Pitfalls of Early Acetaminophen Concentration in Prediction of Toxicity

Spyres MB, O'Connor AD
Department of Medical Toxicology, Banner – University Medical Center Phoenix, AZ

Background

- The value of plasma APAP levels <4 hrs post-ingestion in predicting toxicity has not been established.
- Some authors suggest a >1 hr post-ingestion level <100 mcg/mL excludes the need for therapy[1], and others state an undetectable level between 1 and 4 hrs post-ingestion can exclude significant toxicity.
- This case series illustrates that early APAP levels are unreliable and should not be used to predict toxicity.

Case Series

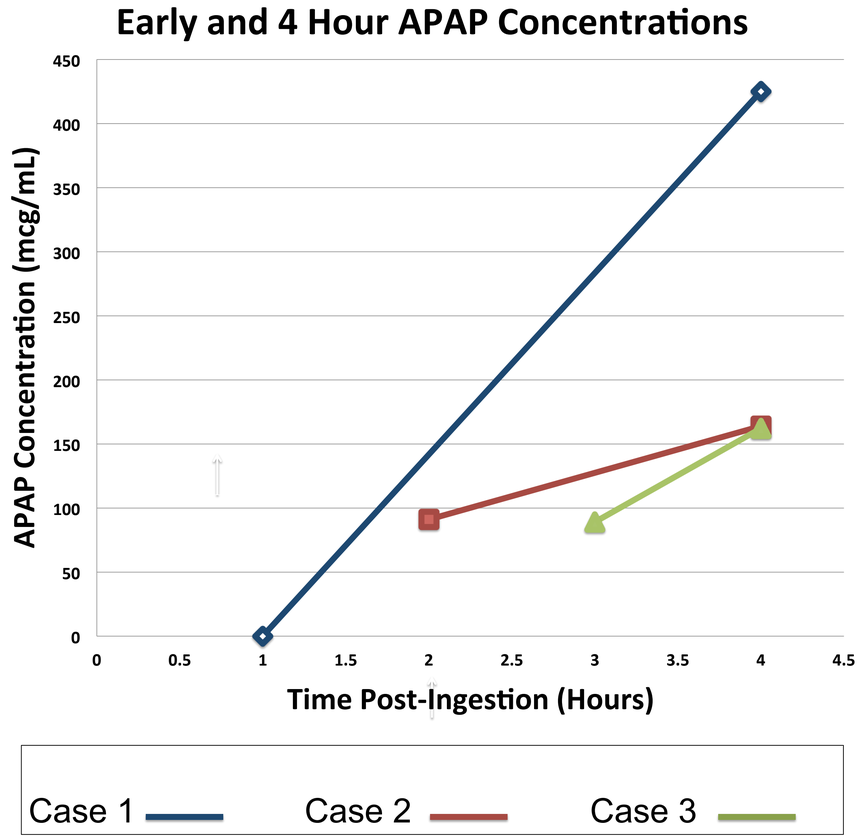
Case 1
- A 16-year-old girl ingested 75 x 500 mg APAP tabs
- APAP level 75 mins post-ingestion was undetectable (<2 mcg/mL)
- 4 hr APAP level was 425 mcg/mL
- PT peaked at 18.7 seconds after initiation of NAC

Case 2
- A 31-year-old man ingested 26 x 500 mg APAP tabs
- APAP level 2 hrs post-ingestion was 91 mcg/mL
- 4 hr APAP level was 164 mcg/mL

Case 3
- A 23-year-old woman ingested 10 x 500 mg APAP tabs, 6 ibuprofen/diphenhydramine tabs, and 20 mL of a codeine-containing cough syrup
- APAP level 3 hrs post-ingestion was 89 mcg/mL
- 4 hour APAP level was 162 mcg/mL
- ALT peaked at 68 IU/L

Case Series Continued

- In each case, N-acetylcysteine was started <8 hrs post-ingestion and discontinued at 21 hrs without complication. No clinically significant coagulopathy or transaminase elevations occurred.



Discussion

- Two studies have investigated early APAP levels and prediction of toxicity. A 1994 retrospective review reported as an abstract concluded a 1 to 4 hr APAP level <100 mcg/mL had a negative predictive value (NPV) of 94.6% for excluding toxicity and could be used to exclude need for therapy.[1] A 2013 prospective study found the same conditions to have a NPV of 98.8%. Including confidence intervals, this gave a false negative rate of 6.5%, leading authors to recommended against reliance on early APAP concentrations to rule out toxicity.[2]
- This case series supports the findings and author conclusions of the 2013 study, and further illustrates that APAP levels < 4 hrs post-ingestion should not be used to predict toxicity or determine need for therapy.
- Case 1 is remarkable for an undetectable level 75 mins post-ingestion followed by a markedly elevated level at 4 hrs. This suggests that clinicians cannot exclude toxicity even when an early initial level is undetectable.
- Case 3 co-ingested an opiate and anti-muscarinic agent possibly contributing to delayed absorption. Case 1 and 2 did not have significant co-ingestants.

Conclusions

Early APAP levels (<4 hrs) should not be used to determine need for antidotal therapy.

References

1. Douglas DR, Smilkstein MJ, Rumack BH. APAP levels within 4 hours: are they useful? Vet Human Toxicol. 1994; 36:350 [abstract]
2. Froberg BA, King KJ, Kurera TD, et al. Negative predictive value of acetaminophen concentrations within four hours of ingestion. Acad Emerg Med. 2013; 20:1072-1075