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CASE REPORT

Clonazepam-induced acute liver injury: A case report

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ABSTRACT

Clonazepam belongs to the benzodiazepine class of drugs (benzodiazepine derivative). It is used both as an anticonvulsant and in the treatment of panic disorder with or without agoraphobia. The most frequent adverse drug reactions of clonazepam are sedation or drowsiness, ataxia or hypotonia, and behavioral disturbances. Hepatomegaly and transient elevations in serum aminotransferases and alkaline phosphatase concentrations may occur in patients receiving this drug, but the frequency of the reaction has not been well defined. Here, we report that an acute psychosis case was the patient's laboratory reports showed a transient elevation in serum transaminases and alkaline phosphatase levels after clonazepam was administered.

KEY WORDS: Clonazepam; Benzodiazepines; Serum Transaminases; Alkaline Phosphatase; Adverse Drug Reaction

INTRODUCTION

Benzodiazepines are class of drugs which are used as anxiolytics, anticonvulsants, and muscle relaxants. Central nervous system adverse effects are common with benzodiazepines, cognitive and behavioral side effects are common when treated for seizures, all the other adverse drug reactions are rare and dose dependent. Elevated serum levels of liver enzymes have been reported, but frequency is not defined. Clonazepam (benzodiazepine) mainly used in the treatment of epilepsy, mania. The principal adverse effect found is drowsiness. Clonazepam is highly protein bound in plasma and undergoes extensive hepatic biotransformation; hence, their metabolism is affected significantly in liver diseases. Acute liver injury related to clonazepam and other benzodiazepines is a major concern.

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CASE REPORT

A 26-year-old male patient, known case of acute psychosis, was maintaining well on medications few days back prior hospitalization. Patient came to the Psychiatry and Behavioural Medicine Department of Amrita Institute of Medical Sciences. The chief complaints while admission was her agitated behavior toward her parents and increased talk which was irrelevant and she claimed to have special powers and increased religiosity. Patient was started on parenteral haloperidol and promethazine for his symptoms of agitation. Chlorpromazine and haloperidol were added for her psychotic symptoms. Clonazepam was added for his symptoms of anxiety. As part of the routine blood investigations done, her liver function tests were done in which there was significant elevation in serum bilirubin (direct), alkaline phosphatase (ALP), and aspartate aminotransferase (serum glutamic oxaloacetic transaminase [SGOT]), alanine aminotransferase (ALT), (serum glutamic pyruvic transaminase [SGPT])

Table 1: Liver enzymes value before and after withdrawal of clonazepam-indicating acute liver injury

Liver function test	Day 1 (before)	Day 2 (before)	Day 1 (after)	Day 2 (after)
SGOT	40.3	59.7	32.8	31.0
SGPT	45.6	50.2	32.0	31.5
ALP	135.3	150.9	135.0	131.3
Bilirubin	1.10	0.13	0.4	0.2

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, ALP: Alkaline phosphatase

levels. Clonazepam was withheld for the next 2 days and again her liver function tests were repeated, and the serum hepatic enzyme levels were found to be on the normal side. The patient had no previous history of liver disease, risk factors for acquiring hepatic injury, and never drank alcohol. Causality assessment was carried out using the Naranjo's scale. The algorithms showed that clonazepam was the "definite" (Naranjo's score 9) cause of this adverse drug reaction.

DISCUSSION

The benzodiazepine group of drugs is a large class, which have multiple clinical uses including management of insomnia, seizures, alcohol withdrawal, and muscle spasm and also have proved use in the management of chemotherapy-induced nausea and vomiting. Clonazepam is a benzodiazepine drug which is mainly used as an anticonvulsant and adjuvant agent in the treatment of epilepsy. The most commonly found adverse effects of clonazepam are drowsiness, lethargy, dysarthria, ataxia, and dizziness; these side effects are dose dependent. Tolerance can be developed to the anti-seizure effect of the drugs and also to the side effects. Clonazepam when compared to other drugs in the benzodiazepine class is rarely associated with causing serum ALT elevations, and clinically significant hepatic injury is very rare, but there are convincing case reports on acute hepatic injury caused by clonazepam on recurrence or reexposure has been reported. The injury is usually mild to moderate. The reason behind the liver injury is probably due to an intermediate metabolite produced by clonazepam. In this case, clonazepam caused significant elevations in the serum SGOT, SGPT, ALP, and total bilirubin levels; this was confirmed because even though the patient was on other medications, the liver function tests came to normal after the withdrawal of clonazepam. There are other case reports of drugs under benzodiazepine category (flurazepam) causing hepatitis, cholestatic jaundice, etc. All these case reports including the case reported above of clonazepam and other drugs of this class was followed by complete recovery without any evidence of residual or chronic injury.

CONCLUSION

Acute psychosis case patient's laboratory reports showed a transient elevation in serum transaminases and alkaline phosphatase levels after clonazepam was administered.

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