Case Report

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Exploring Olanzapine Overdose in an Ethiopian Patient: A Case Report

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ABSTRACT

Background

Olanzapine is an atypical antipsychotic drug that has been Food and Drug Administration (FDA) approved for schizophrenia and bipolar disorder. It has a tolerable side effect profile of some metabolic disturbance, including weight gain and hyperglycemia. Even though it has a broad therapeutic index, ingestion in large amounts can result in toxic manifestations, which are an extension of its pharmacodynamics.

Case Presentation

We are reporting a 58-year-old man who presented after ingesting 90 tablets (450mg) of olanzapine 5mg. He presented with difficulty in communication, with clinical findings of hypertension and tachycardia 8 hours after his ingestion. Additionally, laboratory investigations revealed prolonged QTc and mild hyponatremia.

Discussion

Owing to its broad-spectrum action on different central nervous system receptors, olanzapine has a wide range of clinical presentations. These include agitation, delirium, somnolence, respiratory depression, and hypertension or hypotension. Patients may also experience catastrophic complications such as cardiac toxicity.

Conclusion

This is the first case of olanzapine overdose in an Ethiopian patient, and it has given us insight as to how to approach and manage such patients. Moreover, despite the high dose of ingestion, a benign presentation was witnessed. Hence, we believe this case report will serve as a stepping stone for future such encounters.

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1. Introduction

Olanzapine is a second-generation (atypical) antipsychotic with antagonistic activity on many receptors. These include serotonin (5-HT2A), dopamine (D1, D2, D3, D4), histamine (H1), and muscarinic receptors. It is used for the treatment of psychoses, schizophrenia, schizoaffective disorders, bipolar disorders, and other conditions with psychotic or delusional components.[1]

It is effective against positive and negative symptoms of schizophrenia. Besides its superior antipsychotic efficacy, therapeutic doses (5–20 mg/d) of olanzapine have been reported to produce fewer extrapyramidal symptoms compared to first-generation antipsychotics. In addition, olanzapine has not been associated with agranulocytosis. The most frequent adverse effects of olanzapine are sinus tachycardia, orthostatic hypotension, anticholinergic effects, sedation, and weight gain. The ''atypical'' antipsychotic profile of olanzapine is mainly based on its mesolimbic selectivity and its distinct pharmacodynamic profile. It has a higher binding affinity for 5-HT receptors than for dopamine D2 receptors, high affinities for histaminergic (H1) and muscarinic (M1) receptor subtypes, and relatively low affinities for α-adrenergic receptors.[2]

However, despite its improved tolerability compared to conventional agents, the exact safety profile of olanzapine remains uncertain. For instance, olanzapine has been associated with hyperglycemia, ketoacidosis, new-onset diabetes mellitus, and weight gain. Furthermore, convulsions, neuroleptic malignant syndrome, tardive dyskinesia, and neutropenia have also been reported during olanzapine therapy.

In acute olanzapine overdose, the most frequent symptoms observed were lethargy/coma, tachycardia, anticholinergic syndrome, confusion, and agitation. Patients may also have delirium, miosis, dysarthria, myoclonus, and hypertension or orthostatic hypotension. Because of its profound central nervous system (CNS) depression and the frequently observed miosis, olanzapine overdose tends to mimic opioid overdose. In a few cases of overdose, rapid fluctuations between sedation and agitation or ‘‘agitation despite sedation’’ have been described. These patients are often described as being sedated with an underlying anticholinergic delirium.[3]

In addition, hyperthermia, mydriasis, blurred vision, hypotension, respiratory depression, and leukocytosis have been reported. Moreover, prolongation of the QT interval, hypothesized to occur via direct inhibition of the cardiac delayed potassium rectifier, may play a role in fatal arrhythmias. Still, olanzapine appears to have the least direct effect compared with other antipsychotics. Cardiovascular disease is a significant risk factor for ischemic and thrombotic vascular events, as well as for QT prolongation, and the increased prevalence of coronary artery disease in patients with schizophrenia may be relevant in the context of elevated psychotropic drug concentrations after overdose.[4]

2. Case report

A 58-year-old Ethiopian male known to have major depressive disorder, patient on regular follow-up for 30 years, taking sodium valproate 500 mg Per os (PO) twice daily, **olanzapine 5 mg** PO once daily, and imipramine 10 mg tablet once daily. He was brought to the Emergency Room (ER) by his daughter after he presented with difficulty communicating for an 8-hour duration. He had ingested 90 tablets (450 mg) of olanzapine. He had a history of similar attempts. He had diabetes and hypertension on medication.

On physical examination, he was confused. Vital signs revealed an elevated blood pressure of 198/114 mmHg and a tachycardia of 108 beats per minute. Glasgow Coma Scale (GCS) was 14(E-4, V4,

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M-6). All other system examinations were non-revealing.

Investigations

Laboratory tests, including a complete blood count, liver enzymes, renal function, and cardiac markers, were all within normal limits. Serum electrolytes were unremarkable except for mild **hyponatremia**. Electrocardiogram (ECG) showed Corrected QT interval (QTc)-479ms; QRS-179ms; Index- QTc Prolongation, Nonspecific interventricular conduction delays as shown below.

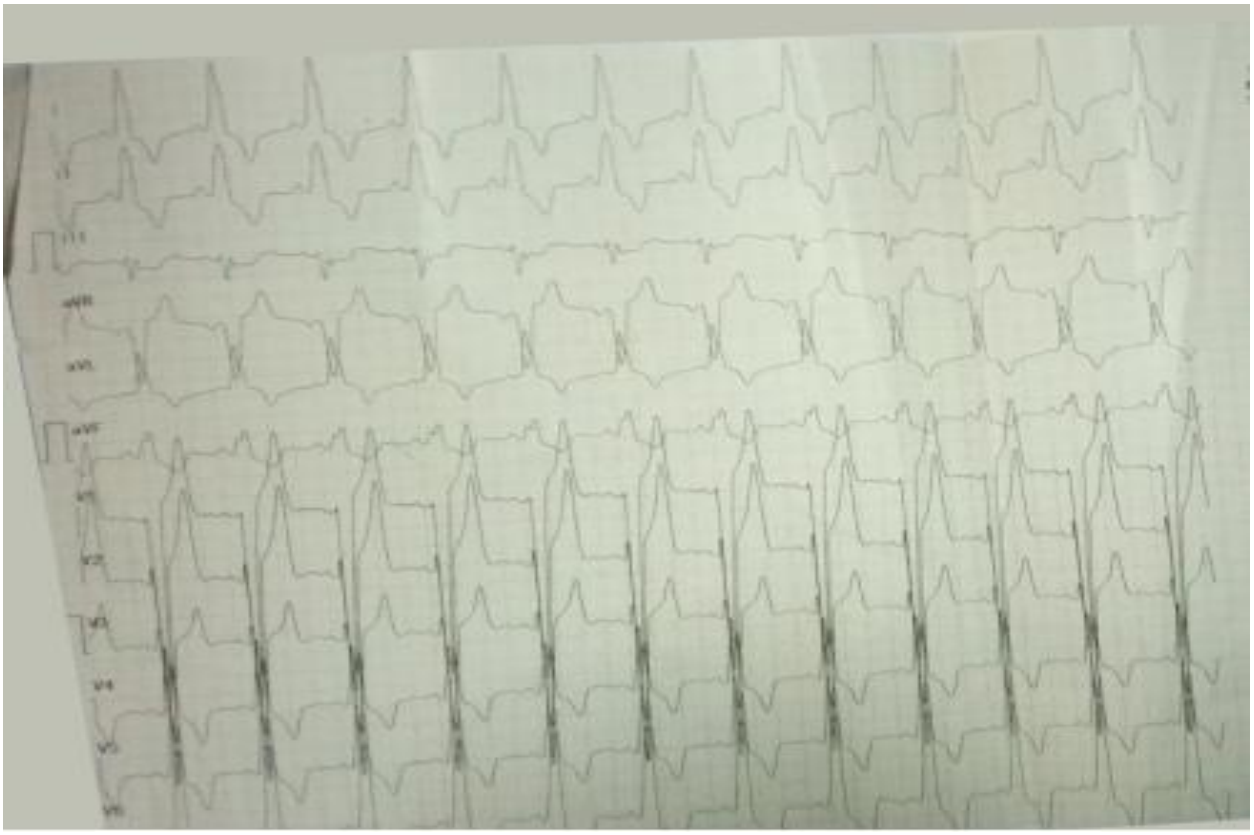

Fig. 1 The patient's ECG showing QT prolongation and interventricular delay

Treatment and outcome

He was put on cardiac monitoring; Olanzapine was discontinued; a single dose of 2 g intravenous **Magnesium** was given; He was not given activated charcoal as he presented far beyond the window of opportunity. His GCS improved, and then he was followed for 48 hours and discharged with an immediate link to a psychiatric ward as his SAD PERSON score was 7.

3. Discussion

Similar to conventional agents, the majority of patients who accidentally or intentionally overdose with atypical antipsychotics will remain asymptomatic or develop only mild to moderate toxicity. Death following an overdose is a rare complication, particularly if treatment is initiated in a timely manner. The toxic and lethal doses are highly variable and depend primarily on the presence of co-intoxicants, age, habituation of the patient, and time from exposure to initiation of treatment. Children and nonhabituated adults are more sensitive to the toxic effects of this agent. The toxic effects that occur following overdose of atypical antipsychotics are essentially an exaggeration of the pharmacologic effects.[5]

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The therapeutic dose of olanzapine ranges from 5 to 15mg per day. However, there are no standard reference values for the expected concentrations of olanzapine after therapeutic administration. In clinical studies, steady-state blood (plasma) concentrations of olanzapine are rarely over 150 ng/mL, but the potential for toxicity has been suggested at concentrations as low as 100 ng/mL.[6]

Olanzapine overdose can present with different clinical pictures. The most common symptoms that arise as a result of olanzapine overdose include central nervous system (CNS) depression with somnolence, blurred vision, low blood pressure, respiratory depression, extrapyramidal and anticholinergic effects, hyperthermia, leukocytosis, and elevated creatine phosphokinase levels.

Some studies point to the possibility of olanzapine overdose mimicking opiate intoxication. Therefore, olanzapine should be added to opioid and α2-adrenergic agonist intoxication in the differential diagnosis of a patient with depressed mental status and miosis. Deaths attributed to probable cardiac toxicity have been continuously reported from olanzapine overdose.

It is postulated that the most probable mechanism of death in an overdose of olanzapine involves cardiac toxicity at the cellular membrane level, although the exact mechanism remains elusive. One possible explanation is that its QTc prolongation occurs by directly inhibiting delayed potassium rectifiers.[7]

The findings in our patients, which are confusion and dysarthria, severe hypertension, mild tachycardia, and investigation results of mild hyponatremia and QTc prolongation, can be explained by the pharmacodynamics of olanzapine.

Olanzapine's antagonist effect on cholinergic and histamine receptors accounts for its manifestation as fluctuating confusion, delirium, and sedation. Hypotension is the usual presentation in patients overdosing on olanzapine, but our patient was an exception. However, since the patient is already a known hypertensive on medication, the marked elevation of blood pressure at the time of presentation cannot solely be attributed to olanzapine overdose, because we do not have his recent blood pressure as a baseline.[8]

The severity of an overdose is related to the amount of the drug ingested.

Table 1: Depicting ingested dose and CNS manifestations, source, Life in the Fast Lane, olanzapine toxicity

Dose (ADULT)	EFFECT
<40 mg	Therapeutic sedation and antipsychotic effects (occasionally used for serotonin toxicity)
40 – 100 mg	Mild-to-moderate sedation with potential for anticholinergic effects.
100 – 300 mg	Sedation with intermittent marked agitation
>300 mg	Increasing sedation progressing to coma requiring intubation. Hypotension

Early identification and institution of treatment are crucial in the management of olanzapine overdose. The management is supportive, as there is no specific antidote for the drug. As it can cause central nervous system depression and respiratory compromise, the ABCs should be tended to as is done in any other poisoning patient. In addition, magnesium sulfate, as it has been done for our patient, helps with the QTc prolongation and resuscitative measures for hypotensive patients. In addition, benzodiazepines can be given for agitated patients; physiostigmine has been reported to reverse agitation and coma caused by olanzapine and catheterization for urinary retention.

4. Conclusion

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This is the first case of olanzapine overdose in an Ethiopian patient, and it has given us insight as to how to approach and manage such patients. Moreover, despite the high dose of ingestion, a benign presentation was witnessed. Hence, we believe this case report will serve as a stepping stone for future encounters. Moreover, it reminds us that even unusual drugs for intentional overdose can be ingested. Hence, clinicians have to be wary in this regard to institute management promptly.

Abbreviations

FDA: Food and Drug Administration
ECG: Electrocardiogram
CNS: Central nervous system (CNS)

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Competing interests

The authors declare that they have no competing interests in relation to the publication of this case report. There are no financial, personal, or professional conflicts of interest that could bias the reporting or interpretation of the findings. The authors have no affiliations or financial involvement with any organization or entity that has a direct or indirect interest in the subject matter discussed in this case report. This competing interests statement is provided in the interest of transparency and to ensure the integrity and impartiality of the research presented.

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