Clinical Practice Algorithm
Acetaminophen Overdose Management in Adults

Presentation

This algorithm only deals with the management of a toxic ingestion of acetaminophen. A toxic ingestion of acetaminophen is considered ≥150mg/kg in a patient without risk, or ≥75mg/kg in a patient with risk*. Many preparations contain other agents and many patients ingest multiple agents; these other agents need to be considered separately. **This algorithm does not address treatment of overdose with extended release acetaminophen products; please refer to the Drug Poison Information Center (DPIC) 513-558-5111.**

Single ingestion ≤ 8 hours after ingestion?

Yes

Check acetaminophen level. *N*-acetylcysteine loading dose should be given pending the level; if waiting for the lab results would delay treatment beyond 8 hours from ingestion

Level above nomogram line?

Yes

Treat with *N*-acetylcysteine using **Treatment Box.** Send baseline LFTs, INR, renal panel.

No

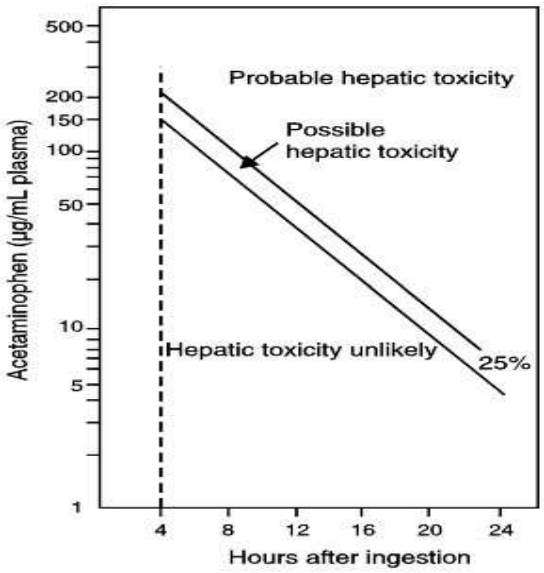
No need for *N*-acetylcysteine?

No

1. ≥8 hours after ingestion
2. Chronic or repeated ingestion
3. Ingestion at unknown time

***Some patients may be at higher risk for liver damage from acetaminophen overdose.**
1. Chronic alcohol use
2. Use of drugs that are enzyme-inducers
3. Malnutrition, HIV, cystic fibrosis, eating disorder

Acetaminophen Toxicity Nomogram



The Rumack-Matthew nomogram, relating expected severity of liver toxicity to serum acetaminophen concentrations.

From Smilkstein MJ, Bronstein AC, Linden C, et al, "Acetaminophen Overdose: A 48-Hour Intravenous N-Acetylcysteine Treatment Protocol," *Ann Emerg Med*, 1991, 20(10):1058, with permission.

TREATMENT BOX

Choosing *N*-acetylcysteine route:

Oral administration of *N*-acetylcysteine is preferred if the patient is cooperative because of safety and drug cost. IV *N*-acetylcysteine (Acetadote®) is FDA approved as safe and effective, but is more expensive and carries a higher risk of anaphylactoid reaction. IV use may be considered at the treating physician's discretion. The following are suggested indications for IV *N*-acetylcysteine:

- Intolerability of oral *N*-acetylcysteine despite adequate anti-emetics
- Coingestant with potential for morbidity necessitating ongoing GI decontamination
- GI bleeding or obstruction
- Medical or surgical conditions precluding oral *N*-acetylcysteine administration
- Acetaminophen toxicity presenting with or developing encephalopathy or hepatic failure (only published experience is with IV *N*-acetylcysteine)

Oral Dosage:

- 140mg/kg followed by 70mg/kg every 4 hours until 36 hours post-ingestion or 36 hours post-arrival if time of ingestion unknown (see stopping *N*-acetylcysteine)
- Repeat dose if emesis occurs within 1 hour of administration
- If emesis occurs, administer ondansetron 4mg IVPB prior to repeating dose or switch to intravenous dosing

IV Dosage:

The following protocol is FDA approved for single ingestions < 8 hours post-ingestion:

- 150mg/kg *N*-acetylcysteine in 200mL of 0.45% Sodium Chloride over 60 minutes followed by
- 50mg/kg *N*-acetylcysteine in 500mL of 0.45% Sodium Chloride over 4 hours (125mL/hour) followed by
- 100mg/kg *N*-acetylcysteine in 1000mL of 0.45% Sodium Chloride over 16 hours (62.5mL/hour)

Stopping *N*-acetylcysteine:

At the end of the 20-hour IV protocol for single ingestions < 8 hours post-ingestion, or at 36 hours post-ingestion for all other patients (including those with oral treatment, multiple or chronic supratherapeutic ingestions, unknown time of ingestion, or late presentation), blood is sent for acetaminophen level, LFTs, INR and renal profile. If the acetaminophen level is zero and the other labs are normal, *N*-acetylcysteine may be discontinued.

All patients with a measurable acetaminophen level or evidence of hepatic or renal injury should *N*-acetylcysteine continued either orally at 70mg/kg every 4 hours or IV at 150mg/kg/24 hours until the acetaminophen level is undetectable, symptoms are resolving, and laboratory indices of hepatic and renal function are either normal or improving (some recommend waiting until post-peak transaminases are < 1,000 IU with resolving symptoms). Labs are usually rechecked at least every 24 hours, more frequently in severe illness as clinically appropriate for the specific patient (e.g. glucose measurements are often more frequent).

Treating reactions *N*-acetylcysteine:

Pruritus, rash and urticaria are common adverse reactions which usually occur near the end of the administration of the loading dose. These symptoms will often resolve with use of antihistamines and reduction or temporary cessation of *N*-acetylcysteine administration. If these symptoms fail to resolve or if more serious signs of anaphylactoid reaction develop such as shortness of breath or hypotension, *N*-acetylcysteine should be discontinued immediately, appropriate therapy undertaken (including antihistamines as well as epinephrine in severe cases), and the patient should be considered allergic to *N*-acetylcysteine from then on. Other adverse reactions include ear pain, nausea and vomiting, tachycardia, skin flushing, pharyngitis, and rhinorrhea.

Contraindications: *N*-acetylcysteine is contraindicated in patients with known hypersensitivity to *N*-acetylcysteine.

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