

DOUBLE-PEAKED ACETAMINOPHEN CONCENTRATION SECONDARY TO INTESTINAL TRAUMA

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ABSTRACT

Background

Reduced gastrointestinal motility can alter the toxicokinetics of acetaminophen poisoning. We report a case of altered acetaminophen toxicokinetics due to delayed gastrointestinal absorption, likely secondary to intestinal trauma/surgery.

Case Report

A 37-year-old woman ingested an unknown amount of acetaminophen and ethanol then stabbed herself in the abdomen. The initial acetaminophen was 1,285.9 µmol/L and the time of ingestion was not known. Intravenous acetylcysteine protocol was started. She developed an ileus post-surgery for the stab wounds. At 31 hours post-presentation, the acetaminophen returned undetectable, and the transaminases were normal. After the resolution of the ileus, repeated acetaminophen peaked at 363.3 µmol/L 52 hours post-admission. At 76 hours post-admission, the acetaminophen was undetectable, and transaminases and coagulation parameters were normal.

Conclusions

Reduction in gastrointestinal motility secondary to trauma and/or surgery must be considered when determining when to initiate or discontinue treatment as well as how long to monitor acetaminophen concentrations.

Key Words: *Acetaminophen, intestinal trauma, gastrointestinal motility, toxicokinetics*

Case Presentation

A 37-year-old, 80 kg woman with a history of chronic depression and suicide attempts was found unresponsive after ingesting an unknown amount of acetaminophen (APAP) and ethanol. She presented with five self-inflicted stab wounds to the abdomen. On arrival, her vital signs were: blood pressure 90/50 mmHg, heart rate 130/minute, respiratory rate 30/minute and Glasgow coma score 10. Endotracheal intubation was performed upon arrival to the Emergency Department (ED). Local wound exploration revealed peritoneal violation.

Gastrointestinal decontamination was not attempted, and the patient was taken for exploratory laparotomy. The initial APAP concentration 2 hours after arrival was 1,285.9 µmol/L, and the time of ingestion was unknown. The initial liver transaminases and INR were within normal limits (Table 1). The serum ethanol concentration was 43.5 mmol/L. Intravenous acetylcysteine (NAC) was initiated in the operating room 2 hours after the patient arrival. The APAP concentration 8 hours post-admission was 487.6

µmol/L. After 21 hours of the NAC protocol, APAP concentration returned at 68.9 µmol/L, and a decision was made to continue NAC infusion at 6.25 mg/kg/h and to repeat the APAP concentration measurement in 4 hours because APAP was still detectable and the patient had an ileus. The APAP concentration was undetectable 31 hours post-admission. However, due to a postoperative ileus, a decision was made to continue NAC treatment and repeat the APAP measurement 4 hours later as APAP absorption may resume after resolution of the ileus. Upon resolution of the ileus, the repeated APAP concentration at 37 hours post-admission was 87.9 µmol/L. At 38 hours post-admission she

was given 650 mg of APAP via rectum as prescribed by the pain service. The incident was reported upon discovery. No other APAP doses were given. The APAP concentration peaked (second peak) at 363.3µmol/L, 52 hours post-admission. On day 4, the ileus resolved, and the APAP concentration returned to <66.0 µmol/L (undetectable); therefore, the NAC infusion was discontinued. Transaminases remained within normal limits throughout hospitalization, and the INR peaked at 1.44, 31 hours post-admission, and was considered secondary to the NAC treatment.

TABLE 1 Laboratory Results Values

Time since admission (Hours)	2 H	8 H	21 H	31 H	37 H	42 H	52 H	76 H
APAP level (µmol/L)	1,285.9	487.6	68.9	<66	87.9	259.3	363.3	<66
AST (IU/L)	18	NA	32	25	21	18	15	12
ALT (IU/L)	25	NA	25	30	22	18	17	21
INR	1.08	NA	1.38	1.44	1.32	1.17	1.15	1.11
Creatinine (µmol/L)	59	NA	42	45	37	37	44	40

Note. APAP: acetaminophen, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, INR: International normalised ratio, IU: international unit, NA: not available

DISCUSSION

Delayed acetaminophen peak concentration and a second peak are important toxicokinetic features when acetaminophen overdose is accompanied by reduced gastrointestinal motility due to co-ingestion of medications or trauma. The above case illustrates the importance of considering altered gastrointestinal absorptive capacity when treating patients with APAP overdose who have sustained abdominal trauma, received surgery, or developed an ileus for other more common reasons i.e. infections or medications. Our literature review revealed no cases of delayed acetaminophen peak concentration or a second

peak following abdominal trauma or surgery. The literature is rich with cases of delayed peak APAP concentration or a second peak due to medication co-ingestions or ingestion of extended release APAP products. In a prospective volunteer study, the time to reach the peak APAP concentration was significantly longer when oxycodone was co-administered with APAP compared to APAP alone or with diphenhydramine (2.87 hours vs. 1.72 and 1.90 hours, respectively).¹ Tighe and Walter reported a delayed toxic peak APAP concentration at 6.75 hours in a 20-year-old woman who co-ingested 13 g of APAP, 2 g of propoxyphene napsylate and 3.75 g of naproxen; she had a nontoxic 4-hour concentration.² In a

case series of 20 patients who had a nontoxic initial APAP concentration at a median time of 4.2 hours (range 4.0–6.3 hours) and a toxic subsequent concentration, the majority of patients ingested APAP-combination products, mostly antihistamines or opioid-containing products.³ An APAP concentration with a double or bactrian peak has been reported in several cases, and most of these were associated with co-ingestion of diphenhydramine or opioids.^{4,6} Both opioids and antihistamines are known to reduce intestinal motility and therefore may delay the absorption of several xenobiotics. This case is unique for two reasons: (1) delayed absorption secondary to trauma and/or surgery rather than co-ingestion and (2) the undetectable APAP concentration prior to the second peak. The possibility of a repeat in-hospital APAP overdose cannot be completely eliminated; however, the patient was under close observation. Although, our patient received 650 mg of APAP for pain control, the second rise in the acetaminophen concentration started prior to the administration of that dose and the peak was higher than would be expected from such dose (expected peak after 650 mg dose ranges from 8 to 20 µg/ml (52.96 to 132.4 µmol/L), our patient had a peak of 363.3 µmol/L).⁷

Patients with APAP overdose who have concomitant painful conditions are at risk of receiving APAP to treat pain. Thus health care teams taking care of such patients must be aware that prescribing APAP to these patients is contraindicated. It might be useful to write in the patient medication record a sentence like “no APAP allowed”. Following a conservative approach, given that APAP was still detectable 3 days post ingestion, criteria to terminate NAC therapy was not met and therefore NAC was continued until APAP was undetectable.

CONCLUSION

Reduction in gastrointestinal motility secondary to trauma/surgery must be considered when determining when to initiate or discontinue treatment, as well as how long to monitor APAP concentrations.

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