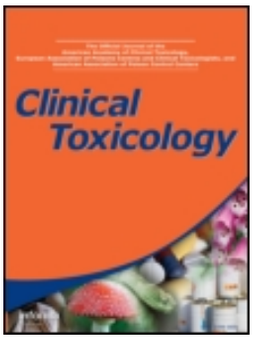

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CASE REPORT

Myoclonic jerks due to acute bromovalerylurea intoxication

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Background. Bromides are still sold as sedatives, antitussives, and anticonvulsants in many countries. Bromovalerylurea is a bromide-containing sedative-hypnotic that is occasionally combined with non-steroidal anti-inflammatory drugs in over-the-counter products. Chronic intake of excessive bromovalerylurea can produce bromide intoxication, but acute bromovalerylurea intoxication presenting with myoclonic jerks has never been described. *Case report*. A 23-year-old woman was brought to our emergency department with unusual drowsiness. Her physical examination was normal except for frequent myoclonic jerks in all extremities that could be triggered by moving the patient or by noxious stimuli. Initial blood tests results were normal; the serum bromide concentration was 81.0 mg/L (reference <10 mg/L). Treatment with intravenous normal saline and furosemide resulted in gradual improvement in her drowsiness and myoclonic jerks. By the second hospital day, she was normal. A brain magnetic resonance imaging (MRI) was normal. At a 2-month follow-up visit, the patient had no neurological sequelae. *Discussion*. Chronic bromide intoxication caused by long-term abuse of bromovalerylurea may present as psychiatric or neurologic abnormalities. Our case of acute bromovalerylurea intoxication presented with severe myoclonic jerks and lethargy. The serum bromide concentration was similar to the reported concentrations in acute bromide intoxications. Treatment with normal saline and diuretics results in increased clearance of bromide and an improvement in clinical effects. *Conclusion*. Myoclonic jerks may be one of the major presentations of acute bromovalerylurea intoxication. Physicians should consider bromide intoxication in the differential diagnosis of the causes of myoclonic jerks.

Keywords Bromide; Bromovalerylurea; Myoclonic jerks; Myoclonus

Introduction

Bromides have traditionally been used as sedatives and are still available as sedatives, antitussives, and anticonvulsants in many countries. Many prescription and non-prescription preparations also contain bromide (1). In the past, bromide intoxications were comparatively frequent but now are rarely encountered in emergency departments (EDs).

Bromovalerylurea is a mild bromide-containing sedative and tranquilizer, which has been used as a non-barbiturate hypnotic and is sometimes combined with non-steroidal anti-inflammatory drugs (NSAIDs) in over-the-counter products. Chronic intake of excessive bromovalerylurea can produce bromide intoxication (bromism) with protean neurological, psychiatric, and dermatological manifestations (2–4). Although some cases of chronic bromovalerylurea intoxications have been published, acute bromovalerylurea intoxications have only been reported in two Japanese journals (5,6). However, in these two cases myoclonic jerks were not reported as a clinical finding. We report a patient who experienced severe myoclonic jerks following acute bromovalerylurea intoxication.

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Case report

A 23-year-old woman was brought to our ED by her family because of unusual drowsiness. She had been well before this incident and had no history of drug abuse. On arrival, she was drowsy but responsive to verbal communication. Her vital signs were as follows: blood pressure, 114/52 mmHg; pulse rate, 84 beats/minute; respiratory rate, 9 breaths/minute; and body temperature, 36°C. Except for frequent myoclonic jerks in her four extremities, the rest of her physical and neurological examination results were normal. The myoclonic jerks occurred many times every several minutes and could be triggered by moving the patient or by noxious stimuli. Between the intervals of myoclonic jerks, there were no abnormal neurological expressions. The patient's serum electrolytes were measured using ion-selective electrodes and were as follows: sodium, 140 mmol/L; potassium, 3.3 mmol/L; chloride, 111 mmol/L; and total calcium, 2.4 mmol/L (9.62 mg/dL) (2.2–2.5 mmol/L, 8.1210 mg/dL). Analysis of

arterial blood gas with oxygen mask supplement yielded the following values: pH, 7.39; HCO_3, 21.6 mEq/L; PaO_2, 195.7 mmHg; and $PaCO_2$, 36.5 mmHg. The anion gap (sodium–chloride–bicarbonate) was 7.4 mEq/L (140–111–21.6). The complete blood count and liver and renal function tests were within normal limits.

The patient's family found several packages (Mylest; Sato Pharmaceutical Co., Ltd, Hsinchu County, Taiwan) that contained bromovalerylurea (100 mg per tablet) alongside her. Acute bromide intoxication caused by bromovalerylurea overdose was highly suspected. Immediately upon arrival at the ED, the patient underwent emergent gastric lavage with normal saline followed by activated charcoal administered through a nasogastric tube. The patient's serum bromide concentration was determined by colorimetry to be 81.0 mg/L (1.0 mEq/L) (reference <10 mg/L).

After the patient was admitted to the intensive care unit, an electroencephalogram was performed and it showed no abnormal epileptic activity. Fluid hydration with intravenous normal saline 4,000 mL over 8 h and furosemide were administered to facilitate the excretion of bromovalerylurea metabolites [bromide, 3-methylbutyrylurea, α-(cystein-*S*-yl) isovalerylurea, and α-(*N*-acetylcystein-*S*-yl) isovalerylurea]. The patient's level of consciousness improved progressively, the frequency of myoclonic jerks decreased gradually, and the intervals between myoclonic jerks increased. Because the patient responded well to hydration and diuretics, no benzodiazepines were prescribed for her myoclonic jerks. On the following day, the myoclonic jerks disappeared completely. The patient stated that she had ingested 45 tablets of bromovalerylurea in a suicide attempt 6 h before being admitted to the hospital. Magnetic resonance imaging (MRI) of the brain was performed 2 days later to look for other pathology that can cause myoclonic jerks or bromide-induced neurological changes in brain; no abnormalities were found. No neurological sequelae were observed at the 2-month follow-up in the outpatient department.

Discussion

Although there has been a reduction in bromide-containing prescriptions, some bromide-containing drugs are still available, such as dextromethorphan hydrobromide, rocuronium bromide, and scopolamine bromide. Bromovalerylurea, a bromide-containing agent used as a hypnotic-sedative or tranquilizer, is popular in some countries, especially in Japan and Taiwan. Several over-the-counter products containing combinations of bromovalerylurea and acetaminophen, caffeine, or NSAIDs, such as Ming-Tong Chih Tong Dan (Ming-Tong Pharmaceutical Co., Ltd, Taichung, Taiwan), Te-Ni-Ton (U Chu Pharmaceutical Co., Ltd, Taoyuan County, Taiwan), and Sedenton (Fuseng Chemical and Pharmaceutical Co., Ltd, Taichung, Taiwan), are available.

Reports of chronic bromide intoxication caused by long-term abuse of bromovalerylurea have been published (3,7). The symptoms of bromide intoxication may present as psychiatric abnormalities, including confusion, self-neglect, fatigue, sluggishness, impairment of memory and concentration, irritability or emotional instability, depression, hallucinations, and schizophrenic-like psychotic behavior, and as neurological abnormalities, such as headache, tremor, slurred speech, spontaneous movements (8), incoordination, and ataxia.

The serum bromide concentrations in acute and chronic bromide intoxication are different. Symptoms and signs of chronic bromide intoxication are seldom seen in cases with serum bromide concentrations <500 mg/L (6.3 mEq/L) (9). A study of healthy volunteers who took sodium bromide orally for 12 weeks found mild sleep abnormalities and concentration difficulties at mean plasma bromide concentrations slightly below 500 mg/L (10). However, the serum bromide concentration indicating acute intoxication is much lower. Following acute exposure to methyl bromide gas, three patients had severe vomiting, tonic convulsions, and clouding of consciousness with plasma bromide concentrations of 72.9, 67.8, and 91.5 mg/L (11). Three fatal cases of acute methyl bromide intoxication had serum bromide concentrations of 110–190 mg/L (12). In our case with acute bromovalerylurea intoxication, severe myoclonic jerks and lethargy were found with a serum bromide concentration of 81.0 mg/L, similar to the reported concentrations in acute bromide intoxication (11).

The anion gap and serum chloride concentration are normal in cases of acute bromide intoxication. However, if an ion-specific electrode is not used or the machine erroneously reports bromide ions as chloride ions, the chloride concentration may be falsely elevated or the anion gap falsely low.

Myoclonic jerks may develop in response to hypoxia, brain trauma, stroke, brain tumor, spinal cord injury, neurodegenerative diseases, central nervous system infections, systemic metabolic disorders, kidney failure, liver failure, or drug and chemical poisoning (13). It is important to distinguish myoclonic jerks from other hyperkinetic movement disorders, such as tics, chorea, dystonia, and tremor (14). Although many drugs (e.g., haloperidol, sulpiride, chlorpromazine, clozapine, antiepileptic drugs, and opiates) can cause myoclonic jerks (13), acute bromovalerylurea intoxication was not found to be associated with myoclonic jerks in a Medline search.

The standard treatment of bromide intoxication is intravenous administration of large amounts of saline, in which the chloride ion competes with and replaces the bromide ion throughout the body and enhances the excretion of bromide by the kidneys. Cases that fail to respond to saline loading can be treated with loop diuretics or mannitol. Hemodialysis can promptly resolve focal neurological signs in patients who fail to respond to saline and diuretics. Although the usual half-life of bromide is 12–14 days without therapy, the calculated half-life deceases to 65 h when treated with saline loading and to 1.65 h when treated with saline loading and diuretics. The half-life decreases further to 1.38 h when treated with hemodialysis in addition to the earlier modalities (15).

Conclusion

Bromide intoxication caused by bromovalerylurea is rarely encountered, especially cases of acute intoxication. Myoclonic jerks may be one of the major presentations of acute bromovalerylurea intoxication. Much lower concentrations of serum bromide can evoke myoclonic jerks in cases of acute bromide intoxication than in cases of chronic intoxication. Physicians should consider bromide intoxication in the differential diagnosis of the causes of myoclonic jerks.

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