

The Use of Fomepizole with N-Acetylcysteine for Acetaminophen Overdose: A Scoping Review

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INTRODUCTION

-Overdoses from acetaminophen (APAP) toxicity is the leading cause of liver transplantation in the United States and the second most common cause globally.
-NAC is the standard treatment for acetaminophen overdose.
-Animal models using fomepizole have shown efficacy in treating APAP toxicity.

OBJECTIVES

-The objective of this study is to determine the effectiveness of NAC vs NAC and fomepizole as adjunct in APAP toxicity and if there is any meaningful benefit to giving fomepizole.

-N-acetylcysteine (NAC) has been the treatment of choice for acetaminophen toxicity, but fomepizole's mechanism of action can play a potential role. This systematic review aims to evaluate the use of fomepizole in acetaminophen overdose.

METHODS

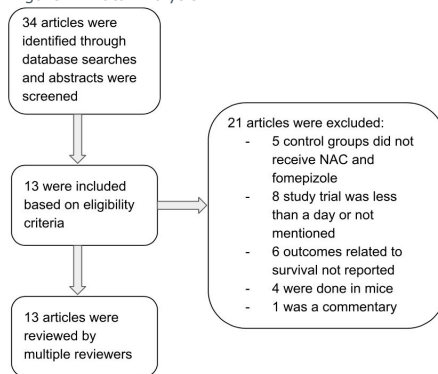
-Study design: This was a systematic review looking at the effectiveness of NAC vs NAC and fomepizole in APAP toxicity. Using the PRISMA criteria, we searched electronic databases (Medline, EMBASE, PubMed ePubs, and The Cochrane Library). We looked for studies including NAC, acetaminophen overdose, and fomepizole.

-Inclusion and Exclusion Criteria: To be included in the review, all literature consisting of randomized control trials, case series, retrospective studies, and case reports were included. Letters, review articles, and commentaries were excluded.

METHODS CONTINUED

-Data Extraction and Synthesis: The five authors each separately screened the publications that met the eligibility requirements. First, **Appendix A** was used to review all citations' titles and abstracts. **Appendix B** was then used to examine the complete text of any citations that might be pertinent.

Figure 1: Data Analysis



RESULTS

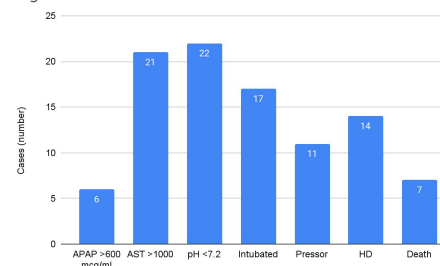
-This systematic review included 13 articles and had a total of 42 patients with cases of acetaminophen overdose. Of the 42 patients, 35 of them survived their overdose when given fomepizole and NAC as treatment. The 7 patients who did not survive were not overdosing on solely acetaminophen.

RESULTS CONTINUED

Kiernan et al. followed a case of a 64 year old woman who was hospitalized with an APAP level of 1,017 µg/ml (therapeutic dose is 10-30 µg/ml)⁵ This was the fourth highest APAP level of a surviving patient. She was given NAC, fomepizole, and hemodialysis and was discharged to a psychiatric unit with normal health about eight days following her presentation to the hospital.⁵

Hidalgo et al. concluded that fomepizole should be given with NAC in APAP overdose due to the high risk of liver failure in patients despite having NAC monotherapy.⁷

Figure 2: Case Characteristics



DISCUSSION

- This literature review shows that there are cases where elevated APAP concentration or complications of metabolic acidosis requiring the need for HD are present despite appropriate NAC treatment.
- Few alternatives are available beyond NAC for APAP concentrations above 600 mcg/ml at 4 hours post-ingestion without the addition of HD treatment.

DISCUSSION CONTINUED

- Results show 35 out of 42 cases survived when fomepizole was used as an adjunct treatment with NAC for APAP toxicity, indicating a favorable outcome.
- A limitation of this review is the inclusion of only case reports. Further studies with randomized clinical trials should be conducted to determine the safety and efficacy of fomepizole as an adjunct treatment option in combination with NAC for the treatment of APAP toxicity.

CONCLUSIONS

-The observed literature on fomepizole as adjunct therapy with NAC for acetaminophen overdose, resulted in positive outcomes in patients who were treated.
-Studies on humans will have to be conducted to determine fomepizole's role in acetaminophen overdose.

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