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Management of poisoning with ethylene glycol and methanol in the UK: A prospective study conducted by the National Poisons Information Service (NPIS)

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Abstract

Background. Poisoning with methanol and ethylene glycol can cause serious morbidity and mortality. Specific treatment involves the use of antidotes (fomepizole or ethanol) with or without extracorporeal elimination techniques.

Methods. A prospective audit of patients with methanol or ethylene glycol poisoning reported by telephone to the National Poisons Information Service (NPIS) in the United Kingdom (UK) was conducted during the 2010 calendar year and repeated during the 2012 calendar year. The study was conducted to determine the frequency of clinically significant systemic toxicity and requirement for antidote use and to compare outcomes and rates of adverse reaction and other problems in use between ethanol and fomepizole.

Results. The NPIS received 1315 enquiries involving methanol or ethylene glycol, relating to 1070 individual exposures over the 2-year period. Of 548 enquiries originating from hospitals, 329 involved systemic exposures (enteral or parenteral as opposed to topical exposure), of which 216 (66%) received an antidote (204 for ethylene glycol and 12 for methanol) and 90 (27%) extracorporeal treatment (86 for ethylene glycol and 4 for methanol). Comparing ethanol with fomepizole, adverse reactions (16/131 vs 2/125, $P < 0.001$) and administration errors, lack of monitoring or inappropriate use (45/131 vs. 6/125, $P<0.0001$) were reported more commonly, while non-availability and inadequate stocks were reported less commonly (6/125 vs 33/131, $P < 0.0001$). There were 8 fatalities and complications or sequelae occurred in 21 patients. Poor outcome (death, complications or sequelae) was significantly associated with older age, higher poisoning severity scores and lower pH on admission ($p<0.001$).

Conclusions. Systemic poisoning with ethylene glycol or methanol results in hospitalisation at least 2-3 times per week on average in the UK. No difference in outcome was detected between ethanol and fomepizole-treated patients, but ethanol was associated with more frequent adverse reactions.

Background

Methanol and ethylene glycol are present in a number of commercial products available to the public, including antifreeze, brake fluids and solutions for wallpaper stripping, window-cleaning and windscreen-washing. Sporadic outbreaks such as an episode of mass methanol poisoning from consumption of illegal spirits in Estonia[1] and ethylene glycol poisoning from contaminated water systems[2] have also been reported.

Although infrequent, systemic poisoning with methanol and ethylene glycol is important because it can cause severe toxicity and, if untreated, is associated with serious morbidity such as renal failure and neurological sequelae, mediated by toxic metabolites formed via alcohol dehydrogenase.[3] These complications can be prevented by administration of the antidotes ethanol or fomepizole, which block alcohol dehydrogenase, but availability of these antidotes is inconsistent in hospitals across the United Kingdom (UK) and also in other countries.[4] Limited information is available about the frequency and management of these poisonings in the UK and in the comparative benefits and adverse effects of antidotes. This information is needed for planning of services including provision of antidotes and renal replacement therapy.

A prospective audit of cases of methanol and ethylene glycol poisoning reported through telephone enquiries to the National Poisons Information Service (NPIS) was therefore conducted during the 2010 calendar year. Its aims were to determine the frequency of potentially serious methanol and

ethylene glycol poisoning in the UK requiring treatment with an antidote and/or haemodialysis, the availability, appropriate clinical use and adverse reactions to antidotes and the frequency of indicators of adverse clinical outcomes, including death, requirement for ITU or HDU admission, haemodialysis etc. The study was repeated during 2012 to increase the number of patients studied, especially those treated with fomepizole as only a small number were collected in 2010. This repeated study also provided additional information on trends in the frequency, management and outcomes of systemic ethylene glycol and methanol poisoning to guide future strategies for improving patient management, including availability of antidotes and laboratory assays.

Methods

All telephone enquiries relating to products containing ethylene glycol and/or methanol made by UK health professionals to any of the 4 units of the National Poisons Information Service (NPIS), located in Birmingham, Cardiff, Edinburgh and Newcastle, were considered for inclusion in the study prospectively over two annual periods which were the complete calendar years for 2010 and 2012. The study population was defined as patients with suspected significant systemic exposures to ethylene glycol and methanol who were admitted to hospital. Significant systemic exposure was defined as a potential systemic exposure to a toxic dose of ethylene glycol or methanol, according to UK treatment guidance (adult ≥10g adult; child 0.1g/kg), where clinical features of toxicity were present and/or where use of an antidote and/or or extracorporeal treatment was recommended by NPIS. Cases were considered for eligibility at the time of the enquiry by specialists in poisons information (SPI) using a pre-defined protocol.

Enquiries from out-of-hours general practitioners (GPs), publically available telephone helplines such as National Health Service (NHS) Direct and other non-hospital sources which did not lead to hospital attendance were excluded from the study as these sources do not provide follow up information and patients with significant exposure will subsequently be referred to hospital.

For patients attending hospitals, telephone follow-up of eligible cases was attempted by the SPI within 4-8 hours of the initial enquiry and repeated

daily until discharge from hospital. If this failed, a follow-up by letter was sent to the responsible clinician.

Details of all calls and information from follow-up were entered contemporaneously as free text into the United Kingdom Poisons Information Database (UKPID), the national database in which clinical data from NPIS enquiries is recorded. Data fields in UKPID included enquiry date/time, patient age and sex, type of caller, source of enquiry, location and circumstances of exposure, product (ingredients, amount, route of exposure, duration and time since exposure), clinical features, WHO/IPCS/EC/EAPCCT Poisoning Severity Score (PSS)[5], investigations and treatments prior to enquiry, treatments recommended and outcome. In addition to these routinely collected data, the protocol specified other clinically-relevant information to be recorded for use in the study, including the timing of antidote and/or extracorporeal treatment, description of adverse drug reactions and the results of biochemical investigations when available (ethylene glycol and methanol concentrations, ethanol concentration, Na+, K+, Cl-, HCO3-, pH, lactate, osmolality, osmolal gap, anion gap). These details were entered as free text in the UKPID record. Final outcomes of follow-up were recorded as complete recovery, sequelae (defined as complication of poisoning persisting at the time of last follow-up), death or unknown. All enquiries and all follow-up data were checked by a SPI (CG) and a clinical toxicologist (RT). Follow-up data received up to 31st May 2013 were used in the analysis, with consolidation of multiple enquiries about the same patient into a single record.

Data relating to the study population were transferred into an Excel spreadsheet for analysis. Descriptive data are reported as means (with standard deviation) or medians (with range). Comparative continuous variables were compared using unpaired t-test (for normally distributed data) and Mann Whitney U test (for non-normally distributed data). Statistical analysis was performed using SPSS V 21(Chicago, IIlinois).

Causality assessment of reported adverse reactions to ethanol and fomepizole was performed independently using the Naranjo Adverse Drug Reaction Probability Scale by two clinical pharmacologists and toxicologists with experience of assessing adverse drug reactions (RT & ST).

A national toolkit provided by the Health Research Authority in the United Kingdom (http://www.hra-decisiontools.org.uk/ethics/) indicates that approval from a Research Ethics Committee is not required for studies that use information collected routinely in any UK administration (England, Wales, Scotland, Northern Ireland) as part of usual clinical care, provided this information is passed to the researchers in a fully anonymised format.

Results

During the 2 years of the study, of 101,594 telephone enquiries made to the NPIS in total, 1315 (1.3%) concerned suspected exposure to ethylene glycol or methanol, involving 1070 individual exposures. These included 418 enquiries related to specifically to ethylene glycol and 28 to methanol, with the remaining enquiries about household products where the ingredients were not specified but ethylene glycol or methanol may have been included.

Non-hospital sources contributed 522 enquiries and there were a further 219 enquiries about topical exposures or systemic exposures unlikely to cause toxicity which were not followed up, leaving 329 systemic exposures eligible for study follow-up. In 71 cases, follow-up was not attempted or failed due to the enquirer not being contactable or declining to provide information, leaving a final study population of 258 cases (243 ethylene glycol and 15 methanol exposures) studied in detail.

In 34 cases, patients were discharged without requiring any specific treatment. Including these, outcomes at hospital discharge or death were known for 194 of the 329 systemic exposures (59%) and for 160 of 224 patients (71%) who received an antidote or extracorporeal treatment. (Figure 1)

An antidote was administered to 216 patients overall, with suspected exposure to ethylene glycol in 204 and to methanol in 12. Overall, 91 received ethanol alone, 85 fomepizole alone, and 40 both antidotes. There was no

difference in the PSS between those treated with ethanol (PSS 0-1 in 62/131(47%), PSS 2-3 in 66/131(50%) and unknown in 3) and fomepizole (PSS 0-1 in 56/125(45%), PSS 2-3 in 68/125(54%) and unknown in 1). Analytical confirmation of exposure was available in 106 cases (49%, ethylene glycol 101, methanol 5) and unavailable in 81 (38%) cases. In the remaining 29 (13%) cases, although antidote treatment was initiated, plasma concentrations were found subsequently to be below the limits of detection for both ethylene glycol and methanol and the antidote was discontinued.

Ethylene glycol exposures

204 of the 243 (84%) suspected ethylene glycol exposures reviewed were treated with an antidote: 83 received ethanol alone, 81 fomepizole alone and 40 both antidotes. Fomepizole was used as the sole antidote in 12 patients with ethylene glycol concentrations >500 mg/L (median 1100, range 584-2140), all of whom made a complete recovery without extracorporeal treatment. The pattern of antidote use for ethylene glycol poisoning, PSS score and ethylene glycol concentrations by treatment group are shown in Table 1. Fomepizole was used more commonly than ethanol in patients with PSS score 3 (43/61, 70.5% vs 32/61, 52.4%, $P<0.05$). There were no significant differences in outcome between patients treated with different antidotes overall or in a subgroup of more severely poisoned patients (PSS 2-3) in whom 6/36 (17%) treated with ethanol only and 6/42(14%) treated with fomepizole only developed sequelae or died. Fomepizole was used for a greater proportion of ethylene glycol cases in 2012 (83/112, 74.1%) compared with 2010 (48/92, 52.2%; $P<0.01$).

Haemodialysis and/or other extracorporeal elimination therapies were used in 86 patients with suspected ethylene glycol exposure, without antidotal treatment in 7 cases and in conjunction with antidotes in 78. In 1 patient who subsequently died, it is not known whether antidotal treatment was administered. More than 1 extracorporeal treatment modality was used in 6 patients and there were no reported adverse events. The type of extracorporeal treatment used for ethylene glycol poisoning, PSS score and ethylene glycol concentrations are shown in Table 2.

There were 5 suspected ethylene glycol related deaths reported in the 2 years studied. In 3 cases, analytical confirmation of ethylene glycol exposure was available and deaths were likely to be due directly to ethylene glycol poisoning. These included: a 35-year old presenting with coma, severe metabolic acidosis (pH 7.13), renal failure (creatinine 220 µmol/L) and ethylene glycol concentration 1935 mg/L; a 33-year old presenting with coma, severe metabolic acidosis (pH 7.14), broad complex tachycardia and ethylene glycol concentration 2010 mg/L who developed cerebral oedema and a 59-year old presenting with profound metabolic acidosis (pH 6.85) and acute renal failure (creatinine 525 µmol/L). In the other 2 cases, the cause of death was unclear. Both antidote and extracorporeal treatments were instituted in 4 patients and antidote treatment only in 1 case.

Complications or sequelae were reported in 21 of the 155 ethylene glycol cases with a recorded outcome, with analytical confirmation of ethylene glycol exposure in 16 of these cases, concentrations below the limit of

detection in 3 cases and unknown in 2 cases. Renal impairment was reported in 20 of these 21 cases at the time of the last follow-up. Sequelae included upper cranial nerve palsy and peripheral neuropathy following intensive care admission for aspiration pneumonia and haemodialysis for acute renal failure (creatinine >1000 µmol/L). A 26-year-old man admitted unresponsive with a pH of 6.68 and ethylene glycol concentration of 133 mg/L developed acute renal failure which resolved, but he had residual cognitive impairment, visual disturbances, refractory seizures and dystonia. MRI findings typical of ethylene glycol poisoning, including low attenuation of the thalamus, basal ganglia, bilateral temporal lobes and occipital lobes, were present.

Patients who died or developed complications or sequelae from ethylene glycol poisoning were older, had significantly higher poisoning severity scores and lower pH on admission than those who made a complete recovery, but the plasma concentrations of ethylene glycol were not significantly different between the two groups (Table 3).

Methanol exposures

12 of the 15 (80%) suspected methanol exposures reviewed were treated with an antidote: 8 received ethanol alone (oral ethanol in 2, intravenous ethanol in 5, both oral and intravenous ethanol in 1) and 4 fomepizole. Fomepizole was used as the sole antidote without extracorporeal treatment in 1 patient with a methanol concentration of 1627 mg/L who subsequently made a full recovery. In addition to antidote treatment, haemofiltration was used in 3 patients and haemodiafiltration in 1 patient. There were 3 suspected methanol related

deaths reported during the 2 year period, but analytical confirmation was only available in 1 patient who had a methanol concentration of 3462 mg/L and an admission pH of 6.6 who died despite treatment with intravenous ethanol and haemofiltration.

Adverse reactions to antidotes

Adverse reactions to antidotes were reported in 18 patients treated for ethylene glycol poisoning and none treated for methanol poisoning. Of these, 11 were treated with ethanol, 2 with fomepizole and 5 with both antidotes. Of 19 adverse reactions reported in 16 (13%) ethanol-treated patients there were 12 reactions in 11 ethanol-treated patients classified as probably related to ethanol use. These consisted of intoxication (7), reduced conscious level (2), nausea and vomiting (1), slurred speech (1), and acute alcohol withdrawal (1). There were 7 reported adverse reactions in another 6 ethanol-treated patients classified as possibly related to ethanol use, which were vomiting (3), nausea (1), drowsiness (1), agitation (1) and headache (1). Adverse reactions were less commonly reported after fomepizole than ethanol use (2/125 vs 16/131, $P < 0.001$). The 2 reactions were both classified as possibly related to fomepizole. One patient had a period of shaking which was treated supportively with full recovery. The cause was uncertain and may have been alcohol withdrawal. Another patient developed angio-oedema which resolved after fomepizole was discontinued and the patient made a full recovery.

Other reported problems associated with antidote use included lack of availability, inadequate monitoring and administration errors (Table 4). Non-

availability and inadequate stocks were reported more commonly with fomepizole than ethanol (33/125 vs. 6/131, P<0.0001) but administration errors, lack of monitoring or inappropriate use were more commonly reported with ethanol than fomepizole (45/131 vs. 6/125, P<0.0001).

Discussion

Systemic poisoning with ethylene glycol (or less commonly methanol) is uncommon, but these data indicate that there are least 2-3 cases per week across the UK. These presentations are associated with significant morbidity and death occurs in an important minority.

The poisoning severity score and pH on admission appear to be predictors of mortality and morbidity. A previous retrospective study has suggested that a high osmolal gap and anion gap and a low pH (<7.22) were associated with increased mortality in toxic alcohol/glycol poisoning[6] and another study in methanol poisoning showed that coma (GCS<8) and low pH (<7.2) were predictors of poor outcome.[7] The actual values for the osmolal gap and anion gap were recorded in only a small number of cases in the current study as a result of enquirers being unable to supply specific information, especially chloride, bicarbonate or plasma osmolality results; this precluded calculation of these parameters and further analysis.

There is marked variability in the management of toxic alcohol exposures in the UK, particularly with respect to use of antidotes. The study suggested that fomepizole is associated with fewer adverse reactions and problems with administration or monitoring compared with ethanol. Adverse events and difficulty in maintaining therapeutic concentrations of ethanol have previously been reported in other studies.[8,9] Nevertheless, the outcome was generally favourable, irrespective of the antidote used, even in a subgroup of patients with more severe symptoms (PSS 2-3). Although some benefits were

seen with fomepizole in a study involving dogs[10], there have been no randomised controlled trials comparing fomepizole with ethanol in humans but a recent systematic review concluded that there are no significant differences in outcome.[11] A statistically significant difference in mortality in a sub-group of patients with low pCO2 was reported in a small study of methanol-poisoned patients when treated with fomepizole.[7] A recent study in a mass poisoning outbreak of methanol found no differences in overall clinical effectiveness between fomepizole and ethanol but there was no comparison in sicker patients in this study.[12]

Fomepizole without extracorporeal removal was used in 13 patients with ethylene glycol or methanol concentrations exceeding 500 mg/L and there was complete recovery in all cases. Recent evidence suggests that fomepizole may obviate the need for haemodialysis in selected cases,[13] but the cost-effectiveness of this treatment strategy is controversial depending on the local cost of intensive care and dialysis over a short period compared to a more prolonged course of fomepizole.[14]

In the UK, joint College of Emergency Medicine/NPIS guidelines on antidote stocking in acute hospitals recommend fomepizole as the antidote of choice for toxic alcohol and glycol poisoning, but an audit conducted in parallel to this study in 2010 showed that only around 20% of acute hospitals in the UK stocked this antidote.[4] The present study has suggested a small increase in the use of fomepizole between 2010 and 2012. Although lack of on-site availability was only reported and documented in 16 cases, this is

likely to be an underestimate as generally the preferential use of ethanol suggests that fomepizole was not immediately available in many cases.

Although limited evidence suggests that haemodialysis is more effective at removing ethylene glycol and methanol, continuous renal replacement methods such as continuous haemofiltration or haemodiafiltration are used frequently due to non-availability of on-site dialysis in many intensive care units in the UK.

Assays for methanol and ethylene glycol are only available on a 24 hour basis in a few hospitals in the UK and antidote treatment is often provided before the results become available. In this study, antidote was administered in 33 patients before methanol or glycol concentrations were reported as undetectable. Such unnecessary use could be reduced by more complete and rapid availability of plasma concentration measurements. Poisoning with methanol and ethylene glycol is too uncommon to justify appropriate assays being provided in all acute hospitals, but these analytical resources need to be available quickly when exposure is suspected. Development of cheap, rapid and effective screening detection methods is also needed to avoid missing these potentially serious cases.

Better methods of organising assays and antidote supply are needed, with resources available on a regional or supraregional basis and a mechanism of distributing costs between hospitals sharing these services.[15]

Further studies are also needed to monitor the availability of antidotes and extracorporeal treatments and the impact of recent guidelines.

Although this is the largest cohort of toxic alcohol exposures reported in the UK, the study has a number of limitations. It was not possible to examine the patients' medical records; data were obtained by telephone follow-up, so inaccuracies or omissions cannot be excluded; detailed follow-up and outcome data were obtained in only 59% of eligible cases and 71% of those receiving antidotal and/or extracorporeal treatments due to difficulties in tracking patients moving through different clinical environments during their hospital stay or refusal to provide patient data over the telephone. We cannot exclude the possibility that outcomes might differ between patients where data is available compared to those where it is not. All cases of poisoning in the UK are not referred to NPIS and those not referred cannot be included in this study, thereby potentially underestimating the number of cases and consequent complications and adverse events. Hospital episode statistics data for England in 2011-2, however, report a total of 112 hospital admissions attributable to toxic effects of methanol (28), glycols (25) and other alcohols (59). Although these data may be affected by inaccuracies in coding, these statistics for England are consistent with the number of annual numbers of cases reported to the NPIS from across the UK in this study. Finally, the data are specific for the UK and the findings in terms of patterns of presentation and availability and use of treatment modalities are not necessarily applicable to other countries. It is likely, however, that similar issues are encountered internationally.

Conclusions

This study suggests that severe poisoning with methanol and ethylene glycol is uncommon in the UK, but when this is encountered, difficulties are often experienced in confirming the diagnosis, in the sourcing and use of antidotes and in accessing haemodialysis when this is necessary. Most hospitals continue to rely on ethanol as an antidote, but problems in administration as well as adverse reactions are more commonly encountered with ethanol. As a consequence many patients require switching to fomepizole, but this is often not immediately available.

Declaration of interest

NPIS received a small unrestricted educational grant to undertake this study from EUSAPharma, the distributor of fomepizole in the UK.

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Table 1. Characteristics and outcome of 204 patients requiring antidote treatment for ethylene glycol poisoning

	2010	2012	Total	Poisoning Severity Score (PSS) at time of enquiry					Plasma concentration	Outcome			
Antidote treatment	n (%)*	n (%)*	n (%)*	0 n (%)**	1 n (%)**	2 n (%)**	3 n (%)**	Not Known n (%)**	Detected Median (Range) mg/L	Complete Recovery n (%)**	Sequelae n (%)**	Death n (%)**	Not known n (%)**
Ethanol only	44 (47.8%)	39 (34.8%)	83 (40.7%)	13 (15.7%)	31 (37.3%)	18 (21.7%)	18 (21.7%)	3 (3.6%)	29 320 (14-2400)	49 (59.0%)	6 (7.2%)	2 (2.4%)	26 (31.3%)
Fomepizole only	34 (37.0%)	47 (42.0%)	81 (39.7%)	7 (8.6%)	31 (38.3%)	13 (16.0%)	29 (35.8%)	1 (1.2%)	40 725 (20-4614)	52 (64.2%)	6 (7.4%)	3 (3.7%)	20 (24.7%)
Both ethanol and fomepizole	14 (15.2%)	26 (23.2%)	40 (19.6%)	4 (10%)	11 (27.5%)	11 (27.5%)	14 (35%)	0 (0%)	30 436 (32-3743)	25 (62.5%)	5 (12.5%)	0 (0%)	10 (25%)
Ethanol oral only	6 (6.5%)	9 (8.0%)	15 (7.4%)	4 (26.7%)	8 (53.3%)	2 (13.3%)	1 (67%)	0 (0%)	4 282 (32-2171)	11 (73.3%)	0 (0%)	1 (6.7%)	3 (20%)
Ethanol iv only	31 (33.7%)	21 (18.8%)	52 (25.5%)	5 (9.6%)	15 (28.8%)	14 (26.9%)	15 (28.8%)	3 (5.8%)	18 316 (14-2400)	28 (53.8%)	4 (7.7%)	1 (1.9%)	19 (36.5%)
Ethanol (oral + iv)	7 (7.6%)	9 (8.0%)	16 (7.8%)	4 (25%)	8 (50%)	2 (12.5%)	2 (12.5%)	0 (0%)	7 320 (54-1250)	10 (62.5%)	2 (12.5%)	0 (0%)	4 (25%)
Ethanol oral + Fomepizole	3 (3.3%)	7 (6.3%)	10 (4.9%)	2 (20%)	4 (40%)	1 (10%)	3 (30%)	0 (0%)	7 420 (32-3743)	6 (60%)	0 (0%)	0 (0%)	4 (40%)
Ethanol iv + Fomepizole	8 (8.7%)	16 (14.3%)	24 (11.8%)	1 (4.2%)	5 (20.8%)	7 (29.2%)	11 (45.8%)	0 (0%)	20 402 (89-1584)	13 (54.2%)	5 (20.8%)	0 (0%)	6 (25%)
Ethanol oral+ iv + Fomepizole	3 (3.3%)	3 (2.7%)	6 (2.8%)	1 (16.7%)	2 (33.3%)	3 (50%)	0 (0%)	0 (0%)	3 510 (150-2581)	6 (100%)	0 (%)	0 (%)	0 (%)

Table 2. Characteristics and outcome of 86 patients requiring extracorporeal treatment for ethylene glycol poisoning

	2010	2012	Total	Poisoning Severity Score (PSS) at time of enquiry					Plasma concentration	Outcome			
Extracorporeal treatment	n (%)*	n (%)*	n (%)*	0 n (%)**	1 n (%)**	2 n (%)**	3 n (%)**	Not Known n (%)**	Detected Median (Range) mg/L	Complete Recovery n (%)**	Sequelae n (%)**	Death n (%)**	Not known n (%)**
Haemodialysis	15 (48.4%)	26 (42.6%)	41 (44.6%)	0 (0%)	8 (22.2.5%)	7 (19.4%)	26 (58.3%)	0 (0%)	30 475 (14-4614)	23 (56.1%)	10 (24.4%)	1 (2.4%)	7 (17.1%)
Haemodiafiltration	4 (12.9%)	12 (19.7%)	16 (17.4%)	0 (0%)	3 (18.8%)	2 (12.5%)	11 (68.8%)	0 (0%)	13 307 (14-3743)	10 (62.5%)	4 (25%)	0 (0%)	2 (12.5%)
Haemofiltration	12 (38.7%)	23 (37.7%)	35 (38.0%)	1 (2.9%)	5 (14.3%)	10 (28.6%)	18 (51.4%)	1 (2.9%)	22 875 (20-2581)	16 (45.7%)	8 (22.9%)	3 (8.6%)	8 (22.9%)

* % receiving each treatment modality in 2010, 2012 and both years.

** % with each PSS score and outcome for each treatment modality

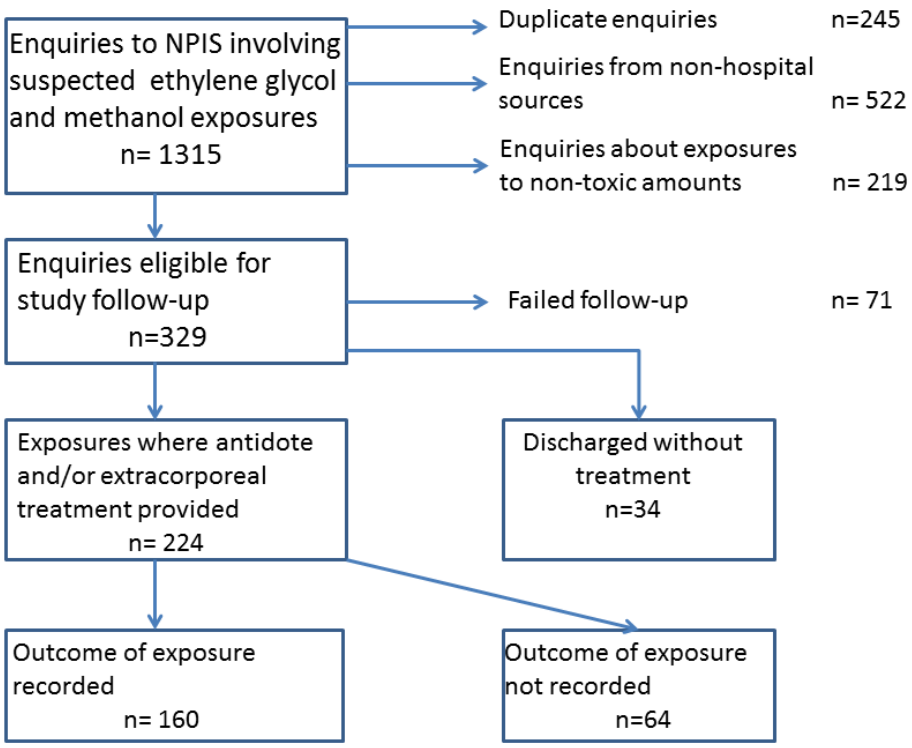
Table 3. Prognostic factors in patients with ethylene glycol poisoning

	n=	Complete recovery n=129	n=	Death or sequelae n=26	P
Mean (±SD) age (years)	127	37 ± 13.7	26	47 ± 15.0	<0.001
Poisoning Severity Score(PSS) mean (±SD)	127	1.6 ± 1.0	26	2.5 ± 0.8	<0.0001
Toxic alcohol concentration (mg/L) median (range)	71	510 (24-4614)	19	654 (14-2530)	ns
Mean (±SD) pH on admission	100	7.26 ± 0.18	24	7.12 ± 0.21	0.001

Table 4. Problems reported with ethanol and fomepizole use

		Ethanol n=	Fomepizole n=
Stocking	Unavailable on site	3	16
	Inadequate stock to complete treatment	3	17
Monitoring	Ethanol concentrations not measured	6	N/A
	Sub-therapeutic ethanol concentrations	18	N/A
Administration	Difficulty in making infusion	4	N/A
	Difficulty calculating infusion rate	4	N/A
	Difficulty with reconstitution	0	1
	Dosing interval wrong	N/A	2
	Concomitant administration of both antidotes	3	3
Inappropriate use	Young children	2	N/A
	Teetotallers	2	N/A
	Ethnic and religious groups	2	N/A
	Severe ethanol intoxication before assay results available	2	N/A
Discontinuation	Too early leading to clinical deterioration	2	0

Figure 1


Enquiries to NPIS involving suspected ethylene glycol and methanol exposures
n= 1315
Duplicate enquiries
n=245
Enquiries from non-hospital sources
n= 522
Enquiries about exposures to non-toxic amounts
n= 219
Enquiries eligible for study follow-up
n=329
Failed follow-up
n= 71
Exposures where antidote and/or extracorporeal treatment provided
n= 224
Discharged without treatment
n=34
Outcome of exposure recorded
n= 160
Outcome of exposure not recorded
n=64

Contributorship statement

ST and HKRT designed the protocol which was modified by all other authors. HKRT made primary contributions to data analysis, interpretation of results, and writing of the manuscript. CG, GJ, SMB contributed to data collection. All authors contributed to interpretation of results, revision of the manuscript and all approved the final manuscript. HKRT is the guarantor.

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Data sharing: No additional data available