Treating acetaminophen overdose

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1 Acetaminophen overdose remains common

A billion doses of acetaminophen are taken safely each year, but 10 000 people in Canada overdose on this medication annually. About one-third are hospitalized for treatment with the antidote, acetylcysteine, and 1%–2% die.[1] Most fatalities result from delayed presentation after deliberate overdose, or from excessive dosing for fever or pain over several days.

2 Clinicians should treat overdoses empirically with acetylcysteine, unless clearly unnecessary

Because the efficacy of acetylcysteine is highly time-dependent, it can be started for any acetaminophen overdose.[2] For acute overdoses that occurred at a reliably known time, acetylcysteine is not needed provided that the patient's peak acetaminophen concentration is below the Rumack–Matthew nomogram treatment line. Death from acetaminophen-induced liver failure is rare if acetylcysteine is started promptly. Dosed correctly, adverse reactions are rarely life-threatening.[3]

3 Acetylcysteine should be continued until the patient meets stopping criteria based on individualized serial testing

Although original treatment protocols stipulated a fixed treatment duration (e.g., 20 h), medical toxicologists now recommend a patient-tailored approach to reduce both over- and undertreatment.[2,4] Serial testing permits more accurate risk stratification and often shortens treatment. Acetylcysteine can be safely stopped when the patient's acetaminophen concentration is undetectable, liver function tests are improving, and the patient is not encephalopathic (Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.210703/tab-related-content).[2,4,6] Acetaminophen concentrations should fall tenfold every 12 hours if absorption is complete and liver function is normal.

4 Massive overdose with early-onset coma and lactic acidosis requires more intense treatment

Acetaminophen directly affects mitochondrial function. Within hours of massive ingestion (i.e., > 600 mg/kg, serum acetaminophen several-fold higher than the treatment threshold), it causes coma, acidosis and hypothermia. Hemodialysis and higher doses of acetylcysteine may be warranted in this context.[5]

5 A medical toxicologist should be consulted for the most current recommendations.

Some poison centres, including those in Ontario and Alberta, now recommend a standardized 1- or 2-bag (i.e., admixture) acetylcysteine infusion protocol. In contrast, the original protocol involved preparing 3 distinct, weight-based bags, which contributed to dosing interruptions and errors.[6] Furthermore, higher acetylcysteine dosing is now recommended for persistently elevated acetaminophen concentrations, and adjunctive fomepizole can be used for the highest-risk patients.

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