Brief safety updates: acetaminophen, ASA and kava

Acetaminophen — unintentional overdoses: Accidental overdoses of acetaminophen are the most common cause of acute liver failure in the United States. For this reason, the US Food and Drug Administration (FDA) may seek to strengthen warning labels for products containing the drug. An FDA scientific advisory committee recommended stronger warnings on packaging after reviewing data including the results of a study involving 258 patients with acute liver failure (ALF) admitted to 17 US academic liver units between January 1998 and October 2000.[1] In the study, acetaminophen was the most common cause of hepatotoxicity and was involved in 38% of the cases of ALF. Of the cases of acetaminophen poisoning, 60% were unintentional overdoses and 38% were suicide attempts. Many of the patients with acetaminophen-related overdoses were seriously harmed: one quarter died, 6% required a liver transplant to survive and about two-thirds recovered spontaneously.[1] The FDA committee also considered data from over 300 cases of acetaminophen-related hepatotoxicity reported to the FDA between 1998 and July 2001.[2] About 60% of the adult cases were in women, 60% of all cases were classified as "severe life threatening liver injury and liver failure" and 8% involved children less than 12 years old.[2] For all adult patients with hepatotoxicity, the mean daily dose of acetaminophen consumed was 6.5 g per day (the median dose was 5 g per day). In 22% of cases, the patient was taking 4 g or less per day.[2] Acetaminophen overdoses are the cause of over 56 000 emergency department visits annually in the United States.[3]

Current recommendations are that adults should not consume more than 4 g of acetaminophen per day (maximum 65 mg/kg per day for children),[4] but if a patient also consumes more than 3 drinks of alcohol a day[5] even that limit may be too high. Many of the accidental poisonings relate to patients exceeding the limit by inadvertently combining preparations of straight acetaminophen with over-the-counter "cold and flu" preparations or opioid combination products (such as Tylenol No. 3 and Percocet).[3] Underlying susceptibilities related to gender, comorbidities or variations in an individual's ability to process the drug may also be involved.[2,3] The number of cases of hepatotoxicity that occur each year in Canada is not known, and Health Canada is not currently reviewing the packaging and warning labels for the drug in this country.

ASA — indications advertised incorrectly: Acetylsalicylic acid (ASA) was recently approved by Health Canada as being indicated for the primary prevention of nonfatal myocardial infarction (MI) in doses of 325 mg or 81 mg (coated)[6] but was also incorrectly promoted for the primary prevention of cerebrovascular accidents (CVA). Bayer is notifying Canadian physicians of the error[7] and is clarifying that ASA is indicated for reducing:

- first, nonfatal MI (but not first, fatal MI) in patients at risk of MI
- vascular mortality in patients with a suspected acute MI
- morbidity and death in patients with unstable angina and previous MI
- transient ischemic attacks (TIAs) and risk of subsequent atherothrombotic CVA (but not first strokes, fatal or nonfatal)
- TIA recurrence after carotid endarterectomy and in hemodialysis patients with silicone rubber arteriovenous cannulas
- venous thromboembolism after total hip replacement
- general pain, fever and inflammation.

The benefits of prescribing ASA for the above indications need to be weighed against the risks of gastrointestinal bleeding, ASA's renal effects and the small but not insignificant increase in the risk of hemorrhagic CVA.[7]

Kava sales stopped: Amid international concern regarding the serious hepatotoxicity associated with kava,[8] Health Canada has stopped sales of the over-the-counter herbal sleep and relaxation aid.[9] Kava, which is known by a variety of names, has been associated with 4 reported cases of hepatotoxicity in Canada (none fatal).[9] Other known adverse effects include a pruritic skin condition (kava dermopathy) and problems with muscle weakness and coordination. Health Canada has ordered stores to withdraw the products and requests that physicians report suspected cases of kava toxicity.

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References

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