Role of fomepizole in the management of ethylene glycol toxicity

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Authors' objectives
To review English-language articles on fomepizole administration in patients with ethylene glycol poisoning.

Searching
MEDLINE (from 1966 to August 2001), EMBASE (from 1988 to August 2001), Current Contents (August 2001) and PubMed (to August 2001) were searched. The search terms reported were 'fomepizole', '4-methylpyrazole' and 'ethylene glycol'. In addition, the references of relevant literature were reviewed.

Study selection
Study designs of evaluations included in the review
All reports published in the English language were eligible for inclusion in the review; there were no exclusion criteria based on the study design or type.

Specific interventions included in the review
Only studies that were of the administration of fomepizole were eligible for inclusion in the review. The reports of fomepizole included in the review described the use of loading doses ranging from 9.5 to over 20 mg/kg intravenously, followed by various follow-up regimens of up to 4 days.

Participants included in the review
Patients with ethylene glycol poisoning were included.

Outcomes assessed in the review
No inclusion criteria for the outcomes were stated in the review. Of the papers included in the review, the clinical outcomes were renal injury, the additional production of ethylene glycol metabolites, the development of cranial nerve palsies, or death.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The categories of data extracted were: bibliographic details; the amount of ethylene glycol ingested; the laboratory findings at admission; the dosing regimen of fomepizole; additional treatment; and outcome.

Methods of synthesis
How were the studies combined?
The findings of the studies were pooled narratively.

How were differences between studies investigated?
The different types of studies were described and discussed separately.

**Results of the review**
One uncontrolled, prospective clinical trial (n=19), one case series (n=11) and 13 case reports were included in the review.

In the prospective study, 17 of the 19 patients required haemodialysis and one died. Renal injury, as defined by elevated serum creatinine, was seen in 9 patients. No information on the incidence of cranial nerve palsies was reported. The results of a pharmacokinetic analysis were reported: the half-life of ethylene glycol was estimated at 19.7 hours when the blood concentration of fomepizole exceeded 8.6 mg/L (considered to be a therapeutic level).

In the case series of 38 patients, of the 11 patients treated with fomepizole, 4 developed elevated serum creatinine and 3 required haemodialysis (one due to high ethylene glycol levels). One patient died but it was unclear if this patient had been treated with fomepizole.

Of the 13 case reports, only one patient died. Three patients developed some degree of renal failure but subsequently recovered. One patient suffered seizures but subsequently recovered. The other 8 patients were discharged from hospital after 2 to 8 days.

Overall, the limited data suggest that fomepizole may be a beneficial treatment in ethylene glycol poisoning. However, in the prospective study, the high success rate may be attributable to the other interventions, in particular haemodialysis. Similarly, in the case series and case reports, the apparent success of fomepizole may be due to the other concomitant interventions.

**Cost information**
It was mentioned that fomepizole is more expensive than ethanol (standard treatment).

**Authors' conclusions**
Fomepizole is an effective alcohol dehydrogenase inhibitor that decreases production of ethylene glycol metabolites. Reduced mortality and morbidity are undetermined because of the small number of patients evaluated to date. There are limited data on the comparative efficacy of fomepizole versus ethanol, and on the administration of fomepizole in children.

**CRD commentary**
This review addressed an appropriate question with appropriate (although very broad) inclusion criteria. The search strategy appears to have been adequate, but important non-English language studies may well have been missed. The reporting of how the review was conducted was poor, with no details of how many reviewers were directly involved, or the level of independent duplication or checking of information for the review. The included studies and case reports were all presented in adequate detail, either in the text or in tabular format. No validity assessment was performed but this was appropriate given the nature of the included studies, particularly as the significance of the poor quality of all the studies was discussed. The narrative pooling of the findings of the individual studies was entirely appropriate given the nature of the evidence.

The authors’ conclusions from their review appear justified, with the proviso that other non-English articles might exist that could provide further information.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors state 'future studies with a randomised design, comparing fomepizole with ethanol and using a more concrete end point such as death will more accurately describe fomepizole's place in therapy'.
Bibliographic details
Pharmacotherapy 2002; 22(3): 365-372

PubMedID
11899949

Indexing Status
Subject indexing assigned by NLM

MeSH
Alcohol Dehydrogenase /antagonists & inhibitors; Antidotes /administration & dosage /pharmacokinetics /therapeutic use; Clinical Trials as Topic; Ethanol /administration & dosage; Ethylene Glycol /blood /metabolism /poisoning; Humans; MEDLINE; Poisoning /drug therapy; Pyrazoles /administration & dosage /pharmacokinetics /therapeutic use; Renal Dialysis; Treatment Outcome

AccessionNumber
12002000697

Date bibliographic record published
28/02/2003

Date abstract record published
28/02/2003

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.