there is a decrease in the partial pressure of CO2 and an increase in the partial pressure of O2 in the blood, leading to the development of respiratory alkalosis. As a result, the haemoglobin dissociation curve shifts to the left, meaning a more durable attachment of oxygen to haemoglobin and less efficient diffusion of oxygen into tissues. At the same time, an increase in 2,3-bisphosphoglycerate (allosteric inhibitor stabilizing the T form, i.e. non-oxygenated haemoglobin and hindering the attachment of O2 to haemoglobin) shifts the haemoglobin dissociation curve to the right, which antagonizes the effects caused by respiratory alkalosis [3, 4, 5, 6, 7, 8].
In addition to hypobaric hypoxia, circulatory hypoxia could be another cause of AMS. It results in a decrease in blood perfusion through tissues and internal organs (e.g. kidneys) [7]. Nevertheless, hypoxia does not significantly affect the kidney function itself, except for minor microalbuminuria. AMS is, therefore, not associated with salt and water retention, or kidney dysfunction [9].

The state of hypoxemia leads to an increase in brain perfusion, an increase in blood volume in the brain, and an increase in the permeability of the blood-brain barrier (this might be caused by hypoxia, oxidative stress, or low-grade inflammation). This results in an increase in brain volume, which hinders the flow of cerebrospinal fluid in the subarachnoid space and leads to fluid retention. Consequently, there is an increase in intracranial pressure. The mechanism is primarily responsible for the main symptom of AMS, i.e. headache, because the pressure on the meninges and large cerebral vessels, which are sensory innervated by the trigeminal nerve, causes the transmission of information to the cerebral cortex about pain [3, 10].

In addition to the speed of climbing and the altitude reached, factors contributing to the AMS progression include low temperature, low humidity, high intensity of solar radiation, extreme physical effort, and individual predispositions [6, 7]. The volume of fluid or medication intake and overall health are also significant [2]. Acute mountain sickness can be mild, moderate, or severe, with the latter leading to death in some cases [11].

The symptoms of AMS are non-specific and rarely occur simultaneously. That is why it is so difficult to notice the onset of the disease. Those symptoms include headache (the main symptom), weakness, fatigue, lightheadedness, dizziness, apathy, gastrointestinal problems (nausea, vomiting, lack of appetite), difficulty sleeping (including the deterioration of the sleep quality), cognitive impairment, mood deterioration, oliguria, heart palpitations, and peripheral oedema [3, 4, 5, 6, 7, 10].

The symptoms of AMS do not tend to appear until after 6-12 hours of climbing. Approximately, the symptoms peak on the 2nd/3rd day of the climb and disappear on the 4th/5th day after the climber returns to the lowlands. Early response to the AMS development signals allows for protecting the individual against the evolvement of high-altitude cerebral and/or pulmonary oedema, which poses a direct threat to health or life [5].

There is also a risk of misdiagnosis of the AMS onset, which can be confused with exhaustion, alcohol intoxication, migraine, dehydration, or hypothermia [5].
There are many measurement scales used to assess the severity of AMS (e.g. Lake Louise Score, AMS-C, Hackett Clinical Score, VAS Scores, Chinese AMS Score) [12]. The Lake Louise Score (LLS) is one of the most common scales used in the diagnosis of acute mountain sickness. Table 1 presents the original version of the LLS. It lists the symptoms that are among the diagnostic criteria for the potential progression of altitude sickness in the patient. If the patient receives more than 3 points, a preliminary diagnosis of AMS can be made. The necessary condition for the diagnosis is the occurrence of a headache as one of the symptoms experienced by the patient [13].

Table 1. The LLS scale created based on self-assessment of the symptoms by the patient; own study based on Altitude pulmonary oedema and high-altitude cerebral oedema in altitude sickness - diagnosis, management, and treatment (Original title: Wysokościowy obrzęk płuc oraz wysokośćowy obrzęk mózgu w chorobie wysokoścórskiej, Siedlecki Z., Grzyb S., Nowacka K., Hagner W.}

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Severity</th>
<th>Points</th>
</tr>
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<tbody>
<tr>
<td><strong>Headache</strong></td>
<td>None at all</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe, incapacitating</td>
<td>3</td>
</tr>
<tr>
<td><strong>Gastrointestinal symptoms</strong></td>
<td>Good appetite</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Poor appetite or nausea</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate nausea or vomiting</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe nausea/vomiting, incapacitating</td>
<td>3</td>
</tr>
<tr>
<td>Fatigue and/or weakness</td>
<td>Not tired or weak</td>
<td>0</td>
</tr>
<tr>
<td>-------------------------</td>
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</tr>
<tr>
<td></td>
<td>Mild</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe, incapacitating</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dizziness/lightheadedness</th>
<th>No dizziness/ lightheadedness</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe, incapacitating</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Difficulty sleeping</th>
<th>Sleep as well as usual</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sleep worse than usual</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Multiple awakenings, night rest ineffective</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Insomnia/Could not sleep at all</td>
<td>3</td>
</tr>
</tbody>
</table>

However, it is worth noting that the Lake Louise Score is based largely on subjective perception and has recently come under heavy criticism due to the excess of false positive results diagnosed based on its criteria [1,4]. A good solution to the problem seems to be a removal of the sleeping difficulties from the score as one of the symptoms indicating the potential development of AMS. According to most researchers, the inability to fall asleep may be related to the impact of hypoxia on the body, and not to the course of acute mountain sickness [1, 5].

Although LLS is the most popular score, it is not the only method to determine the likelihood of developing acute mountain sickness in a patient. For this purpose, a modification of the visual-analogue scale (VAS), among others, which is commonly used in the medical community, turned out to be useful. In this method, the patient is requested to determine the
intensity of specific symptoms of altitude sickness (such as a headache), using a 10-point scale, where 0 means the lack of symptoms, and 10 is the highest imaginable severity of a specific symptom. The results should then be evaluated by a specialist. Although this score, compared to LLS, allows for a more accurate assessment of the severity of specific symptoms, it is largely based on the subjective assessment of both the patient and the doctor, which significantly reduces its practical application. Chinese AMS Score (CAS) is another score used to assess the likelihood of developing acute mountain sickness in a particular patient. It is important to highlight that in the AMS diagnosis, CAS takes into account many symptoms that are omitted in LLS, such as palpitations, shortness of breath, abdominal distension, diarrhoea, constipation, cyanosis of the lips or numbness of the limbs. In addition, headache and vomiting were classified as non-specific symptoms of acute mountain sickness in this score. This is a significant difference compared to LLS, where altitude sickness can be diagnosed after observing a high severity of only these two symptoms. Due to inconsistencies in the above scales, it is reasonable to conduct further research aimed at a deeper understanding of the principles of acute mountain sickness and improving the methods of its diagnosis [12,16].

Correct diagnosis and understanding of the AMS pathophysiology are essential to the implementation of appropriate treatment. However, the prevention of the symptoms is the most important issue.

The most important element of acute mountain sickness prevention is prior acclimatization, i.e. adaptation of the body to the changing conditions. This state is achieved by increasing altitude in a slow and appropriately planned way. With the good health of the climber, the first overnight stop should occur at an altitude of a maximum of 3,000 m above sea level. The next resting location ought to be situated up to 300 m higher than the previous one. After 2-3 days (or 1,000 meters) of climbing, it is also worth introducing at least one all-day rest at the same altitude [2, 11]. A flexible itinerary can be a good precaution, making appropriate modifications to the route plan or extending the necessary rest can be beneficial in terms of protecting the climber's health [17].

Appropriate pharmacological prophylaxis usually contributes to a significant reduction in the time necessary to acclimatize in a high-altitude environment. The drug recommended before climbing high altitudes is acetazolamide [11]. It is usually recommended to take 250 mg of acetazolamide once a day (or 125 mg twice a day) from the first day before climbing for a minimum of 3-5 days [18]. Recent studies, however, suggest that much better effects in the
prevention of acute mountain sickness are achieved by taking 500 mg of acetazolamide per day. As a result of renal carbonic anhydrase inhibition, the drug increases urinary excretion of sodium and potassium ions, as well as bicarbonates, which contributes to hyperchloremic metabolic acidosis. Compensatory mechanisms for acidosis lead to greater stimulation of the respiratory process, resulting in a reduction of resting hypoxemia and improved efficiency in a person at high altitudes [11]. This drug should not be used in people with chronic kidney disease. It should be noted that taking increased doses of acetazolamide may cause drowsiness, paraesthesia, or myopathies. The side effects of the drug also include hand cramps, gastrointestinal problems, dry mouth, rash, or sleeping difficulties [19]. As can be observed, the side effects of acetazolamide are very similar to the symptoms accompanying AMS. Difficulties in getting a good night’s rest do not necessarily have to be a side effect of taking the drug. Studies show that in people living at high altitudes, sleep can consist of unusual dreams and may be interrupted by sudden periods of alertness [20]. In the case of impaired tolerance to acetazolamide, dexamethasone is a good alternative in AMS prevention. A dose of 8 to 16 mg of the drug per day should be taken in divided doses. If climbers have previously had an episode of pulmonary oedema, it is recommended to take nifedipine. It is worth noting that this drug can cause fainting resulting from an excessive decrease in blood pressure. In order to ensure higher protection against the potential risk of pulmonary oedema, it is recommended to take salmeterol in an inhaled form together with nifedipine. However, in this case, possible side effects, such as anxiety, increased heart rate, and muscle tremors should be taken into account [17].

Conquering mountain peaks cannot take place without adequate equipment. Using specialized items often reduces physical load and increases the body’s efficiency, while more efficient preparation for a long-term hike drastically reduces the risk of potential homeostasis disorders. The clothing should be chosen while taking into account the fact that with the increase in altitude, the temperature gradually decreases. However, if the protection from the cold is too extreme, the clothing may cause excessive water and energy loss, contributing to an overall reduction in the body’s efficiency. Appropriate footwear should be tested beforehand so that there are no unnecessary abrasions or wounds, which (due to lower blood oxygenation) heal much slower in high-altitude conditions. As protection against solar radiation, a sun cream with a sun protection factor of at least 50 and glacier glasses ought to be used [17].
In AMS prevention, an adequate diet is also important. It is true that the correct supply of calories can not provide full protection against the disease but it certainly allows for maintaining the correct energy balance during the hike, which contributes to the improvement in physical fitness. A diet rich in carbohydrates and an increase in daily energy supply by about 500 kcal compared to the generally applicable standards will allow for faster acclimatization at high altitudes [21]. Some sources say that supplementation with vitamins A, E, and C for a few days before mountain climbing would be an effective support in the breakdown of free radicals, which tend to accumulate in the body during extreme exercise [22,23].

Adequate physical preparation is of great importance at high altitudes. Preparatory hiking training should begin approximately 4 months before the planned trip. For these preparations, it is recommended to combine circuit training with interval training. Initially, the training is implemented to prepare the respiratory and circulatory systems for greater loads. Another goal of the active preparation should be the increase in strength and muscle mass of the climber. Specialized exercises, containing elements of complex high-altitude climbing, should be performed as the last element of training [17].

In acute mountain sickness prevention, it is also worth taking care of appropriate mental preparation. It is a well-known fact that prolonged hypoxia can contribute to the occurrence of various types of mental disorders, both cognitive and psychotic. Xeno-persecutory attitude, decrease in criticism, anxiety, and positive symptoms are some of the many acute, relenting reactions of the body to staying at high altitudes. It is also worth noting that long-term hypoxia may contribute to the occurrence of high-altitude asthenia, manifested by the impoverishment of short-term memory, reduction of intellectual performance or weakening of eye-hand coordination, among other things. These changes can permanently disrupt the proper functioning of the body. In order to assess the potential risk of the above-mentioned neurological disorders, it is worth seeking psychological and psychiatric expertise before the expedition. It also seems appropriate to perform basic neurological examinations after returning from the high altitude environment in order to quickly detect any kinds of health anomalies [20].
Amount of body water and its distribution can affect the severity of symptoms associated with acute mountain sickness. This is important when assessing the ability to reach a given peak during climbing and safety during the expedition itself.

According to research conducted by E. Ladd and his team, the hydration status was slightly associated with reaching the summit (Denali 6,190 m above sea level). There were no statistically significant differences in hydration between climbers who reached the summit and those who gave up earlier. In both groups of climbers, there were mountaineers with a reduced and normal body amount. Among the ascentionists, 43% developed AMS symptoms, while in the second group, there were 34% of climbers affected. It should be noted that hydration status was assessed by measuring urine specific gravity and the collapsibility of the superior vena cava [24]. In the Hannes Gatterer experiment, it was noticed that the amount of water lost, not the amount of fluid intake, was the differentiating factor for people with AMS(+) and without AMS(-) symptoms. Individuals with higher water retention were more likely to show symptoms of acute mountain sickness and reduced plasma osmolarity was also observed [25]. Another study used the bioelectrical impedance vector analysis (BIVA) method to assess the circadian rhythm of fluids in people in hypobaric hypoxic conditions compared to normoxic conditions. No differences were observed in the experiment. Some individuals developed clinical symptoms of AMS in the first 24 hours after being placed in a hypobaric chamber. An evident decrease in the phase angle (a parameter determining the metabolic level of the cells) was then observed but without a relevant statistical significance. In the further course of the experiment, none of the individuals developed AMS [26]. Giacomo Strapazzon's team also used BIVA measurements and observed the dehydration status of participants with short-term episodes of euhydration. No correlation was observed between BIVA measurements and proBNP concentration. However it was suggested that about 2 litres of fluid per day may be sufficient to maintain hydration homeostasis, but only with minimal physical activity [27]. The amount of water in the body is regulated mostly by the kidneys. Jerôme Biollaz and his team concluded from their experiment that there was no kidney dysfunction or water retention in the course of acute mountain sickness. Fluid balance or urine flow alone did not differ in the group of individuals with AMS symptoms. Only microalbuminuria was detected in both groups. An increase in the concentration of epinephrine, noradrenaline, atrial natriuretic factor, and vasopressin was noted, while the activity of renin, angiotensin, and aldosterone decreased. The concentration of circulating hormones did not differ between those with and without AMS [9]. Alan Richardson studied the changes in the concentration of hormones affecting water and
electrolyte balance in a state of optimal hydration and dehydration and in hypoxic conditions. The results showed that the amount of antidiuretic hormone and aldosterone increased during the study, but did not differ between attempts with different levels of hydration. In his study, no change in the concentration of vestibular natriuretic peptide was observed [28].

It was also shown that dehydration and overhydration may exacerbate the symptoms of AMS as heart rate also changed. With reduced fluid intake, there was an increase in cardiac contractions to compensate for the decrease in ventricular end-diastolic volume. Attention was paid to the body temperature changes and, compared to the state of normal hydration and overhydration, it was lower only in the case of the latter. Such a relationship was noted in the case of conditions of insufficient oxygen supply. Initially, an insufficient amount of water in the body caused worse symptoms, but from the 60th minute of the test onwards, the participants of the experiment showing overhydration reported a worsening headache. It is believed that this may have been caused by an increase in intracellular fluid and swelling of the brain cells. One of the most important factors in the Lake Louise AMS scoring system indicating an increase in symptom severity is headache. It occurred much more often in dehydrated or overhydrated individuals. No difference in ventilation between hydration conditions was noticed. It was found that maintaining the specific gravity of urine < 1.015 g/l and its osmolarity < 400 mOsm·kg⁻¹ together with regular fluid intake in small amounts may reduce the physiological load on the body under hypoxia conditions [29].

High-altitude climbing requires great physical endurance. Hypoxia prevailing at high altitudes causes a decrease in the aerobic and anaerobic capacity of skeletal muscles [7]. Exposure to altitude and dehydration reduces the efficiency of aerobic exercises. These are additive values. Dehydration during heavy physical activity promoted an increase in the incidence and severity of AMS, but not statistically significant [30]. Appropriate hydration during physical exercise is important to prevent an increase in physiological load and reduce the likelihood of headache, fatigue, or nausea [28].

However, an appropriate amount of fluid intake is necessary during high-altitude expeditions to prevent the progression of acute mountain sickness. Weather conditions, physical activity, and planned peak altitude should be taken into account when it comes to the amount of water consumed.
Acute mountain sickness does not have its own pathognomonic symptoms leading to great difficulty in differentiating this condition from others. Diagnosis is based primarily on the physical examination. Symptoms such as headaches, balance disorders, or fatigue are subjective. A decrease in saturation does not always coexist with AMS symptoms. Ultrasound examination may show fluid accumulation in the lungs, but then it already indicates pulmonary oedema. Fatigue can be a result of the physical activity necessary to reach a given altitude. Disorders of the digestive system can be the result of, for example, poisoning, and not an AMS symptom. As mentioned, the inability to fall asleep can be caused by the effect of hypoxia on the body. There are no pathognomonic objective symptoms of AMS development. Hence it can be concluded that a large portion of patients is diagnosed with false positives.

A large discrepancy in the methodology of the experiments that combined the subject of the body’s hydration level and the occurrence of the AMS symptoms can be observed. Hydration monitoring was not standardized. The study by E. Ladd examined the incidence of superior vena cava and the specific gravity of urine, while IB Regli and Giacomo Strapazzon used the BIVA (bioelectrical impedance vector analysis) method [24, 26, 27]. The conditions of the experiments carried out should also be noted. In the study where the difference in fluid retention was presented the amount of water intake and diets were unlimited, but in another study they were controlled. Other researchers have measured the concentration of the hormones affecting water and electrolyte balance in the blood. The conclusions about aldosterone levels were different: one study showed a decrease and the other reported an increase [9, 28].

Differences in conclusions among the available studies may result from different methodologies or conditions in which the experiments were carried out (different FiO2 of oxygen for different altitudes, temperatures, and air humidity). Some participants were placed in specially designed chambers, others were transported to the appropriate altitude by helicopter, or the research was conducted after the active ascent. The time in which the participants stayed under given conditions and physical activity also differed.

Conclusions

Acute mountain sickness is a real problem for participants and organizers of mountain climbing. Symptoms are non-specific and subjective. To prevent their occurrence, appropriate acclimatization, physical preparation, suitable clothing, and pharmacological agents are essential. Studies do not clearly indicate that excessive fluid intake protects expedition
participants from the progression of AMS symptoms. However, in order to maintain body homeostasis during climbing, adequate hydration is essential due to the high physical effort and reduced partial pressure of oxygen.

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**Bibliography:**


