

Trifluoperazine-Induced Cholestatic Jaundice

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Liver injury occurs with many drugs; therefore, a thorough work up is important for establishing the diagnosis. We report a case of trifluoperazine-induced cholestatic jaundice. A 44-year old male with schizoaffective disorder developed an increase in liver enzymes and jaundice after starting treatment with trifluoperazine. Workup for other potential etiologies was negative.

Key words: *Adverse effects, Obstructive jaundice, Trifluoperazine*

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Drug induced liver injury is a common problem and appear to be responsible for 2-5% of the cases of jaundice or acute hepatitis and even fewer cases of chronic liver disease (1). Phenothiazines have been reported to be associated with cholestatic injury. The incidence of cholestasis is about 0.1-2% for chlorpromazine (2,3). Other phenothiazines have also been reported to cause cholestatic jaundice, but no reliable estimate of this incidence is available (3). Phenothiazine-induced jaundice is a form of cholestatic hepatocellular hepatotoxicity. The mechanism of this injury seems to be a combination of physiochemical, immune and direct toxic effect (4).

Associated jaundice and pruritus may be severe, with permanent loss of the bile ducts (5). Jaundice appearing after drug induced hepatocellular liver injury, suggests a serious and potentially fatal liver problem (1). Causality assessment methods provide a uniform approach to determine the likelihood of drug involvement in a suspected episode of hepatitis.

Standard factors that should be considered for determination of drugs as the causative factor include temporal relation (onset of the symptoms between 5 and 90 days after the initial exposure); the course after the patient stops taking the drug (improvement within

weeks); risk factors (such as alcohol use, pregnancy, old age, concomitant use of drugs); causes other than drugs (e.g. viral hepatitis); patient history with regard to previous toxic effects of a particular agent; and response to re-challenge of that agent if performed.(5)

Case Report

A 44-year-old male was admitted to Roozbeh psychiatric hospital in Tehran, Iran so that his psychiatric disturbances would be evaluated. The patients showed a markedly elevated mood. After a complete psychiatric check up, he was diagnosed with schizoaffective disorder. The patient had a history of diabetes mellitus diagnosed 4 years earlier but had a negative history for alcohol abuse, other drug abuse, or previous liver diseases. He received glibenclamide in the past but not on a regular basis and was not taking this medication for about 3 months prior to this hospital admission. At baseline, physical examination was within normal limits and no signs of any hepatobiliary disorder were noted. Trifluoperazine was initiated at 10 mg per day and was titrated to 15 mg per day in a week. Four weeks after the initiation of trifluoperazine, the patient was suffering from nausea, anorexia, pruritus and dark urine. Elevated levels of aspartate

aminotransferase (AST=107 U/l; normal < 49 U/l), alanine aminotransferase (ALT=235 U/l; normal < 49 U/l) and gamma-glutamyltransferase (GGT=279 U/l; normal 0-70 U/l) alkaline phosphatase (ALP=744 U/l; normal 30-120 U/l), and total bilirubin of 3.85 mg/dl (normal 0.1–1.0 mg/dl) were reported after 30 days of treatment. All other routine laboratory findings were within the normal range. Additionally, the serological markers for viral hepatitis were negative. No alternative cause for the liver injury could be demonstrated by ultrasonography. Based on the clinical symptom and abnormalities observed in the laboratory tests, the decision was made to stop all drug treatments (trifluoperazine and biperiden) and to evaluate the clinical response. When trifluoperazine was discontinued, all elevated parameters gradually decreased and returned to near-normal values. At this time, the patient was started on risperidone to control his psychiatric symptoms. The response to risperidone and its side effects was monitored for two weeks until he was discharged from the hospital. The patient's symptoms were improved and no adverse effect was noticed.

Discussion

This case report notes the occurrence of the initial hepatic injury due to the use of trifluoperazine. According to the Naranjo ADR probability scale, the likelihood of an ADR due to the trifluoperazine in this case is probable (6). This finding is based on the fact that liver enzymes were elevated after the initiation of trifluoperazine, and the deterioration of liver function was detected under continued trifluoperazine treatment. Additionally, there was a considerable decrease in liver enzyme levels after stopping trifluoperazine. Other causes of cholestatic jaundice were ruled out and thus, trifluoperazine was recognized as the possible cause of this problem in this patient. Many patients have taken this medication since its introduction in 1958. However, a few cases of cholestatic jaundice induced by trifluoperazine have been reported in the literature. In 1968, Margulies and colleagues reported jaundice in a 26-year old woman with psychosis after taking trifluoperazine for 15 days.(7). However, in general, the low number of reported ADRs may not be a valuable indicator of the risks since the number of the reports is dependent on many parameters such as case recognition, definition and means of reporting ADR. (3)

Conclusion

We suggest that the possibility of cholestatic jaundice induced by trifluoperazine should be considered when clinicians decide to start a patient on this medication. We recommend measuring liver enzyme levels prior to the initiation of trifluoperazine and monitoring the symptoms of jaundice during the treatment to prevent possible complications.

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