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36 HOURS OF COMA BY CLOZAPINE INTOXICATION

Medicine

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ABSTRACT

Clozapine is an atypical antipsychotic drug which is prescribed for treatment-refractory schizophrenia.[1] The risk of adverse hematologic, cardiovascular, and neurologic effects has tempered its use, and reports of overdoses remain rare.[2] Literature is relatively silent on antipsychotic overdose-induced coma. A few studies have so-far documented this rare neuropsychiatric presentation, and all of them were from western countries. We present the first ever report of clozapine intoxication leading to about 36 hours of coma in an adult man from western India.

KEYWORDS

Clozapine overdose, Reversible coma, Antipsychotics.

INTRODUCTION:

Clozapine is an atypical antipsychotic drug used for treatment-resistant schizophrenia and is the prototypical agent of the tricyclic dibenzodiazepine class. Atypical antipsychotics are effective in controlling the positive (hallucinations, delusions) and negative (flat affect, anhedonia) symptoms of schizophrenia with fewer extrapyramidal side effects compared to typical antipsychotics

Despite its clinical superiority in comparison to other atypical antipsychotics, clozapine remains a second-line agent due to its side-effect profile. At standard doses, clozapine has been known to cause agranulocytosis, sedation, and hypersalivation. At toxic doses, clozapine has been reported to cause encephalopathy, dysarthria, ataxia and coma.[3] Previously published reports of clozapine overdose have mainly been characterized by large-dose ingestions in patients who are attempting suicide and are already maintained on clozapine.[3,4] There are few reported cases describing acute clozapine intoxication in clozapine-naïve patients with relatively small exposures.[5]

We report a case of a clozapine-naïve man who presented to the emergency department (ED) with unconscious state, initially thought to be due to an acute ischemic stroke, but ultimately determined to be due to acute clozapine intoxication. Although uncommon, clozapine intoxication should be considered for patients who present with acute onset of neurologic symptoms and possible clozapine exposure.

CASE REPORT:

A 46-year-old man with a history of hypertension and hyperlipidemia was brought to the ED in an unconscious state. The patient's wife has given alleged history of consuming 20 tablets each of clozapine (100 mg), clonazepam (0.25 mg), and folic acid (5 mg) 2 hours back. He was reported to have been found lying beside his cot in an unresponsive state, with empty packs of the tablets scattered around him. On presentation, Glasgow Coma Scale (CGS) score was 6/15 (E1, V1, M4); blood pressure was 86/60 mm Hg; pupils were small-sized but still reacting to light and bilateral planters were equivocal. His electrocardiogram showed mild ST- T wave flattening along with tachycardia and signs of respiratory depression. He was immediately intubated and mechanically ventilated and was put on volume-controlled ventilation. A gastric lavage was performed with activated charcoal. His chest x-ray, MRI brain, abdominal ultrasound, hepatic and renal functions, complete blood count and an arterial blood gas analysis revealed no significant abnormality. There was no evidence of seizure; myocarditis and head injury. For the next 36 hours, the patient remained comatose and moved his limbs transiently on painful stimulus with preserved doll's eye sign. Then patient regained consciousness and was self-extubated. It was followed by intermittent disorientation and labile mood with paroxysmal drowsiness for the next 3-4 hours. Patient was kept in an ICU for a day and then shifted to ward in normal neurological status without any complications.

DISCUSSION:

As compared to earlier reported cases,[6,7] in which as much as 5 g of clozapine could induce 48 hours of coma, our case showed clear discordance with reference to overdose of as low as 2 g of clozapine. Fortunately, unlike in agranulocytosis and myocarditis, clozapine-induced coma continued to show a benign course, with complete recovery as seen in this case. Although research started almost a decade ago, the fatal dose of clozapine is not yet clearly established, unlike that of benzodiazepines, barbiturates, opioids and tricyclic antidepressants and just to speculate, if the usage of clozapine as a means of suicide attempt continues, we wonder whether determination of fatal dose should become clearer during years to come. Primary management of acute clozapine overdose is supportive care. Providers should be prepared to provide airway management given the frequency of somnolence and coma. Hypotension refractory to fluids may be present due to alpha-adrenergic blockade, and vasopressor support may be necessary.[5] To date, no specific antidote available for clozapine. Management of such patients with supportive care, proper monitoring still holds the key to the successful outcome.

CONCLUSION:

Coma due to clozapine intoxication is rare manifestation. It should be promptly identified and treated with supportive care for better outcomes.

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