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EXPERIENCES OF THE CZECH TOXICOLOGICAL INFORMATION CENTRE WITH ETHYLENE GLYCOL POISONING

Martina Křenová[a], Daniela Pelclová[a], Tomáš Navrátil[a], Miroslav Merta[b]

[a] *Toxicological Information Centre, Department of Occupational Medicine, 1st Faculty of Medicine, Charles University and General Teaching Hospital, Prague*
[b] *1st Medical Department – Clinical Department of Haematology and Nephrology, 1st Faculty of Medicine, Charles University and General Teaching Hospital, Prague*
e-mail: martina.krenova@centrum.cz

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The objective was to evaluate the severity of ethylene glycol (EG) intoxications in a 3-year retrospective study of the calls to the Toxicological Information Centre (TIC). Data about clinical course of patients with EG poisoning reported to the TIC in the years 2000–2002 were analysed. They were completed by the data from discharge records from the hospitals and by toxicological analyses. The χ-square test, Student's t-test, Fisher's test and the calculation of linear correlation coefficient were used for statistical analysis. The significance level was set at 0.05. TIC received total 188 calls concerning EG, from which 33 discharge reports were gained. There were 30 males (age 5–74 years) and 3 females (age 10–54 years). The patients ingested 252 ml on average (30–1000 ml); lethal dose (100 ml) was exceeded in 14 patients. Mean time interval from ingestion to admission was 3 hours (3–24 hours), mean length of hospitalisation 6 days (1–76 days). Fourteen patients developed metabolic acidosis, nine unconsciousness, thirteen signs of nephrotoxicity and nine signs of hepatotoxicity. Three patients died. Antidote ethanol was given in 30 patients. Other treatment included haemodialysis (20 cases) and B vitamins (23 cases). Ingested dose and the time interval between ingestion and admission correlated with severity of kidney damage. These data confirm that EG poisoning could seriously threaten the life. Renal parameters were abnormal in 30 % of patients who were discharged from the hospital. Those patients will be followed to evaluate the reversibility of EG toxic kidney damage.

INTRODUCTION

In the Czech Republic acute intoxications with ethylene glycol (EG) represent a serious clinical problem[1]. According to the statistical analysis of the Institute of Health Information and Statistics of the Czech Republic 125 patients were intoxicated with EG during the period 2000–2002.

EG is a colourless, odourless and sweet-tasting compound. It causes intoxication with a poor prognosis and high mortality. EG is a common main constituent (about 90 %) of most antifreeze solutions. It is also used as a foam stabilizer, a constituent of hydraulic brake fluid, softening agent for cellophane and as a component for chemical synthesis. Non-intentional ingestions frequently involve exposure of children to toxic antifreeze products and drinking antifreeze with EG instead of ethanol by ethyl alcohol abusers. Intentional ingestions result from suicidal attempts.

The commonly quoted EG minimum lethal dose is 1–1.5 ml/kg or approximately 100 ml for an adult[2]. However, this value is based on the extrapolation from animal studies performed during the 1930s and on case reports from the 1940s (ref.[3–5]). The toxic EG blood level is approximately 0.2 g/l and the lethal EG blood level about 2 g/l (ref.[2]). Significant toxicity of EG metabolites, such as glycol aldehyde, glycolic, glyoxylic and oxalic acids, eliminated by the kidneys leads to severe multi-organ damage and to acute renal failure[6,7]. The first step of this metabolic pathway is catalysed by enzyme alcohol dehydrogenase in the liver. Thus, inhibitors of alcohol dehydrogenase (ethanol or fomepizole) prevent the biotransformation of EG to toxic metabolites.

The classical pathologic finding is acute tubular necrosis of proximal tubular cells and the presence of calcium oxalate crystals in the proximal tubules[4]. Although renal function following EG intoxication usually returns to normal range, haemodialysis may be required for months and some renal damage may persist[8–11]. Early diagnosis, intensive treatment with the antidote ethanol, elimination of the poison by haemodialysis and correction of acid-base balance abnormalities are crucial measures for the therapy.

The Czech Toxicological Information Centre (TIC) has been working in Prague since 1962. Nowadays it answers calls received during 24 hours from hospitals and public all over the country using both it's own Czech database and databases Poisindex by Micromedex and INCHEM.

The objective of this study was to evaluate retrospectively the severity of EG intoxications in a 3-year study of the calls to the TIC.

MATERIALS AND METHODS

Data concerning clinical course of patients with EG poisoning reported to the TIC in the years 2000–2002 were analysed. They were completed by the discharge records data from the hospitals and by toxicological analyses. Following factors were analysed: age, sex, amount of EG ingested, delay between the intake of EG and admission to the hospital, days of hospitalisation, serum EG levels, biochemical markers of nephrotoxicity (serum creatinine above 110 μmol/l) and hepatototoxicity (activity of aspartate aminotransferase (AST) above 0.72 μkat/l and activity of alanine aminotransferase (ALT) above 0.78 μkat/l), symptoms, outcome of intoxication and treatment. The χ-square test, Student's t-test, Fisher's test and the calculation of linear correlation coefficient were used for statistical analysis. The significance level was set at 0.05.

RESULTS

The TIC received totally 188 calls concerning EG intoxication during the period 2000–2002, from which thirty-three discharge reports were gained. There were two children (age 5 and 10 years), twenty-nine males (age 15–74 years) and two females (age 17 and 54 years). Eleven patients committed suicide attempts, fourteen patients ingested EG by mistake. The reason of ingestion remained unknown in eight persons. Several of them probably considered EG to be an alcoholic beverage. In ten patients other poisons were co-ingested. It concerned ethanol in nine patients and rodenticide bromadiolone in two patients.

The ingested dose of EG was known in twenty-three patients. They ingested 252 ml of EG on average (range 30–1000 ml). The potential lethal dose (100 ml) was exceeded in fourteen patients. In nine patients the time of intoxication was unknown. Sixteen persons were admitted to the hospitals 1–6 h after poison ingestion; five after 6–12 hours; two after 12–24 h and one after 72 h after EG ingestion. Mean length of hospitalisation was six days (1–76 days). EG blood level on admission was measured in fifteen patients (mean value 1.8 g/l, range 0.2–8.0 g/l).

Fourteen patients developed severe metabolic acidosis (pH < 7.2). In nine patients mildly elevated activity of liver enzymes was observed. The mean maximal AST and ALT activity was 11.3 μkat/l and 8.4 μkat/l, respectively. In all but one the hepatic function recovered completely during discharge. Thirteen patients developed laboratory signs of nephrotoxicity (range maximal serum creatinine level 121–1115 μmol/l). In this group of patients the ingested dose was known only in seven patients (mean value 417 ml). The mean length of hospitalisation was twenty-eight days. Serum creatinine level was still elevated in ten patients during discharge from hospitals. Further symptoms and complications were present: sopor or coma in twelve patients; hypertension or elevated blood pressure in nine patients; tachycardia in seven patients; bronchopneumonia in four patients; muscular cramps in three patients; miosis in two patients; brain oedema in two patients; toxic cardiomyopathy in one patient and respiratory failure in one patient. Three patients died. The reason of death was metabolic failure in two cases and asystole in one case.

The antidote ethanol was given in thirty patients. Other treatment included haemodialysis (twenty cases), B vitamins (twenty-three cases) and symptomatic treatment.

In patients the ingested dose over 150 ml correlated with the kidney damage (p = 92.5 %), with the level of metabolic acidosis (p = 99.2 %) and with the degree of depression of the central nervous system (p = 92.5 %). The time interval between ingestion and admission correlated with the metabolic acidosis (p = 93.4 %), with the kidney damage (p = 93.8 %), depression of the central nervous system (p = 97.6 %) and with the length of hospitalisation (p = 95 %).

DISCUSSION

Accidental or suicidal EG ingestion is one of the most severe causes of poisoning in the Czech Republic[1]. The difference of the number of intoxicated patients with EG between the Institute of Health Information and Statistics of the Czech Republic and TIC is caused by the holes in the statistical system (not all patients with EG intoxication are not reffered to the Institute) as well as by more calls to the TIC concerning one patient intoxicated with EG. Results of our study indicate that the potential toxic dose is ingested very easily. It could be as little as one draught. Adult men are the most endangered population probably due to better accessibility to EG containing products to them, especially antifreeze fluids.

Our analysis of outcome and treatment of patients with EG intoxication confirmed that the most important prognosis factors are the ingested dose and the early antidotal treatment. Even though the mean ingested dose 252 ml of our patients is, according to the literature, lethal, the mortality was only 9 % probably because 48 % of our patients were admitted earlier than 6 hours after EG ingestion and 70 % during the first 24 hours.

In comparison with studies from Poland or Sweden, the mortality rate in our patients is lower. Stompór et al.[12] presented an analysis of EG acute intoxication treatment results in a group of thirty-six patients (mean EG blood level on admission 1.3 g/l). Eighteen persons (50 %) died. Only 11 % of their patients were admitted earlier than 6 hours after EG ingestion. The dose taken by our patients is comparable with the results of Sydor et al.[13] in a group of fifteen patients, who ingested 400 ml EG on average and the mortality was 53 %. The main reason of the high

mortality was again a long time interval between poisoning and admission to hospital. In the study of Hylander et al.[14] and Karlson-Stiber et al.[15] mortality was 17 % from thirty-six patients intoxicated with EG. The ingested dose of EG was known only in eight patients (mean value 481 ml). From six patients who died, four were admitted 12 hours after intake and two patients 24 hours after intake. Of the seven survivors, two patients were admitted within 6 hours, one patient within 12 hours and four within 24 hours after intake.

In our group the typical features of poisoning were: metabolic acidosis, various degree of depression of the central nervous system, nephrotoxicity, hepatotoxicity and cardiovascular complications. Most patients were treated with the antidote ethanol, correction of metabolic acidosis and B vitamins. Haemodialysis treatment was introduced for toxin elimination as well as for correction of acid-base balance disturbances and in eleven patients as a treatment of acute renal failure. The outcome was mostly favourable and mortality very low.

However, renal parameters were still elevated in 30 % of patients who were discharged from the hospital. Relatively rare case reports[10, 11, 16] show that the renal function in the surviving patients after some time usually returns to normal values. However these data are limited. Therefore our patients, who were discharged with abnormal markers of nephrotoxicity, will be followed-up to evaluate the reversibility of EG toxic kidney damage.

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