

## **The prevention of acute mountain sickness – the effect of theophylline and acetazolamide in prevention of acute mountain sickness**

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### **Background and aim of the study**

The acute mountain sickness (AMS) has an incidence of 40 to 60 % in all subjects travelling to an altitude higher than approximately 2500 m, depending on the speed of the ascent [1]. The symptoms are headache, gastrointestinal disturbances, dizziness and sleepiness.

The main factor to develop acute mountain sickness is the exposure to hypobaric hypoxia. This leads to an increase of the intracranial pressure accompanied by a hydrostatic cerebral oedema. The exact pathophysiology remains nevertheless unclear [2].

Various controlled studies have shown, that the application of acetazolamide in dosages of 500 mg / die prevents the development of acute mountain sickness. The mechanism of action is the increase of ventilation (as a reaction to the induced metabolic acidosis). New data have shown, that the drug theophylline is able to prevent symptoms of acute mountain sickness at a comparatively low dose [3].

The aim of our recent project on the Jungfraujoch is the comparison of the effectiveness of theophylline and acetazolamide in the prevention of acute mountain sickness, leading to a better understanding of the pathophysiology of AMS and a contribution to the therapeutic possibilities.

The following hypotheses shall be proven:

1. Theophylline (500 mg/die orally as retarded preparation) is as effective as acetazolamide (500 mg/die orally) in the prevention of AMS (according to the symptom score) compared to placebo in subjects exposed to an altitude of 3554 m.
2. The average oxygen saturation during acute exposure to 3554 m is significantly higher using acetazolamide or theophylline compared to placebo.
3. Acetazolamide and theophylline improve both the development of high altitude related sleep disorders.

### **Importance of the project**

The aim of the study is to show that the oral application of retarded theophylline in a daily dose of 500 mg (plasma level ~ 5mg/dl) is as effective as the application of 500 mg of acetazolamide concerning the prevention of AMS. Furthermore, the study contributes to the understanding of height-dependent change of sleeping pattern [4].

With theophylline being effective in this comparison study, travellers will have a good alternative to acetazolamide with low side effects in case they have to travel acutely above a height of 3000 m. This would be an advantage especially for patients with accompanying pulmonary diseases as the prevention with the acetazolamide (an antagonist of the enzyme carboanhydrase) is not favourable because of the occurring metabolic acidosis with an increase of respiratory effort.

### **Measurements and examinations**

The incidence of AMS is increased by fast ascent to high altitude and accompanying heavy exercise. This was simulated by the rail ascent to the Jungfrauoch (3580 m) and then physical exercise with an ascent to the Mönchsloch hut. AMS was prevented either by theophylline or acetazolamide (versus placebo), each 500 mg/die, starting three days before the arrival on the Jungfrauoch.

The study-duration was three days per person and a total of 36 volunteers were tested in a double-blind, randomised and placebo-controlled method.

From the first evening on the Jungfrauoch (2-3 h after arrival on 3580 m) the following tests have been carried out for the following three days:

- AMS-symptom-score (18.00, 8.00, 12.00)
- Blood gases: pO<sub>2</sub>, pCO<sub>2</sub>, pH (18.00, 8.00)
- Oxygen saturation (18.00, 8.00, 12.00)
- Pulse rate (18.00, 8.00, 12.00)
- Blood pressure (18.00, 8.00, 12.00)
- Blood samples (18.00, 8.00)

On both nights we performed full polysomnographic measurements with electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), electrocardiogram (ECG) and oxygen saturation. Furthermore we documented episodes of snoring, thorax and abdominal movements, airflow on nose and mouth and periodic leg movements.

### **Expected results:**

As shown in a previous study, theophylline is effective in prevention of acute mountain sickness. This study will show the effectiveness of theophylline compared to the "gold standard" acetazolamide.

The study was completed in December 2000. Due to the very time consuming manual analysis of more than 70 polysomnographic measurements, the results of the study are not yet available. But the next report of the International Foundation HFSJG will certainly include the main results of this study.

References:

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