



Accurate Clinic

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Tylenol (acetaminophen) Safety

The safe maximum dose of Tylenol (acetaminophen) in the presence of liver disease such as Hepatitis C is not well defined.

I recommend limiting the daily intake of Tylenol in the presence of liver disease to be no more than 2-3gms (2000-3000mg)/day and preferably under 2gms/day. At the same time, I recommend that the liver enzymes be monitored and the dose of Tylenol be modified as indicated. Finally, I advise that any patient with liver disease discuss their dosing of Tylenol with their liver specialist for further guidance.

Upon searching for guidelines, I found the following articles that shed some light on the subject, although ultimately the answer remains obscure.

Cleveland Clinic Center for Continuing Education

January 11, 2005

There is a lot of confusion about the safety (or lack of safety) of acetaminophen use in those who have established liver disease such as hepatitis C. After all, a massive overdose of this medication will cause liver failure. At the same time, modest doses of acetaminophen (for example, 3 grams per day or less) seem to be well tolerated in those with liver disease including those with hepatitis C. It should be clear that no medication including this one should be taken unless really necessary. There is a further warning for products containing acetaminophen that those who drink considerable amounts of alcohol should not use this agent. All medications have the potential to cause harm. But considering the alternatives for controlling pain and fever, acetaminophen has an excellent track record in those with hepatitis C.

Hepatitis C Association

<http://www.hepcassoc.org/news/article110.html>

Acetaminophen, When Taken as Directed, is Safe for Patients with Liver Disease

March 21, 2005

Contrary to common perception, clinical data demonstrate that acetaminophen is an appropriate pain relief choice for patients with chronic liver disease. According to a systematic literature review of the data, which is published in the current issue of the American Journal of Therapeutics, there is no evidence that acetaminophen at therapeutic doses aggravates liver disease.

Studies showed that patients with liver disease are able to metabolize acetaminophen appropriately. The review article concludes that acetaminophen at recommended doses, when taken as directed, can be used safely in patients with liver disease and is a preferred analgesic



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because it lacks the gastrointestinal toxicity, renal toxicity and inhibitory actions on platelet aggregation associated with aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs).¹

"The results of this review refute the popular misconception that liver disease patients should avoid using acetaminophen to manage their pain," said lead author Dr. Gordon Benson, professor emeritus, Department of Medicine, University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School. "Liver toxicity with acetaminophen appears to occur only in those who consume an overdose of the drug."

The studies included in the systematic literature review demonstrated:

-- Administration of the maximum recommended dose (4 g / d) of acetaminophen for 13 days to 20 patients with stable chronic liver disease did not result in any evidence of toxicity.²

-- In patients with chronic hepatitis C, administration of acetaminophen (3 g / d for seven days) did not affect serum levels of alanine aminotransferase (a common liver function test).³

-- Repeated administration of the maximum recommended acetaminophen dose for over five days to six patients with chronic liver disease did not lead to accumulation.⁴

-- Available studies in patients with chronic liver disease have shown that although the half-life of acetaminophen may be prolonged, cytochrome P-450 (CYP2E1) enzyme activity is not increased and glutathione stores are not depleted to critical levels in patients taking recommended doses.

Alcohol-associated acetaminophen hepatotoxicity has not been reported in prospective studies of alcoholics taking therapeutic doses of acetaminophen. To date, there have been no prospective studies evaluating use of acetaminophen in chronic drinkers with underlying liver disease.

"These study data provide a better understanding of how patients with liver disease are able to metabolize acetaminophen, without increased risk of hepatotoxicity," said Dr. Benson. "For liver disease patients who don't want to risk the side effects of NSAIDs, acetaminophen is a superior pain management choice."

Acetaminophen is a commonly used analgesic/antipyretic that is recommended for management of mild-to-moderate pain and fever. It has been available without a prescription for almost 50 years in the United States.⁵ It is widely accepted that acetaminophen is safe and well tolerated at recommended doses. Its analgesic and antipyretic efficacies are generally considered equivalent to those of aspirin.⁶

McNeil Consumer & Specialty Pharmaceuticals, a division of McNeil-PPC, Inc., markets prescription and over-the-counter (OTC) pharmaceutical products. The company's OTC products include complete lines of **TYLENOL®** acetaminophen, which celebrates 50 years of trust and



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innovation in 2005, and MOTRIN® IB ibuprofen for adults and children. Prescription products include CONCERTA® (methylphenidate HCl extended-release tablets) and FLEXERIL® (cyclobenzaprine HCl 5 mg tablets). Other McNeil Consumer & Specialty Pharmaceuticals brands include IMODIUM® A-D anti-diarrheal, ST. JOSEPH® 81 mg Adult Aspirin and NIZORAL® A-D Shampoo.

1 Benson GD, Koff RS, Tolman KG. Therapeutic use of acetaminophen in patients with liver disease. *Am J Ther.* 2005; 12(2): 133-141.

2 Benson GD. Acetaminophen in chronic liver disease. *Clin Pharmacol Ther.* 1983;33:95-101.

3 Dargere S, Collet T, Crampon D, et al. Lack of toxicity of acetaminophen in patients with chronic hepatitis C: a randomized controlled trial. *Gastroenterology.* 2000;118:A947.

4 Benson GD. Acetaminophen in chronic liver disease. *Clin Pharmacol Ther.* 1983;33:95-101.

5 Prescott LF. Paracetamol: past, present and future. *Am J Ther.* 2000; 7:143-147.

6 Benson GD, Koff RS, Tolman KG. Therapeutic use of acetaminophen in patients with liver disease. *Am J Ther.* 2005; 12(2): 133-141.