

Acetazolamide and sulfa allergy: how to deal with sulfa allergy at altitude?

To the Editor Each year millions of people travel to high-altitude regions all over the world – the Himalayas in Asia, Alps in Europe, Rockies in the United States, and Andes in South America. It is more and more common to climb a few-thousand peaks in search of adventure. An increase in the number of tourists visiting high-altitude regions gives a false impression that mountain climbing is much easier than it really is. It is very common, especially in the Himalayas, that people who travel to high-altitude regions have no altitude experience. In this letter, I would like to report the cases of 2 patients who were seen at the Himalayan Rescue Association (HRA) Clinic in Manang, which lies at an altitude of 3500 m in the Annapurna region of Nepal. Both patients had a history of sulfa allergy and had travelled to high-altitude areas for the first time.

The first patient was a middle-aged woman with a history of hyperparathyroidism, diet-controlled diabetes, and allergy to sulfonamide. She was seen at the HRA Clinic in the late afternoon with the symptoms of acute mountain sickness. The patient complained of headache, dizziness, and significant weakness. She did not have any altitude experience before. A physical examination revealed no pathological findings, except for significant weakness. She was able to sit and walk but with support. She was in poor general state but she was conscious and logically answered the questions. Saturation was 96%; there were no dehydration signs; the Glasgow Coma Scale (GCS) score was 15/15. During history taking, she reported that on the same day she had climbed from Manang (3500 m) to Yak Kharka (4000 m). During the ascent, she experienced a mild headache, which persisted until Yak Kharka but later resolved after paracetamol use. She then started to feel dizzy and unstable to walk. Because of sulfa allergy in history, she did not take acetazolamide. She decided to descend to Manang to the HRA Clinic.

The other patient, a 22-year-old woman without any history of disease and drug use but with a history of sulfa allergy, was seen at the HRA Clinic in Manang with symptoms of acute mountain sickness. The patient complained of headache

and significant weakness. She did not have any previous altitude experience. A physical examination revealed no pathological findings, except for significant weakness. She was conscious and logically answered the questions. Saturation was 91% and the heart rate was 91 beats/min; there were no signs of dehydration; the GCS score was 15/15. The Lake Louise scale score was 4 points (weakness, 2 points; headache, 2 points). After a more detailed history taking, the patient reported that on the same day she had climbed from Tilicho Base Camp (4100 m) to Tilicho Lake (4900 m). During the climb, she developed a headache but she continued to ascend. Then, headache increased to 3 points in the Lake Louise scale score and new symptoms developed: dizziness, weakness, nausea, dyspnea, and tachycardia. The patient decided to descend to Tilicho Base Camp (it took 2.5 h), where she was waiting 1.5 h for horses to descend. Given a history of sulfa allergy, she did not take acetazolamide but 4 mg of dexamethasone. Her condition improved. In the afternoon, she got to the HRA Clinic.

During their stay at the HRA Manang Clinic, both patients were closely observed, no drugs were administered, and after a few hours, they were discharged and remained under the care of their friends.

Sulfa allergy complicates pharmacological prophylaxis or treatment of acute mountain sickness.¹ In patients with a history of anaphylaxis to sulfonamide, acetazolamide is contraindicated.¹ Our patients knew about their allergy, which is particularly important while travelling into remote areas with limited access to medical services, such as the Himalayas.

A rapid ascent to altitudes above 2500 m is associated with a risk of developing different types of altitude illnesses including acute mountain sickness, high-altitude cerebral edema, or high-altitude pulmonary edema.¹ It is possible to avoid these conditions by proper acclimatization. A gradual and slow ascent is of vital importance. It is typically recommended to increase the sleeping elevation not more than 500 m per day over 3000 m.³ Every 3 to 4 days, a 1-day rest should be considered.¹ In planning the rate of the ascent, the altitude at which someone sleeps

is considered more important than the altitude reached during the waking hours.¹ Both our patients had had a good acclimatization schedule before they reached Manang and, as recommended, they took a day rest in a village at an altitude of 3500 m. However, it was risky to climb from Manang (3500 m) to Tilicho Base Camp (4100 m) because of the altitude difference exceeding 500 m. In addition to a gradual ascent, prophylactic medications should be considered for use in moderate-to-high risk factors of acute mountain sickness, such as very rapid ascent, history of mountain sickness during the climb above 2500 to 2800 m on 1 day, or an increase in sleeping elevation of more than 500 m above 3000 m.¹ The recommended prophylactic dose of acetazolamide for adults is 125 mg twice daily.¹ However, this does not concern individuals with sulfa allergy. If these individuals are at a moderate or high risk of mountain sickness and if there is any likelihood of hypersensitivity reactions to acetazolamide, they may use dexamethasone instead.^{1,3} Usually, it is started on the day of ascent and used at a dose of 2 mg every 6 hours or 4 mg every 12 hours. Dexamethasone should not be used longer than 10 days because of adrenal gland suppression.¹ Individuals who reach the target altitude and stay there for several days may stop prophylaxis after 2 to 3 days.^{1,3} Medication use should also be stopped when a descent is started.^{1,3} However, it should be remembered that drugs cannot be used as a substitute for physiological acclimatization.

Before they reached Manang, both patients had relaxed their climbing schedules and gained altitude at a slower rate. However, as they climbed higher, problems began to arise. They ignored the first symptoms of the disease, which led to the worsening of their general state. The symptoms of acute mountain sickness developed within hours. Although both patients were well acclimatized at the initial height (Manang, 3500 m) and they did not experience any symptoms, a further climb was devastating. One of the patients took dexamethasone and started to descend when she developed symptoms of acute mountain sickness. Of note, none of the patients had any previous altitude experience but they knew not to take acetazolamide because of the allergy. However, in this situation, they should have followed more rigorous rules of acclimatization. Normally, it is recommended to increase the sleeping elevation by less than 500 m but some reports even suggested less than 300 m for good acclimatization.^{2,4}

A gradual ascent can be an alternative. Before ascending to the target altitude, it is suggested to stay for several nights at an intermediate height. For example, if a person is planning a prolonged trek at 3000 m to 4300 m, he or she should acclimatize at 1800 m to 2500 m 2 to 4 days earlier.⁵

To summarize, sulfa allergy may be a problem especially in those who are not aware of their allergy and travel to remote areas. As these cases illustrate, people with allergy to sulfonamide

in history and contraindication to acetazolamide use who travel to high-altitude regions should pay special attention to staged ascent and the first symptoms of mountain sickness. For safety reasons, it is strongly recommended to follow the rules of proper acclimatization and not to ignore the first signs of acute mountain sickness. Individuals with sulfa allergy should consider to gain altitude at a rate not exceeding 300 m every 24 hours. It may prolong acclimatization time, which may be difficult to accept when trekking time is limited. When travelling to high mountains, it is necessary to have a time margin to avoid pushing oneself to reach the peak despite the presence of symptoms. Further climbing is strictly prohibited when the first symptoms of the disease appear. People with known hypersensitivity to sulfa drugs and no altitude experience should choose mountains of moderate height for their first trek or consider staying at moderate altitude for several nights before climbing a few-thousand peak. It is suggested for such individuals to have dexamethasone in their first aid kit. A medical consultation is strongly recommended a few months before travelling to mountainous regions.

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Author name and affiliation Marta Kurdziel (Himalayan Rescue Association, Manang Clinic, Manang, Nepal; Department of Cardiology, Silesian Center for Heart Diseases, Katowice, Poland).

Correspondence to: Marta Kurdziel, MD, Śląskie Centrum Chorób Serca, Oddział Chorób Serca i Naczyń, ul. M. Curie-Skłodowskiej 9, 41-800 Zabrze, Poland, phone: +48-32-273-26-81, fax: +48-32-373-38-19, e-mail: kurdzielmarta@gmail.com.

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