Alcoholic liver disease: Is acetaminophen safe?

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Evidence-based answer

Yes—acetaminophen is a safe and effective analgesic that can be appropriately used for adult patients with stable chronic alcoholic liver disease for at least a short period of time (studies have been limited to a maximum of 48–72 hours), up to the maximum recommended dosage of 4 g daily (strength of recommendation: **A**, based on 2 RCTs and other studies). There are little data to guide longer-term use of acetaminophen in this situation.

Clinical commentary

"Lesser of all evils"

Selecting an appropriate analgesic for patients with chronic alcoholic liver disease is complicated. Narcotics are potentially addictive, and nonsteroidal anti-inflammatory drugs (NSAIDs) can cause gastrointestinal bleeding and other adverse events. Alcoholic liver disease predisposes patients to these potential drug-related complications, so these options are not ideal.

Acetaminophen is the "lesser of all evils" in this population, based on some data suggesting it is safe when used within approved dosing parameters. However, these parameters vary significantly.

Although a maximum daily dose of 4 g is widely accepted as normal, the American Geriatric Society recommends no more than 2 to 3 g daily for older patients with hepatic insufficiency or a history of alcohol abuse.

Moreover, the American Liver Foundation issued a warning to not exceed 3 g daily for any prolonged period of time in response to a 2006 clinical trial that demonstrated aminotransferase increases in healthy volunteers treated with 4 g of acetaminophen daily for 14 days.[1]

Regardless of the exact maximum dose, none are greater than 4 g daily.

Always judiciously monitor dosing of acetaminophen because patients continue to experience unintentional overdose and hepatic failure caused by inadvertent use of multiple acetaminophen-containing products.[2]

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Do not exceed 3 g daily for any prolonged period, according to a warning from the American Liver Foundation

Evidence summary

Acetaminophen, while widely used, is hepatotoxic in supra-therapeutic doses.[3] Many studies purporting to show evidence of hepatic damage from therapeutic doses of acetaminophen have also been reported. Particularly in the 1970s and 1980s, there were a number of case reports and small literature reviews indicating that hepatic injury among

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Therapeutic dosing of acetaminophen in the alcoholic patient is not associated with hepatic injury

regular users of alcohol (particularly chronic alcoholics) who take acetaminophen with therapeutic intent could be a "therapeutic misadventure."[4]

Recent studies suggest short-term safety

• **A systematic review** (published in 2000) identified reports of acetaminophen toxicity, poisoning, or adverse events for alcohol patients.[5]

Researchers found 7 articles classified as Class I (studies utilizing randomized controlled trials) or Class 2 data (studies utilizing prospective, nonrandomized trials), and 20 articles that provided Class 3 data (retrospective case reviews and case reports).

The studies of Class I and 2 data indicated therapeutic dosing of acetaminophen is safe for patients with liver disease, whereas the Class 3 (lower-quality) data suggest acetaminophen is toxic for patients with liver disease.

This review concluded that, based on all the methodologically sound studies available (specifically those using the stronger evidence), therapeutic dosing of acetaminophen for the alcoholic patient is not associated with hepatic injury.

• **In a randomized, double-blinded,** placebo-controlled study, 102 alcoholic patients were given 4 g of acetaminophen daily for 2 days.[6]

Liver enzymes were monitored for an additional 2 days. There was no elevation in aminotransferases when compared with the control group of 99 patients who received the placebo. The mean AST level on day 4 was 38.0 ± 26.7 U/L in the treatment group and 37.5 ± 27.6 in the placebo group.

In this brief study, there was no increase in liver toxicity among alcoholic patients given the maximal therapeutic dose of acetaminophen.

Recommendations from others

American College of Gastroenterology. The American College of Gastroenterology states that it's generally safe to take acetaminophen in the amount specified in the package labeling. Furthermore, they recommend that patients diagnosed with liver conditions consult their physician for advice on dosing for acetaminophen or any other pain reliever.[7]

In *Liver and Biliary Disease*, the author concludes that chronic alcoholics are at increased risk for hepatotoxicity secondary to acetaminophen even at therapeutic doses; therefore, advise them to take no more than 2 g daily.[8] ■

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