

ACUTE METHANOL INTOXICATIONS REGISTERED IN VARNA REGION (BULGARIA) FOR A 25-YEAR PERIOD

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ABSTRACT

This retrospective study was conducted to follow out acute intoxications with methanol in Varna region (Bulgaria) for a 25-year period (1991-2015). At that time, 98 patients with methanol poisoning were registered in the Clinic of Toxicology of Military Medical Academy in Varna, Bulgaria. The average age of the patients was 44.5 years. The diagnosis was made based on symptoms and was confirmed by gas chromatographic analysis of methanol concentration. The majority of poisonings were accidental – 88.9 %, and only a small part was with suicidal intentions (9.2%). Lethal outcome was registered in 38 patients. Eight of the survived patients (13.3%) were with residual visual impairment and six of them had permanent neurological complications.

Keywords: acute poisoning, intoxication, methanol, coma, convulsions

INTRODUCTION

Methyl alcohol (methanol, wood alcohol) is a component of many commercial products such as solvents, detergents, paints, varnishes, fuels, antifreeze, denatured alcohol, car windows washing liquid, and may be found also in home-made alcohol beverages (1,2). It is used in chemical production and in laboratory practices. Methanol poisonings are infrequent,

but in most cases they are causing life-threatening injuries (3,4,5). Methanol itself is a relatively low-toxic compound (5). Ingested orally, it is rapidly absorbed by the gastrointestinal tract. Around 90-95% of it is metabolized by the liver enzymes alcohol dehydrogenase and aldehyde dehydrogenase to highly toxic metabolites - formaldehyde and formic acid, which are the ones that cause organ damage and death of the poisoned patients. In many countries, methanol is the leading cause of intoxications as a result of the use of illegal and non-standard alcohol (6). Methanol poisonings are the result of accidental or deliberate ingestion of fluids containing methanol. Intoxications are mostly single cases, however, mass poisonings are reported as well (7,8). Despite the intensive treatment, lethality in this kind of poisoning is high and visual impairment, blindness and serious

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disorders of the central nervous system (CNS) have been established in part of the survivors.

In this regard, we aimed to investigate the incidence of acute methanol poisoning, mortality rates and complications of methanol poisoning in Varna region (Bulgaria) for a 25-year period (1991 – 2015).

MATERIALS AND METHODS

The study was performed as a retrospective review of the hospital charts of all patients who had been treated for methanol poisoning from 1991 to 2015 (25 years) in the Clinic of Toxicology of Military Medical Academy in Varna, Bulgaria. The treatment of patients included gastric lavage, administration of sodium bicarbonate (for correction of acidosis), ethanol (as an antidote), and hemodialysis, when needed. Fomepizole is not available in Bulgaria. The definitive diagnosis of each poisoning was based on a positive history of alcohol consumption (home-made, smuggled, industrial), clinical manifestations, metabolic acidosis with an increased anion gap, and gas chromatographic analysis of the patients' blood.

Gas chromatograph 5890-series II Hewlett Packard with flame ionization detection (GC-FID), Headspace sampler 19395A and HP 3396 Series II Integrator was used for the determination of methanol in blood samples.

RESULTS AND DISCUSSION

During the 25-year period, ninety-eight patients have been treated for acute methanol intoxication in the Clinic of Toxicology of Military Medical Academy in Varna, Bulgaria, and all of them were included in the study. Of them, 74 (75.5%) were male and 24 (24.5%) were female, the ratio of men to women was 3.1:1. Acute intoxications with methanol occurred significantly more often in men than in women (9,10,11). This is a result of a more frequent use of alcoholic beverages by males. Compared to all intoxications during the studied period, the incidence of acute poisoning with methanol was low (0.6%). Despite their low frequency, methanol intoxications are very important for toxicological practice as they are associated with the development of life-threatening injuries and complications, and a high mortality rate (2,3,12,13,14,15).

Age distribution shows that the majority of the patients are in active working age (up to 60 years) –

88 people (89.8%) (Fig. 1). These findings coincide with studies of other authors (13,16,17).

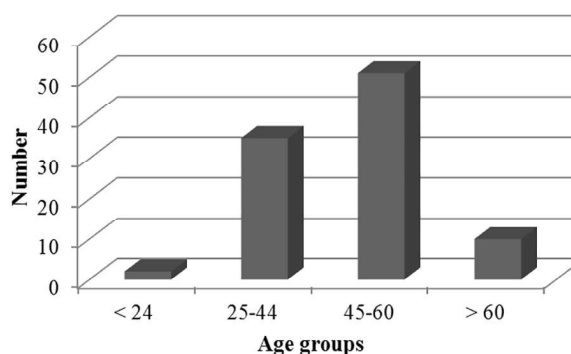


Fig. 1. Age distribution of methanol-poisoned patients

The majority of poisonings were accidental and without intent – 89 cases (90.8%) and only 9 cases (9.2%) were with deliberate intake of methanol, i.e. suicidal. The high rates of accidental poisonings could be contributed to the physicochemical properties of methanol which is similar in color, smell and taste to ethanol. The alcohol combustion liquid used in the households should contain ethyl alcohol that is denatured with methanol, which should amount up to 1% and be dyed with methyl violet that imparts a blue-violet color of the finished product. Unfortunately, many companies that produce alcohol for combustion are using the less expensive methanol as a raw material instead of ethanol (18). The oral intake of such alcohol is the major cause of methanol poisoning in our study.

The blood concentrations of methanol in methanol-poisoned patients were in the range of 100 to 4860 mg/dL upon arrival at the hospital as estimated by gas-chromatographic methods. In 8 patients (8.2%) methanol blood concentrations from 100 to 200 mg/dL were established. These were below the lethal concentration. For all other patients, the initial values of the methanol in the blood were higher than the lethal ones (above 200 mg/dL) (Tabl. 1).

The average duration of the registered by us latent period from the ingestion of methanol until the first non-specific symptoms of the methanol poisoning of the CNS and GI tract (headache, dizziness, nausea, vomiting) was 12.5 hours. Patients, who did not seek immediate medical help after the first symp-

Table 1. Concentration of methanol in hospitalized patients' blood

Concentration of methanol in patients' blood, mg/dL	Cases	Percent, %
100 – 200	8	8.2
210 – 1000	21	21.4
1100 - 2000	29	29.6
2100 - 3000	19	19.4
3100 - 4000	16	16.3
4100 - 5000	5	5.1

toms, were hospitalized later with the complete clinical picture of methanol poisoning - visual impairment, coma, convulsions, severe metabolic acidosis, respiratory disorders and hemodynamics.

The main methods recommended for the treatment of the severe methanol poisoning include gastric lavage, administration of sodium bicarbonate (for correction of acidosis), ethanol (as antidote), and hemodialysis, if necessary (5,7,12,19). The early initiation of this treatment can improve the prognosis (20). In our treatment regimen, intravenously administered ethanol was used as an antidote. The concentrations of methanol and ethanol in the blood were monitored in the next 1-2 days by gas chromatographic analysis. Our goal was to achieve therapeutic concentrations of ethanol in the range of 100-150 mg/dL (21). We did not apply fomepizol, which has 8000x greater affinity to alcohol dehydrogenase (ADH) than ethanol because it is not registered in Bulgaria. The data in the literature indicates that both antidotes have similar effects on the outcome of the treatments of the poisoning (5,8,12,22,23). Hemodialysis is a key element in the treatment of serious poisoning with methanol and is a general method for its elimination, as well as its toxic metabolites (5,24,25).

All patients with methanol poisoning in the Clinic of Toxicology received such treatment. Despite all undertaken measures 38 patients (38.8%) died. Various clinical findings at the time of admission have been suggested as poor prognostic factors, such as severity of acidosis, high serum levels of methanol or the long time elapsed from consumption to the time of admission, the presence of hyperglycemia, coma, and seizures (6,7,8). Our results con-

firm the previously established by other authors high lethality rate in methanol intoxications (6,8,14,15).

In eight of the surviving patients (13.3%) visual impairments were registered, 4 of them ended up with complete blindness. Poisoning is often accompanied with blindness and ocular disorders in patients, who survive methanol intoxication (7,9,26,27,28). Some of the eye damages are irreversible (26). In the other patients, we have achieved partial success by therapeutic application of 2-3 courses of 10 sessions each of hyperbaric oxygenation during the recovery period. Formic acid is the toxic metabolite in methanol intoxication, which inhibits the mitochondrial electron transport chain by inhibiting the enzyme - cytochrome c oxidase. Cytochrome oxidase is an important energy-generating enzyme crucial for the proper functioning of highly oxidative tissues (e.g. retina) and its inactivation is responsible for the retinal and optic nerve toxicity in methanol poisonings.

Serious neurological complications were established in six patients (10%) at discharge from the hospital. Neurological complications are typical of methanol poisoning. Necrosis and hemorrhage in putamen and white brain matter are being described and they are often the cause of death (1,4,29,30). Cerebral hemorrhages are registered in patients with low blood pH, higher base deficit, hyperglycemia and high lactates at admission (17).

CONCLUSION

Our study confirms that acute poisonings with methanol are relatively low in frequency but are characterized by life-threatening complications and high mortality. Oral ingestion is the major route of methanol intoxications. Methanol poisonings are mostly random and, very rarely, they are a result of suicide attempts. They affect more often men and people of working age. We have established a high mortality rate (38.8%), despite the proper treatment.

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