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## Prevention and treatment of high altitude cerebral edema (HACE)

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### Summary:

High altitude cerebral edema (HACE) is often a severe and potentially fatal manifestation of acute mountain sickness (AMS). It usually develops within the first 2 in individuals rapidly ascending at altitudes above 4000 m. The main cause of HACE is hypoxia, because of reduced oxygen level at high altitude.

The aim of this study was to assess the methods of prevention and treatment of high altitude cerebral edema (HACE). Our study material consisted of publications, which were found in PubMed, ResearchGate and Google Scholar databases. The first step was to find proper publications from the last 30 years. The second step was to carry out an overview of the found publications.

Methods of prevention of acute mountain sickness are highly effective in high altitude cerebral edema prevention. Many studies established the role of gradual ascent and staged ascent as well as administration of acetazolamide and dexamethasone in AMS prevention, and therefore in HACE prevention. Methods of treatments of acute mountain sickness are highly effective in high altitude cerebral edema treatment. Several researches proved the role of descent, administration of acetazolamide and dexamethasone, oxygen therapy as well as use of portable hyperbaric chamber in AMS treatment, and therefore in HACE treatment. However HACE treatment requires greater descent and larger doses of dexamethasone. Also duration of recovery is longer.

**Key words:** high altitude cerebral edema, HACE, prevention, treatment

## **INTRODUCTION AND PURPOSE**

High altitude cerebral edema (HACE) is often a severe and potentially fatal manifestation of acute mountain sickness (AMS). HACE has relatively lower incidence rate than AMS and is normally preceded by symptoms of AMS. It usually develops within the first 2 in individuals rapidly ascending at altitudes above 4000 m [1]. The neurological features of HACE are characterized by neurological disorders of varying degree: disturbance of consciousness, ataxia, papilledema, urinary retention or incontinence, abnormal plantar reflexes, pupil difference, visual field loss, speech difficulty and hearing loss [2]. Early recognition of symptoms of HACE is essential, because this condition may rapidly progress to death [1].

The main cause of HACE is hypoxia, because of reduced oxygen level at high altitude. Hypoxia leads to cerebral vasodilatation, that effects increased both cerebral blood flow and cerebral blood volume. This process causes cerebral capillary hypertension, that results in increased capillary permeability and therefore capillary leakage. Hypoxia also induces synthesis of vascular endothelial growth factor, bradykinin, histamine, arachidonic acid, oxygen free radicals and nitric oxide. These biochemical factors lead to altered permeability of the blood-brain barrier, that effects fluid penetration. This processes result in increased intracranial pressure and therefore cerebral edema [2].

The aim of this study was to assess the methods of prevention and treatment of high altitude cerebral edema (HACE). Our study material consisted of publications, which were found in PubMed, ResearchGate and Google Scholar databases. In order to find the proper publications, the search has been conducted with the use of a combination of key words like: "high altitude cerebral edema", "HACE", "prevention", "treatment". The first step was to find proper publications from the last 30 years .The second step was to carry out an overview of the found publications.

## **DESCRIPTION OF THE STATE OF KNOWLEDGE**

### **Prevention**

None of the studies have prospectively examined the efficacy of methods of prevention of high altitude cerebral edema, and therefore further research is needed. However many researches that have assessed prospectively different methods of prevention of acute mountain sickness, revealed their effectiveness in HACE prevention. Therefore it is reasonable to use them due to similar pathophysiology of AMS and HACE [2,3]. Bloch et al.,

Beidleman et al. and Baggish et al. proved that gradual ascent and staged ascent are highly effective in preventing of acute mountain sickness [4,5,6]. Forward et al., van Patot et al., Gertsch et al., Basnyat et al. (2011) and Basnyat et al. (2011) in their researches established a role of acetazolamide in prevention of acute mountain sickness [7,8,9,10,11]. Johnson et al., Ellsworth et al. (1987), Ellsworth et al. (1991) and Maggiorini et al. proved the effectiveness of administration of dexamethasone in AMS prevention [12,13,14,15].

Gradual ascent and staged ascent remain the most effective methods of prevention of high altitude cerebral edema. Individuals travelling above 3000 m should not increase their sleeping elevation by more than 500 m/day and should include a rest day (ie, no ascent to higher sleeping elevation) every 3 to 4 days. The recommended adult dose of acetazolamide for HACE prevention is 125 mg every 12 h. The pediatric dose is 2.5 mg/kg/dose (maximum 125 mg/dose) every 12 h. The recommended adult dose of dexamethasone for HACE prevention are 2 mg every 6 h or 4 mg every 12 h. Very high doses (4 mg every 6 h) may be considered in very high-risk situations, such as military or search and rescue personnel being airlifted to altitudes >3500 m with immediate performance of physical activity, but should not be used except in these limited circumstances Dexamethasone should not be used for prophylaxis in pediatric patients [3].

## **Treatment**

None of the studies have prospectively examined the efficacy of methods of treatment of high altitude cerebral edema, and therefore further research is needed. However many researches that have assessed prospectively different methods of treatment of acute mountain sickness, revealed their effectiveness in HACE treatment. Therefore it is reasonable to use them due to similar pathophysiology of AMS and HACE [2,3]. Bärtsch et al., Hackett et al. (2001), Hackett et al. (2004) and Imray et al. proved that descent is the primary method of AMS treatment [1,2,16,17]. Ferazzini et al., Hackett et al. (1988), Hackett et al. (2004), Levine et al., Wright et al. and Keller et al. established the role of dexamethasone in AMS treatment [2,18,19,20,21,22]. Pollard et al. reported the use of dexamethasone in treatment AMS in pediatric patients [23]. Grissom et al. showed the role of acetazolamide in AMS treatment [24]. Freeman et al., Austin and Zafren reported the use of portable hyperbaric chambers in the treatment of high altitude cerebral edema [25,26,27].

Before initiating treatment of high altitude cerebral edema, consideration should be given to other causes of symptoms resemble to HACE [3]. Differential diagnosis shall include: carbon monoxide poisoning, dehydration, exhaustion, hypoglycemia, hypothermia, and

hyponatremia [2]. If HACE is suspected or diagnosed, dexamethasone with acetazolamide should be administered, oxygen therapy should be started and descent to lower elevation should be initiated. Individuals should try to descend at least 1000 m or until symptoms resolve. The recommended adult dose of acetazolamide for HACE treatment is 250 mg every 12 h. The pediatric dose is 2.5 mg/kg/dose (maximum 125 mg/dose) every 12 h. The recommended adult dose of dexamethasone for HACE treatment is 8 mg once, then 4 mg every 6 h. The pediatric dose is 0,15 mg/kg/dose (maximum 4 mg/dose) every 6 h. Oxygen should be delivered by nasal cannula or mask at flow rates sufficient to achieve an SpO<sub>2</sub> >90%. If descent is infeasible or delayed, oxygen therapy should be continued or the individual should be placed in a portable hyperbaric chamber [3].

## **CONCLUSIONS**

1. Methods of prevention of acute mountain sickness are highly effective in high altitude cerebral edema prevention.
2. Many studies established the role of gradual ascent and staged ascent as well as administration of acetazolamide and dexamethasone in AMS prevention, and therefore in HACE prevention.
3. Methods of treatments of acute mountain sickness are highly effective in high altitude cerebral edema treatment.
4. Several researches proved the role of descent, administration of acetazolamide and dexamethasone, oxygen therapy as well as use of portable hyperbaric chamber in AMS treatment, and therefore in HACE treatment.
5. However HACE treatment requires greater descent and larger doses of dexamethasone. Also duration of recovery is longer.

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