



AASLD Position on Acetaminophen

Acetaminophen is the most widely used analgesic in the world, and is a major ingredient in more than 300 over the counter headache and cold formulations and prescribed medications in the United States.

Rates of both adult and pediatric acetaminophen related toxicity have been increasing steadily over the past decade. As a result, acetaminophen is now the most common cause of acute liver failure, and causes liver failure three times as often as all other drugs combined.

In 2005 acetaminophen toxicity led to 106,000 emergency room visits in adults and 25,000 visits in children. In that year, 73,000 patients were hospitalized and there were 333 deaths. Most emergency room visits, hospital admissions and deaths resulted from acetaminophen taken in combination with other agents.

Half the all acetaminophen-related liver failure cases are unintentional, occurring when acetaminophen is inadvertently taken in combination with other analgesics or when taken with alcohol. In addition, more than 35% of unintentional overdoses involve use of different formulations taken simultaneously. In addition, narcotic containing acetaminophen compounds, the top generic prescription drug in the US, represent a problem in this regard as well. Evidence from the Acute Liver Failure Study Group

suggests that narcotic compounds are involved in 2/3 of the unintentional cases. Many patients tell us that they have taken the narcotic to excess for weeks or months. We suspect that a gradual increase in dose occurs due to addiction, eventuating in overdoses that do not differ clinically from one-time overdoses.

In summary, acetaminophen poisoning often involves multiple preparations taken simultaneously, the use of narcotic combinations and impulsive behavior involving lack of understanding of possible injury related to these behaviors.

It is now clear that regulatory interventions can reduce acetaminophen toxicity. For example, legislation introduced in the United Kingdom in 1998 limits the maximum number of tablets sold at one time, highlights the dangers of acetaminophen overdose using explicit warning labels and mandates blister-packaging. Within a year following introduction of this legislation, deaths from acetaminophen decreased by 21% with a simultaneous 66% decrease in liver transplantation for acetaminophen related acute liver failure. Despite these interventions, the total number of acetaminophen tablets sold did not decrease significantly.

When the Food and Drug Administration (FDA) Advisory Committee on Non-Prescription Drugs (NDAC) last met in September 2002, their discussion of changes in package labeling for acetaminophen and the problem of unintentional overdoses did not consider the issue of suicidal ingestions or potential strategies to prevent unintentional or

suicidal overdoses, such as limiting package size, blister packing or unbundling of the narcotic-acetaminophen compounds.

The Acute Liver Failure Study Group and the American Association for the Study of Liver Diseases propose that the FDA convene the NDAC to provide recommendations to reduce both unintentional and suicidal overdoses by using the following strategies:

More Explicit Packaging to Reduce Unintentional Overdoses:

1. Mandatory clear labeling of all acetaminophen preparations outlining:
 - a. Risk of exceeding the recommended daily dose.
 - b. Risk of combining acetaminophen with alcohol.
 - c. Clearer labeling of acetaminophen in combination products.
 - d. More detailed labeling should provide specific information that acetaminophen overdoses can kill.
2. Each combination medication should include acetaminophen on the front of the package in a large font.

Unbundling of Prescription and Non-Prescription Narcotic-containing Compounds.

1. Hydrocodone and acetaminophen do not need to be combined. Acetaminophen is not necessary or should be provided in lower doses per capsule.

Reducing Overdose with Suicidal Intent:

1. Use of blister-packaging to limit impulsive overdoses.
2. Limiting the number of capsules available for purchase to 16 or 24.

The above position was authored by Jonathan Schwartz, MD; Todd Stravitz, MD; and William M. Lee, MD of the ALF Study Group