

CASE REPORT

Drug-induced hypoglycemia presenting as acute mountain sickness, after mistaking acetohexamide for acetazolamide

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Acute mountain sickness (AMS) can present with a wide variety of symptoms in unacclimatized persons who rapidly ascend to altitudes >2500 m. The clinical manifestations of drug-induced hypoglycemia, including adrenergic and neurologic symptoms, have significant overlap with the AMS symptom complex. These similarities can lead to confusion in the diagnosis of hypoglycemia versus AMS, particularly for diabetics ascending to altitude. A case is described in which the oral hypoglycemic agent acetohexamide, instead of acetazolamide, was mistakenly self-administered for the prophylaxis and treatment of altitude illness. Improper self-medication by travelers in remote areas may be more common than is currently recognized.

Key words: high altitude, hypoglycemia, AMS, mountain sickness, acetohexamide, acetazolamide, oral hypoglycemic agents

Introduction

Acute mountain sickness (AMS), resulting from rapid ascent of unacclimatized persons to 2500 m or higher, can present with a wide variety of symptoms including headache, anorexia, nausea, malaise, dizziness and lassitude, [1–3]. Acetazolamide has been shown to be effective in the prevention [2–5] and treatment of AMS [6,7].

The clinical manifestations of drug-induced hypoglycemia also vary widely. As serum glucose levels fall, prodromal sympathomimetic symptoms including diaphoresis, tremulousness, tachycardia, weakness, coolness of the skin, hunger, and anxiety occur. Later, neurologic symptoms of prolonged central nervous system (CNS) glucose deprivation develop, including headache, nausea, confusion, memory loss, visual disturbances, and uncoordination [8].

There is obvious overlap of symptoms between AMS and hypoglycemia. In the most advanced cases, each may result in seizure, coma, and death. This report presents a case in which the oral hypoglycemic agent acetohexamide was mistakenly administered instead of acetazolamide for the prophylaxis and treatment of AMS during ascent; resulting in symptoms common to both drug-induced hypoglycemia and AMS. Iatrogenic problems resulting from the incorrect use of medications by travelers in remote areas may be more common than currently recognized.

Case report

A previously healthy 37-year-old physician filled several prescriptions in Guam for travel-related medications while en route to Nepal. The physician–patient flew to Kathmandu (elevation

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1400 m) and stayed 3 nights while finalizing logistics for her trek to the Mount Everest region. Six years earlier she had trekked to 5400 m in the same area and experienced mild AMS. The evening prior to her flight from Kathmandu to Lukla (2900 m), she began a 250-mg oral prophylactic course of what she thought was acetazolamide (Diamox, Lederle, Wayne, NJ). In fact, she self-administered acetohehexamide (250 mg). The pill bottle was labeled acetohehexamide, which she had been informed, incorrectly, by the pharmacist was the generic form of Diamox.

During the following 5 days, the patient gradually ascended by foot to 4300 m, continuing daily 250-mg doses of acetohehexamide at bedtime. On the second day of ascent, the patient experienced mild headache after arriving at 3500 m and this was resolved by the following morning. During further ascent, the patient experienced lightheadedness, tremulousness, tachycardia, hunger, and weakness. These symptoms were more pronounced at night and the patient attributed them to AMS. She continued her ascent as symptoms resolved each day after the morning meal. On day 5 she arrived at 4300 m and experienced progressively worse symptoms over two consecutive nights. These began 2 hours after she took her usual bedtime dose of acetohehexamide. The additional symptoms included severe headache, pronounced fatigue, anxiety, and nausea. In an effort to treat worsening symptoms of suspected AMS, she added promethazine with codeine and ibuprofen to her evening acetohehexamide. Further ascent was avoided. She noticed that the symptoms resolved markedly after the morning meal, and food intake was maintained throughout the day.

On day 7, the author, who was staffing a nearby clinic, was consulted. The patient complained of a very difficult night (Lake Louise AMS symptoms score 13 of 18 [9]). All symptoms resolved after eating breakfast that morning. The patient denied any chronic medical problems or use of other medications. Physical examination was unremarkable; pulse was 68 and regular, respirations were 16. The patient was discovered to be taking acetohehexamide, an oral hypoglycemic agent, and not acetazolamide.

The suspected diagnosis was drug-induced hypoglycemia with possible concurrent AMS. The acetohehexamide was discontinued and all recurrent nocturnal symptoms resolved by the second evening after the drug was discontinued.

Discussion

The physician–patient experienced symptoms of hypoglycemia while unknowingly treating herself with an oral hypoglycemic agent for suspected AMS. The symptom complex of AMS and hypoglycemia have significant overlap. Because she believed the drug was acetazolamide, and suspected AMS, she continued to take the drug despite worsening symptoms of hypoglycemia. The patient's actual blood glucose level was not documented because of a lack of equipment. Because the level of blood glucose does not correlate well with the substrate requirement of the CNS and symptoms of hypoglycemia [10], determination of blood glucose level in this patient may not have contributed to the diagnosis.

Acetohehexamide is a first-generation sulfonylurea. This class of drugs stimulates the release of insulin from the pancreas and these agents are commonly used to treat mild diabetes mellitus. The usual dose of acetohehexamide in diabetics is 250 to 1500 mg per day. The duration of action is from 12 to 24 h, with maximal activity reached within 3 h. Such longer-acting agents in particular have a well-recognized risk of hypoglycemic episodes that may be severe and prolonged, lasting as long as several days. The hypoglycemic effect of these agents is potentiated by concomitant use of numerous drugs, including salicylates, phenylbutazone, sulfonamides, and alcohol. These are commonly ingested at altitude [11].

The patient incorrectly attributed her symptoms to AMS and continued self-treatment. Her initial symptom of headache, that resolved before further ascent, was suggestive of AMS secondary to rapid ascent. However, her later symptoms of tremulousness, sweating, tachycardia, hunger, and weakness were consistent with the early adrenergic response to drug-induced hypoglycemia. With continued use of the oral hypoglycemic agent acetohexamide, additional symptomatology developed that was suggestive of CNS glucose deprivation. It is unlikely that hypoglycemia would have occurred without the acetohexamide, since fasting blood glucose is reported to increase during acclimatization at 4000 m [12].

It was unlikely that the patient's progression to moderate neurological dysfunction, including severe headache, fatigue, anxiety, and nausea, was caused by AMS. In the context of a recent increase in altitude, the patient's initial Lake Louise AMS symptom score suggested significant altitude illness. However, this scoring system lacks specificity. Her combined symptoms were consistent with hypoglycemia, but less consistent with AMS. Tremulousness, hunger, and the relief of symptoms after eating are not symptoms of AMS. The remarkable presentation of symptoms 2 h after ingesting acetohexamide during a fasting state, and the improvement each morning with breakfast, is a strong indication for drug-induced hypoglycemia. Additionally, all symptoms resolved by the second night following discontinuation of the hypoglycemic agent.

Paresthesia of the lips and fingers, and increased urinary frequency are commonly reported side effects of acetazolamide but are not found to occur with acetohexamide or as symptoms of hypoglycemia. In double-blind controlled trials the side effects of acetazolamide enabled subjects to identify the drug and a nonblind bias [2,5] was introduced. The absence of these common side effects might create suspicion that the self-administered drug was not acetazolamide.

Acetohexamide and acetazolamide have several potentially confusing elements. Both are sulfa drugs with similar generic names and dosage schedules and both are available as white ovoid tablets in preparations of 250 and 500 mg. In this case, both the pharmacist and physician-patient were aware of the product name, Diamox, but unfamiliar with the generic names acetohexamide and acetazolamide. The routine use of both generic and product names for drugs interchangeably by physicians, pharmacists, and patients may contribute directly to prescribing errors.

Known diabetics on hypoglycemic medications who ascend to altitude may face additional risks resulting from the potential confusion of AMS and drug-induced hypoglycemia. First, as in this case, diabetics on hypoglycemic agents who are actually experiencing a hypoglycemia episode could incorrectly attribute their symptoms to AMS and improperly continue their hypoglycemic agent, thereby worsening their condition. Second, it has been reported that insulin-dependent diabetics are at increased risk of death from diabetic ketoacidosis while at altitude [13]. The potential difficulty in distinguishing hypoglycemia from AMS could falsely lead insulin-dependent diabetics, who are actually suffering from AMS, to withhold necessary insulin—resulting in diabetic ketoacidosis or other complications. Additionally, insulin has decreased potency after freezing and subfreezing temperatures are commonly encountered at high altitudes.

This case illustrates the potential for iatrogenic problems with the use of medications promoted and made available for self-treatment in remote areas. Prescription medications, including acetazolamide, are commonly carried by trekkers in Nepal. Increased familiarity with the medications prescribed or carried and the illnesses likely to be encountered may minimize similar incidents among both physicians and nonphysicians. Strict use of generic names, except when clinically significant differences are known between products, may minimize prescribing errors. The importance of using simple, safe, and effective interventions when available, is

emphasized. Had descent been selected over continued chemotherapy for suspected worsening AMS, this situation could have been averted early.

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