Antidepressant-Induced Liver Injury Underestimated
Megan Brooks  | December 31, 2013

All antidepressant drugs may potentially cause liver injury, even at recommended doses, and some groups are more vulnerable than others, French researchers report.

"Antidepressant liver toxicity has been underestimated in the scientific literature," say Gabriel Perlemuter, MD, PhD, from AP-HP Hôpital Bicêtre, Kremlin-Bicêtre, France, and colleagues.

In some cases, antidepressant-induced liver injury can be irreversible. Given that there currently is no strategy available to prevent antidepressant-induced liver injury, "early detection and prompt drug discontinuation remain critical," they say.

Their research was published online December 20 in the American Journal of Psychiatry.

Liver Injury Unpredictable

The investigators reviewed clinical data on antidepressant-induced liver injury from 158 reports, including 88 case reports, 38 original articles, and 32 reviews.

They calculate that 0.5% to 3% of patients treated with antidepressants may develop asymptomatic mild elevation of serum alanine aminotransferase (ALT) levels.

In most cases, liver damage is "idiosyncratic and unpredictable, and it is generally unrelated to drug dosage," they say. Liver damage may occur between several days and 6 months after initiation of an antidepressant.

All antidepressants can induce hepatotoxicity, especially in elderly patients and those who take multiple pharmaceutical agents. However, there is not enough evidence to draw "rigorous conclusions" about the prevalence and severity of antidepressant-induced liver injury, the investigators say.

Based on the evidence, the antidepressants associated with highest risk for hepatotoxicity are monoamine oxidase (MAO) inhibitors, tricyclic/tetracyclic antidepressants, nefazodone, bupropion, duloxetine, and agomelatine. Those with seemingly lower risks are citalopram, escitalopram, paroxetine, and fluvoxamine.

Life-threatening or severe drug-induced liver injury has been reported for some antidepressants, including MAO inhibitors, tricyclic/tetracyclic antidepressants, venlafaxine, duloxetine, sertraline, bupropion, nefazodone, trazodone, and agomelatine, Dr. Perlemuter and colleagues report.

Although no dose-response relationship has been clearly demonstrated, it is best to stick to the minimum effective dosages of antidepressants to reduce the risk for liver injury, they advise.

Use With Caution

Dr. Perlemuter and colleagues say that antidepressants with a higher potential for hepatotoxicity "should be used with caution in elderly patients, in patients with coprescriptions, and in patients with substantial alcohol use, illicit substance use, or evidence of chronic liver disease."

"Systematic pretherapeutic screening and regular assessment of hepatic enzymes during treatment may be useful for antidepressants with a high potential for hepatotoxicity and for patients with known risk factors," they add.

It is also important to tell patients taking an antidepressant about the possibility of liver abnormalities, to encourage
them to report any clinical symptoms suggestive of liver problems, and to stop treatment if jaundice develops, the researchers say.

Antidepressants "should be discontinued immediately" in any patient with suspected drug-induced liver injury, they write.

Dr. Perlemuter has received travel funds from Janssen, Gilead, and Roche, consulting fees from Bayer, Biocodex, Physiogenex, and Servier, and royalties from Elsevier-Masson. The original article contains a complete list of author disclosures.

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