Case Report

Acute-onset psychosis induced by a therapeutic dose of parenteral hyoscine butylbromide: A case report

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ABSTRACT

Anticholinergic medications are frequently prescribed for gastrointestinal and genitourinary spasms. Psychosis, when present, results from anticholinergic overdose or toxicity. In the literature, anticholinergic-induced psychosis at therapeutic doses in patients with normal cognition is extremely uncommon. Here, we describe the case of a 28-year-old female who presented with auditory and visual hallucinations, stereotypy, and agitation after receiving a single intramuscular injection of 20 mg hyoscine butylbromide for dysmenorrhea. Even though it is rare for a therapeutic dose of hyoscine butylbromide to cause psychosis, clinicians should maintain a high index of suspicion and be cautious when administering or prescribing anticholinergics.

Key words: Anticholinergics, Hallucination, Hyoscine butylbromide, Physostigmine, Psychosis

For decades, antispasmodics have been used to relieve abdominal cramping in the gut [1]. The quaternary amine antimuscarinic medication, hyoscine butylbromide, is indicated for the alleviation of gastrointestinal (GI) and genitourinary spasms, as well as the symptoms of inflammatory bowel disease [2]. It is also used before invasive radiologic and diagnostic procedures to prevent GI spasms. As an anesthetic premedication, it induces sedation and decreases secretions in the oropharynx and bronchi [3]. It is one of the most widely used anticholinergic and antispasmodic drugs currently available [2]. Toxic effects of anticholinergics are typically caused by overdosing; however, anticholinergics can sometimes cause mild toxicity as a side effect. The synergistic actions of most anticholinergics increase the risk of toxicity [4]. Like other anticholinergics, hyoscine butylbromide has multiple adverse effects affecting nearly all organs [3]. Despite reports of central nervous system (CNS) symptoms such as headaches and drowsiness, acute psychosis from hyoscine butylbromide in a patient with normal cognition is very rare, especially at a therapeutic dose.

We report the case of a 28-year-old female patient who presented to the emergency unit with symptoms of auditory and visual hallucination after receiving hyoscine butylbromide for dysmenorrhea. We are reporting this case to raise awareness among health-care professionals about the potential for hyoscine butylbromide to induce acute psychosis at a therapeutic dose in patients without a history of psychotic disorders.

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CASE REPORT

A 28-year-old female patient presented to the emergency room with complaints of auditory and visual hallucinations 60 minutes after receiving a single intramuscular injection of 20 mg hyoscine butylbromide from a pharmacy following episodes of dysmenorrhea. Her symptoms included hearing her mother's voice begging her to go to the market and seeing insects crawling over her tummy and legs. She was also noted to pick up an imagined object off the floor at regular intervals. She imagined herself meeting the President of the United States. She exhibited stereotypic movements and was agitated occasionally. There was no history of dry mouth and eyes, impaired vision, palpitations, dizziness, or urine retention. There was no fever, no head trauma, and no symptoms of liver or kidney disease in the patient. She has no previous history of a similar presentation, nor has she ever been treated for a psychotic disorder. She was not on any medications or being treated for any chronic diseases. She does not consume alcohol, smoke cigarettes, or use psychotropic substances.

She was hyperactive and had a heart rate of 98 beats/min, blood pressure of 120/80 mmHg, a respiratory rate of 24 cycles/min, oxygen saturation of 98% in ambient air, and a temperature of 37.2°C. Her skin was not flushed, and her pupils were normal

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size and reactive to light bilaterally. She recognized previously familiar people, and her sensorium was clear. There were no obvious focal neurological abnormalities. Other aspects of her physical examination were otherwise unremarkable.

The results of the laboratory tests were normal, as shown in Table 1. Drug toxicology testing was not done, and hence, the level of hyoscine was not measured. A consideration of hyoscine butylbromide-induced acute psychosis was entertained. The Naranjo adverse drug reaction probability scale [5] yielded a score of 7, which indicated that hyoscine butylbromide was the most likely cause of the symptoms of acute psychosis in this patient.

The patient was treated with 10 mg of diazepam intravenously to calm her down and relieve her agitation. She was admitted to the hospital for observation and strict monitoring. We opted not to give her any further medication but to observe her until the effect of the drug wore off. Her symptoms (hallucinations and abnormal movements) were significantly improved after about 6 hours. By the following day, the symptoms were completely resolved, and she was discharged and counseled to be cautious when using anticholinergics, especially hyoscine butylbromide, in the near future. At the follow-up 2 weeks later, the patient had completely recovered with no evidence of a recurrence of symptoms.

DISCUSSION

Anticholinergics can generally induce psychosis when administered in excess of the therapeutic dosage range [6-8]. In this index case, however, psychosis was caused within the therapeutic dosage range, with no additional peripheral or cognitive anticholinergic symptoms following the administration of hyoscine butylbromide. According to Naranjo's adverse drug reaction probability scale [5], hyoscine butylbromide is the probable causative factor. This case exemplifies that psychosis can occur from anticholinergics, in this case, hyoscine butylbromide, even at normal doses.

Table 1: Laboratory test results of the patients

Investigations	Patients' values	Reference range
Hemoglobin	13.5 g/dL	11–15.5 g/dL
Hematocrit	40.1%	36–48%
White blood cells count	6×10^9/L	$4–11\times10^9$/L
Neutrophils	62.2%	40–70%
Lymphocytes	34.1%	20–40%
Eosinophils	2.9%	1–4%
Basophils	0.8%	0.5–1%
Platelets	276×10^9/L	$150–450\times10^9$/L
Erythrocyte sedimentation rate	12 mm/h	0–20 mm/h
Random plasma glucose	85 mg/dL	70–140 mg/dL
Serum creatinine	0.9 mg/dL	0.7–1.4 mg/dL
Aspartate aminotransaminase	12 IU/L	5–36 IU/L
Alanine aminotransaminase	18 IU/L	7–55 IU/L
Thyroxine (T4)	8.2 µg/dL	4.6–12 µg/dL
Triiodothyronine (T3)	115 ng/dL	90–215 ng/dL
TSH	2.6 mIU/ml	0.4–4.5 mIU/mL

TSH: Thyroid-stimulating hormone

Hyoscine butylbromide is a derivative of hyoscine, which is extracted from the leaves of the Australian Duboisia tree [3]. It is a non-selective muscarinic acetylcholine receptor antagonist that binds to a set of muscarinic receptors (M1–M5). This controls acetylcholine and dopamine release indirectly [2,9]. The M2 and M3 receptors are the predominant subtypes of muscarinic receptors found in the GI tract [2]. It is believed that hyoscine inhibition of the M2 muscarinic receptor in the axon terminal increases acetylcholine levels in the substantia nigra, hence elevating striatal dopaminergic levels [10]. Positive psychotic symptoms, including hyperactivity and stereotypy, may occur from such activity [11]. In contrast, the blockage of M4 subtype receptors has been associated with memory and attention difficulties [12].

Even though hyoscine butylbromide blocks acetylcholine at muscarinic receptors at therapeutic doses, it can also do the same at nicotinic receptors at high doses [2]. The effects on the CNS are uncommon because hyoscine butylbromide is poorly absorbed (2–10% when administered orally) and cannot readily cross the blood–brain barrier [3]. At therapeutic doses (20–80 mg), blood concentrations are difficult to detect [13]. After intravenous administration, the drug is rapidly distributed into the tissues ($t_{½}$=29 min) [3].

As might be anticipated based on the mechanism of action of hyoscine butylbromide, the potential side effects and adverse consequences are many and affect nearly all organ systems. The most common side effects are blurred vision, sensitivity to light, high intraocular pressure, dry nose, occasional bronchospasm, fast heart rate, palpitations, constipation, dry mouth, dry throat, and urine retention [3,14]. The CNS side effects are more likely secondary effects generated by the drug's direct action, as the drug does not readily cross the blood–brain barrier [3]. The CNS side effects, such as headache and drowsiness, have been reported, however, psychosis induced by hyoscine butylbromide has been described infrequently [15]. The majority of recorded cases of anticholinergic-induced psychosis were due to an overdose of medication [6-8]. In this index case, however, psychosis occurred following a single therapeutic dose of hyoscine butylbromide. Das *et al*. [16] also reported a similar outcome when an anticholinergic was administered at a therapeutic dose.

The type and intensity of adverse effects are highly dependent on the route of administration. At therapeutic doses, the effects of oral administration are substantially less prevalent than an identical dose given parenterally [3]. Fortunately, the most common side effects are usually minor and resolve on their own as the drug is eliminated from the body [3,14]. It is worth noting that hyoscine butylbromide, being a quaternary ammonium derivative, does not readily reach the CNS. As a result, anticholinergic adverse effects on the CNS are uncommon [2,3].

Anticholinergic toxicity manifests as flushing, fever, dry mucous membranes, altered mental status or delirium, mydriasis, diplopia, and urine retention. Infrequently, patients may have seizures, jerking movements, and rhabdomyolysis [6,7].

An association with electrocardiogram abnormalities (QT and QTc prolongation) has been established [7]. A person with anticholinergic intoxication is described as "red as a beet, hot as a hare, dry as a bone, blind as a bat, and mad as a hatter." This depicts a patient's flushed skin, high body temperature, dry mucous membranes, blurred vision, and confusion or delirium [17]. Other than hallucinations and stereotypy, our patient did not manifest most of the toxic symptoms.

In the majority of cases, hyoscine intoxication can be treated by discontinuing the offending drug and providing supportive care [17]. Benzodiazepines can be used to alleviate patients' agitation and restlessness. Physostigmine, an inhibitor of acetylcholinesterase, reverses both central and peripheral signs of anticholinergic toxicity [17]. Parenterally administered doses of 0.5–2 mg are advised [7,18]. Patients with toxic psychosis who pose a threat to themselves, or others may require hospitalization for close monitoring and management. Although our patient had anticholinergic-induced psychosis, she was not treated with physostigmine. She was observed and monitored until the effect of the offending drug wore off. The serum concentration of hyoscine butylbromide could not be determined due to a lack of measurement facilities.

CONCLUSION

Psychosis caused by a single therapeutic dose of hyoscine butylbromide is uncommon. Consequently, physicians require a high index of suspicion to entertain this possibility. Patients experiencing behavioral problems following the use of anticholinergics should be assessed thoroughly. Physostigmine, an inhibitor of acetylcholinesterase, has proven to be an effective treatment for anticholinergic toxicity. Clinicians should therefore use caution when prescribing anticholinergics.

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