Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

ToxTidbits: Antidote Facts

1-800-222-1222

Acetylcysteine (intravenous)

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, intravenous acetylcysteine is indicated in patients unable to tolerate oral acetylcysteine, and patients who present with evidence of fulminant hepatic failure.

Adverse Effects/Contraindications: Caution should be used in patients who have experienced previous hypersensitivity or anaphylactoid reactions with IV acetylcysteine, as well as in patients with asthma. The most common anaphylactoid reactions include rash, flushing, and bronchospasm.

Dosing: Adults and children should receive 150 mg/kg administered over 60 minutes, followed by 50 mg/kg administered over 4 hours, followed by 100 mg/kg administered 16 hours. The total dose is 300 mg/kg delivered over 21 hours. AST/ALT, INR, and acetaminophen level should be checked before discontinuing the IV acetylcysteine after 21 hours, because longer infusions may be necessary in some patients based on these and other criteria. Dilution volume should be reduced in patients weighing < 40 kg in order to avoid complications of fluid overload. Please call the Maryland Poison Center for specific dosing information for adults and pediatrics.

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 intravenous acetylcysteine:

- *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.*
- *Doyon S, Klein-Schwartz W. Hepatotoxicity despite early administration of intravenous N-acetylcysteine for acute acetaminophen overdose. Acad Emerg Med 2009;16(1):34-39.*
- *Klein-Schwartz W, Doyon S. Intravenous acetylcysteine for the treatment of acetaminophen overdose. Expert Opin Pharmacother 2011;12(1):119-30.*
- *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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