ACUTE INTOXICATIONS WITH ETHYLENE GLYCOL IN VARNA REGION: 25-YEAR EXPERIENCE

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ABSTRACT

Ethylene glycol (EG) is a bivalent alcohol. It is composed of many commercial and industrial products such as anti-freeze, coolants, deicing fluids, brake solutions, detergents and lacquers and is used as an organic solvent of many substances. Accidental and intentional poisonings with EG are rare, but potentially lethal and are a challenge to the clinical toxicology. Retrospectively, we followed the acute intoxications with EG for a 25-year period (1991-2015) in the Varna region, Republic of Bulgaria. The subject of the study were 95 patients with acute EG poisoning, at an average age of 46.8 years (21-77), who had received treatment at the Clinic of Toxicology and the diagnosis was confirmed by gas chromatographic method. EG intoxications are specific to the male gender, at male:female ratio of 6.9:1. All poisonings resulted from oral intake, mainly of anti-freeze, 92.6% of them being accidental and only 7.4% - deliberate. A lethal outcome was registered in 8 (8.4%) patients. Extreme renal insufficiency occurred in 9 (10.3%) of the surviving patients. *Scr Sci Med.* 2017;49(4):42-46

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INTRODUCTION

Ethylene glycol (EG) intoxications are a result of accidental oral ingestion or intentionally consumed as an alcohol substitute by alcoholics. EG has a relatively low toxicity (1-3). It is rapidly absorbed in the gastrointestinal tract (GIT). About 80% of EG is metabolized in the liver by the enzyme alcohol dehydrogenase (ADH), with a half-life of about 3-5 hours. The resulting metabolites include glycoaldehyde, which is then metabolized to glycolic, glyoxylic, and oxal-

ic acids. These acids, along with the excessive lactic acid, are responsible for the anion gap metabolic acidosis, organ damage, acute renal failure, and death of patients (4,5). Acute EG poisoning is not common, however, it is life-threatening and with a high risk of lethal outcome (6-9).

In this regard, we set our goal to investigate acute intoxications with EG for a 25-year period in the Varna region.

MATERIALS AND METHODS

The subject of the study were 95 patients with acute EG poisoning treated at the Clinic of Toxicology in 1991-2015, a period of serious socio-economic changes in the Republic of Bulgaria. The study is retrospective, analyzing disease histories and personal outpatient maps of treated patients, as well as forensic medical reports from the autopsy of deceased patients. Diagnosis was based on the history of anti-freeze ingestion, typical symptoms, severe metabolic acidosis, and confirmed by gas chromatography using the GS 5890-series II Hewlett Packard Gas Chromatograph with the FID Headspace sampler 19395A and the HP 3396 Series II Integrator.

RESULTS

During this period, 17438 patients with acute intoxication were treated in the Clinic of Toxicology. Poisonings with EG were recorded in 95 of them or in 0.5% of the cases. We confirmed the low incidence of EG intoxications (10). There was a much higher incidence of EG intoxications in men - 83 cases (87.4%), at male to female ratio of 6.9:1 (Fig. 1), which was, probably, due to the more frequent contact of men with technical liquids, including anti-freeze.

Figure 1. Sex distribution of EG poisonings

Acute EG intoxications occurred at any age. Mean patient's age in our study was 46.8 years (21-77). The patients of an active working age prevailed (in 61% of the cases) (Table 1).

Table 1. Age distribution of EG poisonings

Age	Cases	Percent, %
< 24	5	5.3
25 - 44	32	33.7
45 - 60	21	22.1
> 60	37	38.9
All	95	100

Most EG poisonings were a result from oral intake. The occasional, unintentional intoxications were 88 (92.6%), and suicide attempts were only a small percentage (7.4% or 7 cases).

In 8 patients (8.4%), a fatal outcome was recorded, the mean age of the deceased patients was 56.6 years (44-77). Using gas chromatography, a gold standard for the diagnosis of EG poisoning (11), we detected its concentration in blood and urine. In patients with EG blood levels below 20 mg/dL, we started an antidote treatment with intravenous ethanol, because in Bulgaria we haven't got experience using fomepizole yet, which has been recommended in recent years in EG and methanol poisoning (12). In the next few days, we monitored EG and ethanol concentrations in the blood. In patients with an EG blood concentration above 20 mg/dL, we performed immediate hemodialysis to remove EG and its metabolites from the blood. These patients did not develop any clinical signs of poisoning. Nine (10.3%) of the patients who had survived the poisoning developed acute renal failure (ARF) and required hemodialysis treatment in order to restore their renal function. The maximum number of hemodialysis procedures we have administered in one patient was 20.

DISCUSSION

EG absorption through the lungs and skin is limited and rarely can lead to clinical signs of poisoning. EG is a colorless, odorless, relatively sweet alcohol (13) that is absorbed very quickly in GIT and reaches maximum serum concentrations after 1 to 4 hours. EG is metabolized up to 80% in the liver and the metabolites and non-metabolized EG part are excreted by the kidney (14,15). EG is metabolized to ox-

alic acid through a series of metabolic reactions. In the liver, ADH initially metabolizes it to glycol aldehyde. This first reaction is rate-limiting and can be blocked by the administration of antidotes such as ethanol or fomepizole (12). The next step is biotransformation of glycoaldehyde to glycolic acid with the participation of aldehyde dehydrogenase (ALDH). Further metabolism to glyoxalic acid and oxalic acid is a slower and longer process.

Symptoms that develop during the first few hours after EG ingestion are mainly due to its central nervous system (CNS) action (as with ethanol) such as euphoria, speech abnormalities, ataxia, consciousness suppression and coma. Possible manifestations by GIT are nausea and vomiting. The manifestations of GIT and CNS develop in the first 12 hours after EG ingestion (4,16). In the next 12 hours, tachycardia, arterial hypertension, tachypnoea, dyspnoea, cyanosis as well as pulmonary edema and acute heart failure may occur. The symptoms occurring 12-24 hours after EG ingestion as well as the metabolic acidosis are mainly due to EG metabolites (2,14). After 24 to 72 hours, posterior bladder damage up to ARF occur due to acute tubular necrosis (17) that is, usually, reversible. Glyoxalic and oxalic acids exacerbate metabolic acidosis and cause cardiopulmonary lesions. Glyoxalic acid is toxic to renal tubular cells. Oxalic acid reacts with calcium ions and forms calcium oxalate crystals, which are deposited in the kidneys, brain, pericardium, liver, and blood vessels and damage them. Usually, such injuries are reversible, however, in some cases, permanent lesions are registered (15,18). Emerging hypocalcaemia causes cardiac arrhythmias, tetanus muscle contractions and seizures (19).

A typical clinical picture of intoxication develops in the patients with suicidal attempts and those who have taken more EG but have not sought medical attention by the end of the first day after swallowing. Normally, EG lethal dose is 1.4 mL/kg b.w. (4). The prognosis of EG poisoning is poor in the presence of coma, seizures, severe metabolic acidosis (20), respiratory and circulatory lesions (21) at the beginning of treatment and advanced age of the intoxicated patients (22). Early onset of treatment may improve the prognosis (23). In case of severe EG poisoning, white matter brain necrosis, predominantly

in the frontal lobe, basal ganglia, thalamus, midbrain and pons are described (24,25).

Hemodialysis, along with the antidote, is a cornerstone in the treatment of severe EG poisoning and is a major method for elimination of EG and its metabolites (3,26,27). This therapeutic option is recommended with blood glucose concentration above 50 mg/dL (1). In the USA and the UK, the most common cause of extracorporeal treatment is EG poisoning (28). It is also a primary method of treatment in patients who have developed ARF. We have performed hemodialysis in 34 (35.8%) of patients.

The lethality rate found by us is the same (29) or lower than that reported by other researchers (30,31). The lower lethality rate in our study is due to the large number of occasional intoxications in which patients seek medical care immediately or soon after EG ingestion. In these cases, clinical symptoms of poisoning are usually not available at the time of treatment, and metabolic acidosis is mild or lacking.

CONCLUSION

Acute EG intoxications are rare, but potentially life-threatening and pose a challenge to clinical toxicology. The main route of EG intoxications is oral. Poisons with EG are predominantly random, rarely due to suicidal attempts and are more specific to male gender. We have recorded a lethality rate of 8.4%. Hemodialysis is a main method of treatment, both in the early phase of intoxication, during the elimination of EG and its metabolites, and in ARF development. The medico-social significance of EG poisonings is determined by its possible lethality, serious complications, prolonged and costly treatment.

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