

Comment on Fomepizole and Acetaminophen Overdose

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We read with interest the case report by Haider et al.¹ However, the title incorrectly asserts “severe acetaminophen toxicity”, which was clearly absent in this case. For more than 4 decades, we have defined “toxicity” by elevated transaminase activities and “severe toxicity” by either aspartate transaminase or alanine transaminase $\geq 1,000$ IU/L.² If the patient’s transaminases do not increase, there is no toxicity. Prompt treatment with IV N-acetylcysteine (NAC) and fomepizole prevented hepatotoxicity, although IV NAC alone likely would have been sufficient because of the timely start of antidotal treatment.

Fomepizole fully blocks CYP2E1 and prevents oxidative metabolism of acetaminophen (APAP).³ Although the co-ingested oxycodone likely delayed complete absorption of APAP, fomepizole prolongs the elimination half-life.⁴ Rampon et al described 6 patients with similarly high APAP concentrations who received IV NAC and fomepizole. Five of the 6 had normal transaminases throughout their course, and the sixth had the highest aspartate transaminase and alanine transaminase of 51 and 79 IU/L, respectively. Five of the 6 also had APAP concentration curves that paralleled the treatment line, which suggested an approximate half-life of 4 hours (Figure 1).

Indications for fomepizole in acute APAP overdose are evolving, but the current data comprise only case reports (of which this is another) and small case series. Some authors suggest thresholds of any [APAP] >600 mg/L, any cross product of [APAP] and the higher transaminase $>10,000$ IU-mg/L², or any APAP overdose with metabolic acidosis.⁵ However, we often consider adding fomepizole for patients with [APAP] above the 300 line.

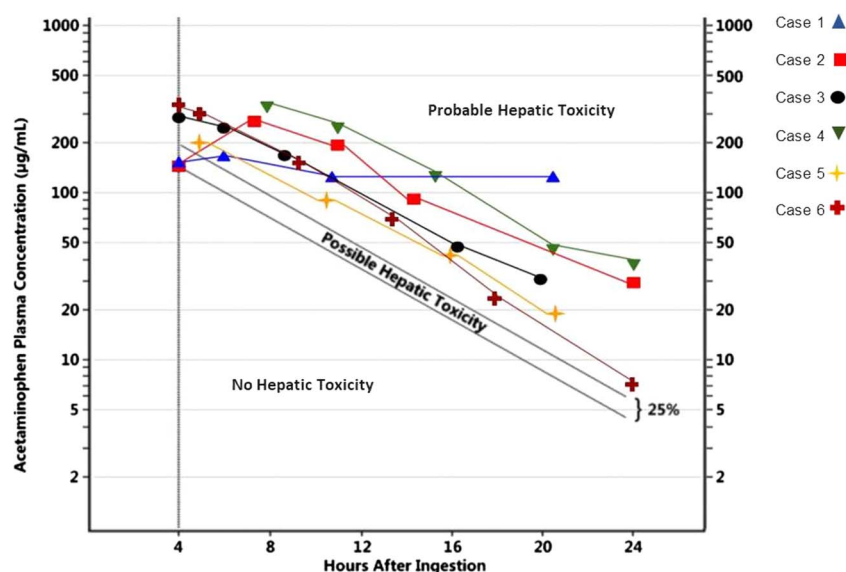


Figure 1. Serial acetaminophen concentrations in 6 patients treated with IV N-acetylcysteine and IV fomepizole from Reference 5 (available as open access under Creative Commons CC BY license).

REFERENCES

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