Case Report

Olanzapine overdose presenting with acute muscle toxicity

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ABSTRACT

Olanzapine is a commonly prescribed atypical antipsychotic drug that is being increasingly used as an intentional overdose. It usually presents with reduced and fluctuating level of consciousness and coma. It may rarely present with muscle toxicity by binding to HT2A receptor in skeletal muscle and increasing its permeability. We report a case of such poisoning which had no obvious symptoms but was brought to emergency due to overdose and was found to have acute muscle toxicity as evidenced by raised creatine phosphokinase (CPK) levels. From this, we also want to emphasize that CPK levels should be checked in all the patient’s prescribed olanzapine to look for muscle toxicity.

Key Words: Creatine phosphokinase, olanzapine, overdose

INTRODUCTION

Olanzapine is a commonly prescribed atypical antipsychotic of thienobenzodiazepine group. Due to its improved safety profile and efficacy at therapeutic doses, it has rapidly gain popularity for the treatment of psychiatric disorders such as schizophrenia. Although its dopamine antagonistic property has been described as being the cause for its antipsychotic activity, its multi-receptor action, i.e., antagonism to dopaminergic D1, D2, D4, serotoninergic 5-HT2A, 5HT2C, histaminergic H1, cholinergic M1-5, and α1-adrenergic receptors, results in variable clinical symptoms during acute poisoning. However, till date, there is no antidote for this poisoning and supportive management remains the mainstay of therapy. The severity of symptoms correlates with the amount of the drug ingested as well as with co-ingestion of additional drugs. Here, we report a case of olanzapine overdose mainly characterized by increased creatine phosphokinase (CPK) values with minimal presence of other symptoms of toxicity.

CASE REPORT

A 25-year-old male weighing around 50 kg, with background history of schizophrenia, under treatment with olanzapine for 6 months presented to emergency department with somnolence and vomiting after 12 h of self-ingestion of 400 mg of olanzapine.

At presentation, his Glasgow Coma Scale (GCS) was 12/15. His pulse rate was 90 beats/per min, blood pressure 110/60 mmHg, respiratory rate 16 breaths/min, oxygen saturation 92% on room air, and temperature of 98.5°F. Respiratory, cardiovascular and per abdominal examinations were normal. All the routine laboratory parameters including complete blood count, chest X-ray, 12 lead electrocardiogram (ECG), renal function, urine routine and microscopic examination, and random blood sugar were within normal limits. Arterial blood gas showed respiratory alkalosis. CPK levels were 5780 U/L, serum alanine aminotransferase (ALT) was 146 U/L, and serum aspartate aminotransferase (AST) was 100 U/L.

He was started on normal saline 175 ml/h and vitals were monitored continuously. Urine output of over 3 ml/kg/h was aimed. He had gradual improvement in GCS over 2 days. CPK levels were 4000 U/L; ALT was 100 U/L, AST was 60 U/L on the 2nd day. CPK level was ordered...
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daily thereafter which revealed CPK of 3000 U/L on day 3, 1500 U/L on day four and it progressively decreased to 100 U/L on day 7 [Figure 1]. The patient was admitted to Intensive Care Unit and then transferred to ward.

He did not receive any intramuscular injection, nor developed fever, seizure, electrolyte abnormalities during hospital stay and was discharged home after 8 days of hospital stay. He did not develop any complications during the follow-up period of 2 weeks.

**DISCUSSION**

This case illustrates a rather uncommon presentation of olanzapine overdose in the form of acute muscle toxicity. Although such rise in CPK is said to occur at higher doses, our patient did not have other symptoms that would usually occur at such doses such as agitation, hypotension, tachycardia, miosis, deep coma, or ECG abnormalities. He did not have any co-existing medical illness, did not take any other drugs, and had no history of trauma, restraint, or any clinical symptoms and signs of infection which could explain the rise of CPK. Normal saline was used as hydration therapy with target urine output of over 3 ml/kg/h. Serum creatinine was stable. Acute kidney injury was avoided with adequate hydration.

Olanzapine overdose is commonly seen in clinical practice, especially among psychiatric patients, who attempt suicide by ingesting their own prescribed medications. Clinical picture of olanzapine overdose can be quite variable due to their multi-receptor action and may depend on the dosage. However, most patients present with neurological symptoms. In a retrospective analysis by Palenzona et al., the most frequent findings were somnolence (77%), agitation (42%), and miosis (31%). With increased severity patients may develop coma and require mechanical ventilation.

Olanzapine undergoes first-pass metabolism (40%) by the capacity-limited isozyme cytochrome P450 2D6, large overdoses result in nonlinear pharmacokinetic behavior, with disproportionate increases in the serum concentration relative to dose and potentially severe adverse effects. Instead of linear and dose proportionate pharmacokinetics as described in therapeutic range, a two-phase elimination is observed at acute overdosage.

Acute muscle toxicity in olanzapine poisoning shows a dose-dependent effect. It has been reported to be present in up to 17% of patients with olanzapine overdose. It has high binding affinity for the 5-HT2A receptor expressed by human skeletal muscle cells and mediates cellular glucose uptake. Increased muscle cell membrane permeability, as a consequence of 5-HT2A receptor blockade, has been proposed as a mechanism by which CPK could diffuse into the circulation across the very high trans-membrane gradient. Neuroleptic malignant syndrome, a potentially life-threatening adverse reaction to antipsychotic drugs, though uncommon with atypical antipsychotics, has also been reported to occur after increased dose of olanzapine administration. A rapid loading causing a sudden and massive downregulation of dopaminergic transmission is considered to be the cause.

Considering our patient who ingested 400 mg of olanzapine and developed increases CPK level. These finding was consistent with similar types of study. However, agitation, hypotension, tachycardia, miosis of both eyes and deep coma with a GCS value of 3 ECG abnormalities was not seen in our patient.

Although the usual dose range for olanzapine is 5–15 mg/day, there are no standard reference values with respect to the expected concentrations of olanzapine after therapeutic administration. In clinical studies, steady-state blood (plasma) concentrations of olanzapine are rarely over150 ng/ml, but the potential for toxicity has been suggested at concentrations as low as100 ng/ml. There are reports of survival and complete recovery following ingestion of about 800 mg. We, however, did not measure serum olanzapine level as this facility was not available in our center.

To conclude, olanzapine overdose can cause acute muscle injury, presenting with elevated CPK levels. CPK levels should be initially checked in these patients and then monitored. Adequate hydration can avoid acute kidney injury. The understanding of its pathophysiology, though, is still unclear and needs further investigations.

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**Conflicts of interest**
There are no conflicts of interest.
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