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Fomepizole for the treatment of ethylene glycol poisoning

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Keywords

Ethylene glycol, fomepizole, outcome

Comments

The authors comment that it is impossible to compare fomepizole with an untreated control group given the high morbidity and mortality as a result of EG poisoning, and that no attempt was made to compare the antidotes ethanol and fomepizole (Level V evidence). Unfortunately little prospective information is available on ethanol treatment nor its effects on EG metabolism, but it certainly has major drawbacks. Central nervous system depression, unpredictable ethanol pharmacokinetics and hypoglycaemia make the prospect of an alternative antidote very attractive. The major drawback of fomepizole is cost, although the hidden costs associated with ethanol treatment (prolonged duration of intensive care unit stay and the possible increased use of haemodialysis) may mean that this is not a real problem.

Introduction

Untreated ethylene glycol (EG) poisoning results in production of toxic metabolites, metabolic acidosis, renal failure and high mortality. With prompt diagnosis and treatment the prognosis is very good. Traditionally the antidote ethanol has been given which inhibits alcohol dehydrogenase and therefore the metabolism of EG to the toxic metabolite glycolic acid and eventually oxalic acid. This study investigates the use of the new alcohol dehydrogenase inhibitor, fomepizole, in the treatment of EG poisoning.

Aims

To investigate the safety and efficacy of fomepizole when used as an antidote in EG poisoning. Specifically the development of renal failure, cranial neuropathies and the production of EG metabolites were studied.

Methods

Nineteen patients with EG poisoning and a plasma EG concentration = 20 mg/dl were treated with iv fomepizole until plasma EG concentration was reduced to less than 20 mg/dl. The treatment regime for fomepizole consisted of a 15 mg/kg loading dose followed by 10 mg/kg every 12 h. After 48 h the dose was increased to 15 mg/kg 12 hourly since earlier pharmacokinetic studies had shown increased fomepizole metabolism in human volunteers. Haemodialysis was also administered according to certain predefined indications that included severe acidosis, rapidly rising creatinine and high initial EG levels. Comprehensive clinical and laboratory safety monitoring was performed along with serum assays to elucidate the pharmacokinetics of fomepizole and metabolism of EG.

Results

One patient who had an acute MI, prior to enrollment in the study, died as a result of cardiogenic shock. No patients had cranial neuropathy and few adverse events were reported due to fomepizole - those that were might well have been a consequence of EG poisoning.

In all patients there was a progressive decrease in plasma glycolate and urinary oxalate concentrations and increase in arterial pH and serum bicarbonate with fomepizole therapy. This was associated with clinical improvement.

Seventeen patients required haemodialysis. Nine patients had deterioration in renal function during treatment, although these patients presented later, had high baseline creatinine concentrations and very high glycolate levels (97.7-264.4 mg/dl). However in only three of these patients did the creatinine concentration not return to normal at follow up (133-336 ?mol/l). None of the patients with normal baseline creatinine levels or baseline glycolate levels less than 76.8 mg/dl developed renal impairment.

Discussion

Fomepizole appears to be a safe and useful antidote in the management of EG poisoning, and inhibition of EG metabolism was demonstrated by the reduction in plasma glycolate and urinary oxalate concentrations.

Traditionally patients with EG levels greater than 50 mg/dl have received haemodialysis because of unpredictable ethanol pharmacokinetics. However haemodialysis may not be necessary using the antidote fomepizole in all cases where EG levels are greater than 50 mg/dl, provided baseline renal function and acid-base is normal.

References

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