Acetaminophen Poisoning: The Pharmacist's Role in Prevention

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Case: A 52 y/o woman was seen in hospital for possible sepsis. A high serum acetaminophen level, increased creatinine, and severely elevated liver enzymes, INR, and lactate were found on the initial workup. She had been taking acetaminophen with codeine and extra strength acetaminophen chronically for arthritis pain. Despite the antidote and aggressive supportive care, she developed encephalopathy and died on her ninth hospital day.

Acetaminophen (**a**cetyl-***p***-**a**mino**p**henol, APAP) poisoning is the leading cause of liver failure in the western world and is a public health problem.[1] The BC Drug and Poison Information Centre (DPIC) helped manage over 1,900 acetaminophen poisonings and overdoses in 2014. Many, like the case above, were potentially preventable, but the issues are complex. For National Poison Prevention Week (March 15-21, 2015), we would like to highlight acetaminophen poisoning and what pharmacists can do to help.

Toxicity

Acetaminophen at normal doses (up to 75 mg/kg/d for children under 12 years, and up to 4,000 mg/d in adults) is generally safe, although there is evidence that some patients may have toxicity at lower doses.[2] With excessive dose, liver damage (caused by a reactive metabolite that is normally detoxified by glutathione) is the main toxic effect. N-acetylcysteine, a glutathione precursor, is very effective in preventing and treating liver damage from acetaminophen when used early, but its effectiveness decreases with time once a toxic exposure has occurred.[3] Patients who delay seeking medical attention after an acute overdose or those who have taken excessive amounts over time due to therapeutic error or misuse are at risk for more severe outcomes. If untreated, a toxic APAP exposure may progress to acute liver failure with coagulopathy, renal failure, metabolic acidosis, and encephalopathy. About one-third of patients who develop acute liver failure will die without a transplant.[4] Early coma and acidosis (before liver damage) can also occur in massive overdose due to mitochondrial dysfunction.[5]

Who gets poisoned and why? DPIC's experience

Children 5 years and younger

Almost all of the 783 APAP exposures in this age group were unintentional and included 160 therapeutic errors. Common scenarios included products within easy reach, double doses, confused measurements. Most of these exposures were managed at home, but there were still over 110 hospital visits and several hospital admissions as a result.

Older children and adolescents aged 6-19 years

In this age group the majority (80%) of the almost 300 exposures were intentional, leading to almost 200 hospital visits and over 100 hospital admissions.

Adults 20 years and older

In adults, suspected suicide accounted for 46% of the 829 exposures, while misuse, abuse, and unintentional therapeutic error accounted for 41%. Adult APAP poisonings led to almost 600 hospital visits and over 300 admissions. While most hospitalisations involved intentional overdose, 36 hospital admissions were for unintentional overdose. Five patients died.

Factors associated with APAP overdose are numerous and beyond the scope of this article. However, a few points from the literature are notable:

- Intentional overdose: Availability has been identified as a main reason for choosing APAP for overdose. In one study, half of the patients who overdosed on APAP took the overdose less than an hour after thinking about it; two thirds of these took what was already in the home.[6]
- Unintentional overdose: In one survey, patients with chronic or ongoing pain were more

likely (odds ratio [OR] 4.6-4.9) to take more than 4 grams of acetaminophen per day. Reading the label did not reduce that risk, but knowledge that APAP was an ingredient, knowledge of the labelled per-dose and daily maximums, and having the attitude of starting with low doses (increasing as necessary) were associated with lower risk (OR 0.5-0.6).[7]

Prevention and the pharmacist's role[10,11]

Efforts to reduce intentional and unintentional poisonings have been made at the regulatory and industry level, with the US and UK leading the way. Examples include restricting availability, improving packaging and labelling, reformulating products and reducing recommended doses, and awareness campaigns.[2,8-10] Examining all the prevention options is beyond the scope of this article. However, pharmacists play an important role in the safe use of acetaminophen, and given its widespread use, individual efforts may save a liver or a life:

- encourage patients to check ingredients and doses, and help them understand labels
- encourage patients to use the lowest effective dose and increase only if needed; counsel patients, especially those with chronic pain, not to exceed recommended doses
- consider lowering maximum daily dose in patients with chronic liver disease and in those taking other potentially hepatotoxic phamaceuticals including natural and herbal products.
- ask about other acetaminophen use when dispensing or recommending a product with acetaminophen, and ensure patients understand the total amount of acetaminophen from all sources that they can safely take
- ensure caregivers understand how to dose children's acetaminophen products - provide the proper dose for a child's age and weight, demonstrate dosing devices
- encourage safe storage and disposal of all medications

For more patient education tips on acetaminophen use:

http://www.safemedicationuse.ca/newsletter/newsletter_Acetaminophen.html

http://www.knowyourdose.org/

If you suspect overdose call the Poison Control Centre at 604-682-5050 or 1-800-567-8911.

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We are grateful to all the First Nations who have cared for and nurtured the lands and waters around us for all time, including the x?m??k??y??m (Musqueam), Sk?wx?wu?7mesh U?xwumixw (Squamish Nation), and s?l?ílw?ta? (Tsleil-Waututh Nation) on whose unceded and ancestral territory our centre is located.