Neuroleptic malignant syndrome associated with the use of injection zuclopenthixol acetate

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Zuclopenthixol is available in two parenteral formulation, i.e., in the form of acetate and decanoate. It has high affinity for dopamine D1 and D2 receptors. There is limited literature of association of neuroleptic malignant syndrome with the use of zuclopenthixol monotherapy. These case reports have mostly implicated zuclopenthixol decanoate and also zuclopenthixol acetate. In this report, we present a case of neuroleptic malignant syndrome associated with use of zuclopenthixol acetate.

CASE REPORT

A 35-year-old male presented to the emergency with altered sensorium, fever, and stiffness of limbs. Exploration of the history revealed that he has been consuming alcohol for the past 10 years in a dependence pattern characterized by craving, tolerance, and withdrawal. Just before presentation, he was consuming about 750 ml of Indian made foreign liquor per day.

Ten days before the presentation, while the patient was lifting a heavy object at his home, he developed severe backache and remained bedbound. In view of the severe pain, he was not able to go out to take alcohol. After about 72 h of the last intake of alcohol, the patient developed withdrawal symptoms in the form of irritability, visual and auditory hallucinations, agitation, sweating, palpitations, misrecognition, and disturbed sleep with reversal of sleep-wake cycle. These symptoms would often fluctuate and worsen with movement.

Zuclopenthixol has a high affinity for dopamine D1 and D2 receptors, which is used in parenteral form to manage acute agitation and psychosis. There are very few reports of neuroleptic malignant syndrome (NMS) associated with the use of zuclopenthixol monotherapy. These case reports have implicated both zuclopenthixol decanoate and zuclopenthixol acetate. In this case report, we present a case of NMS associated with the use of zuclopenthixol acetate, in the background of agitation due to the alcohol withdrawal state.

Keywords: Neuroleptic malignant syndrome, side effect, zuclopenthixol

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over 24 h with evening worsening of symptoms. Over the next 3–4 days, the symptoms kept on increasing and his agitation increased markedly, leading to a consultation with the local practitioner. In view of the marked agitation, he was given injection zuclopenthixol acetate 200 mg thrice on the same day. Within 12–14 h of the last injection, the patient developed fever, stiffness in limbs, perfuse sweating, increase in symptoms of intermittent agitation, and altered sensorium. In view of these symptoms, he was referred to a tertiary care hospital for further management.

Detailed exploration of history did not reveal evidence of any other substance use, any other psychotic symptoms, seizures, head injury, hematemesis, meleana, and depressive features.

On examination, he had profuse sweating, his pulse rate was 130/min, the temperature was 102°F, and blood pressure was 80/50 mmHg, with marked fluctuation in the vital signs over the time. He had features of dehydration. Neurological examination revealed marked lead pipe like rigidity, diminished reflexes, flexor plantar response, pupils of normal size, and normal bowel sounds. On mental status examination, he was mute. However, there were no other signs of catatonia.

On investigations, he was found to have raised serum creatinine phosphokinase levels (839.9U/L; reference laboratory value: 26–308 U/L) and leukocytosis. Other investigations in the form of renal function test, liver function test, serum electrolytes, blood glucose levels, blood and urine culture, magnetic resonance imaging of the brain, and cerebrospinal fluid analysis did not reveal any abnormalities.

In view of the temporal correlation of onset of symptoms after the use of zuclopenthixol acetate, a diagnosis of NMS was considered. An additional diagnosis of alcohol dependence syndrome, currently in withdrawal, was also considered. The patient was started on supportive management to address the dehydration and was given Thiamine 500 mg thrice daily. In addition, he was started on tablet bromocriptine 5 mg thrice daily and lorazepam 2 mg/day. With this intervention, his symptoms improved over a 1 week and tablet bromocriptine was tapered off after 1 week of being asymptomatic. He was educated about alcohol dependence, and relapse prevention counseling was started. He was also attached to the orthopedic services for the evaluation of his backache.

**DISCUSSION**

There is limited literature on the association of NMS with zuclopenthixol. In our literature search, we could only find five publications, reporting association of NMS with zuclopenthixol in 7 cases. Out of the 7 cases, in 3 cases, NMS was associated with zuclopenthixol decanoate,[6,8] and in the other 3 cases, NMS was associated with zuclopenthixol acetate.[9] NMS was also associated with the use of oral zuclopenthixol hydrochloride in one case, who had previously developed NMS with haloperidol.[10] In all the previously reported cases of NMS associated with zuclopenthixol acetate, the patients were receiving additional antipsychotic medication. However, in the index case, zuclopenthixol acetate was used as monotherapy. In 3 out of the 7 reported cases, the patients were managed with bromocriptine and in 3 cases, management was limited to the use of benzodiazepines. In the index case, we used both, as the patient was exhibiting symptoms of NMS, in the background of alcohol withdrawal state. Previous reports have shown that NMS can develop after 1 day to 11 days of use of zuclopenthixol acetate.[6] In the index case, NMS developed within 1 day of last dose of zuclopenthixol acetate. This was possibly due to the use of higher doses administered over a short period in the index case. Existing literature clearly suggests an association of higher doses and rapid increase in the dose of antipsychotics with NMS.[7,8]

Few case reports suggest that NMS can mimic alcohol withdrawal delirium.[11] Further, only one case report in the existing literature suggests the development of NMS after intravenous administration of Haloperidol in a patient of alcohol withdrawal delirium, much like index patient and authors concluded that even a small dose of neuroleptic drugs can precipitate NMS in an already exhausted patient.[10] Similar incident has been reported during benzodiazepine withdrawal.[11] Index case possibly developed alcohol withdrawal delirium to start with, which was misinterpreted as psychosis in view of psychotic symptoms and marked agitation. This possibly led to the administration of higher doses of zuclopenthixol over short span of time. Alcohol withdrawal and agitation contributed to the development of dehydration and exhaustion, which are known risk factors for NMS.[8,9] These factors possibly contributed to the development of delirium.

Accordingly, it can be said that clinicians should properly evaluate the patients presenting with psychotic symptoms for delirium, associated with alcohol withdrawal, and cautiously use antipsychotics for the management of alcohol withdrawal delirium.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will
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Conflicts of interest
There are no conflicts of interest.

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