Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

ToxTidbits: Antidote Facts

1-800-222-1222

Acetylcysteine (oral)

Acetaminophen is a commonly used analgesic and antipyretic. Acetaminophen toxicity may occur acutely when supratherapeutic amounts are ingested purposefully or unintentionally, or chronically when supratherapeutic amounts are ingested over an extended period of time. Liver failure, including coagulopathy and hepatic encephalopathy, and kidney failure may occur in severe toxicity. However, if treated early, patients with acetaminophen poisoning generally recover uneventfully.

Mechanism/Indications: Acetaminophen is metabolized to a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI), that is detoxified by conjugation with glutathione. In overdose, hepatic stores of glutathione are depleted and NAPQI binding to hepatocytes induces cell death and hepatic necrosis. Acetylcysteine replenishes hepatic glutathione and may also act as a glutathione substitute, combining directly with the toxic metabolite. Additionally, acetylcysteine acts as a free radical scavenger, reducing the cytotoxic effect of NAPQI. Acetylcysteine should be considered in any patient who presents with a serum acetaminophen concentration above the toxicity line on the Matthew-Rumack nomogram, or those patients with ingestion of greater than 200 mg/kg or 10 grams (whichever is less) and unknown time of ingestion or acetaminophen concentration will not be available within 8 hours. Acetylcysteine should also be considered in repeated supratherapeutic ingestions and in patients presenting with hepatotoxicity and history of acetaminophen use. In addition, oral acetylcysteine may be indicated in patients that experience serious adverse reactions with intravenous acetylcysteine.

Adverse Effects/Contraindications: Nausea, vomiting and diarrhea are common. The only contraindication to oral acetylcysteine use is hypersensitivity to the medication.

Dosing for acute overdose: Adults and children should receive a 140 mg/kg loading dose, followed by 70 mg/kg every 4 hours for 72 hours (a total of 17 maintenance doses). Some patients may be candidates for a shorter duration of therapy (36 hours); contact the Poison Center for recommendations. Methods used to limit nausea and vomiting include premedication with anti-emetics, diluting the dose 1:4 with soda or juice, and administering via nasogastric tube. If the dose is vomited within one hour of administration, the Maryland Poison Center recommends repeating it.

Dosing for repeated supratherapeutic overdose: Initiate therapy as above. Discontinue when acetaminophen concentration is undetectable and liver enzymes are clearly declining. Call the poison center for specific patient guidelines on dosing and discontinuation of acetylcysteine.

(cont. on pg. 2)

Acetylcysteine (continued)

For more on oral acetylcysteine:

- *Betten DP, Cantrell FL, Thomas SC, Williams SR, Clark RF. A prospective evaluation of shortened course oral N-acetylcysteine for the treatment of acute acetaminophen poisoning. Ann Emerg Med 2007;50(3):272-279*
- *Bond GR. Is oral acetylcysteine protocol the best treatment for late-presenting acetaminophen poisoning? Ann Emerg Med 2009;54:625-627.*
- *Heard KJ. Acetylcysteine for acetaminophen poisoning. NEJM 2008;359(3):285-292.*
- *Hendrickson RG, Howland MA. Antidotes in Depth: N-Acetylcysteine. In: Hoffman RS, Howland MA, Lewin NA Nelson LS, Goldfrank LR, editors: Goldfrank's Toxicologic Emergencies. 10th ed. New York NY, 2015;465-472.*
- *Yarema MC, Johnson DW, Berlin RJ, et al. Comparison of the 20-hour intravenous and 72-hour oral acetylcysteine protocols for the treatment of acetaminophen poisoning. Ann Emerg Med 2009;54(4):606-614.*

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