ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

"How long do I need to watch this patient?"

Emergency departments are busy environments and adequate patient flow is crucial to keep them operating efficiently. Although poison centers are often asked "how long do I need to watch this patient?", this question doesn't always have a clear answer.

In an asymptomatic patient, clinicians often call to ask when we would expect to see symptoms. The answer varies widely depending on the clinical situation, ingested agent, formulation, amount, and if there are co-ingestants. Many immediate release medications have an onset of approximately 30 minutes to 4 hours depending on pharmacokinetic/pharmacodynamic interactions. However, this may be altered in overdose. Four drugs provide excellent examples. Acetaminophen overdoses are associated with slow gastric emptying (see figure) *(Am J Emerg Med 2004;22:548-54)*. Aspirin forms a pharmacobezoar; in one study the longest delay to a measurable serum salicylate concentration was 225 minutes *(Clin Toxicol 2018;11:1-4).* Bupropion is available as extended release and has a toxic metabolite; one study showed a mean time to seizure of 7 hours with a maximum delay of 24 hours *(Am J Emerg Med 2009;27:911-5)*. Finally, valproic acid demonstrates slow absorption in overdose. A patient about which our poison center was consulted had 4 plasma valproic acid concentrations over an 8-hour period that were very low (< 10 mcg/mL) and subtherapeutic, but climbed to almost twice the maximum therapeutic concentration 14 hours after ingestion. We take all of these factors into account when making recommendations about minimum periods of observation for patients. In the asymptomatic patient, the answer should be and usually is… it depends.

Another question we are asked is "how long will symptoms last?". Again, the answer varies. Not only is absorption affected by large doses, but also metabolism and elimination can be affected by elevated concentrations. Phenytoin, for example, is poorly absorbed in large overdoses. In addition, its elimination changes from first-order (50% reduction over a period of time) to zero-order (fixed amount removed per period of time) when serum concentrations are above the therapeutic range. The half-life of phenytoin ranges from 7-42 hours, due to changes in metabolism at different serum concentrations. Practically speaking, 5 half-lives removes ~97% of any xenobiotic, which is great, as long as 3% of the original serum concentration is not enough to produce symptoms. Take baclofen, for example. If the peak concentration is 15 mcg/mL following an overdose, at five half-lives the serum concentration is 0.46 mcg/mL. This concentration can result in severe effects including seizures, PVCs, hypertension, bradycardia, and hypothermia *(Pediatrics 1998;101:1045-8).* So, if asked when a symptomatic patient will be clear of toxic effects, the answer should be and usually is… until they're asymptomatic.

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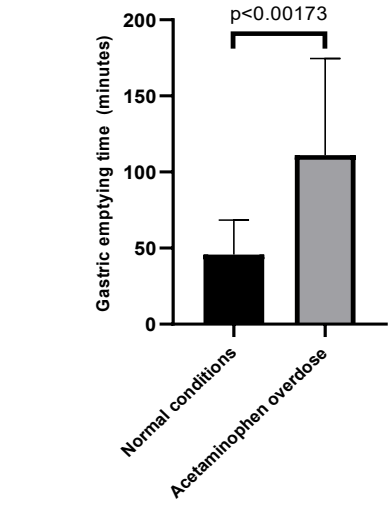

This figure shows the time to emptying of 50% of stomach contents after overdose of acetaminophen and under normal conditions. The doubling of gastric emptying time suggests that acetaminophen slows gastric emptying. *(Am J Emerg Med 2004;22:548-54)*

Did you know?

Multiple examples reinforce the concept of delayed absorption after overdose.

Medical examiners have described finding a paste of pills and gastric fluids in patients who died of acetaminophen overdose. Additionally, in a prospective study designed to investigate pill burdens after oral overdoses, endoscopy identified pill contents in 19/42 patients between 2 and 4 hours after ingestion, and in 3 patients, pill contents were identified after 12 hours. This was seen regardless of the type of medication ingested *(Medicine 2015;94(4):e463).*