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THE USE OF HAEMODIALYSIS AND 2,3 PROPANESULPHONATE (DMPS) TO MANAGE ACUTE ORAL POISONING BY LETHAL DOSE OF ARSENIC TRIOXIDE

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Abstract. The paper discusses a case of oral acute poisoning by dental paste containing arsenic trioxide. A 33-year-old woman ingested 1/3 of the dental paste package, which corresponds to 1850 mg pure arsenic trioxide. Acute gastroenteritis and oral mucosa burn developed within 3 hours since the poisoning. Considering the amount of the ingested poison, highly exceeding the lethal dose, haemodialysis was undertaken.

During the treatment, DMPS (Unithiol) was administered, with the patient's consent. The patient recovered completely, with no complications or side-effects of the therapy.

Arsenic is known to have many allotropic variations and its physical and chemical properties are intermediate between those of metals and non-metallic substances. Under conditions of occupational exposure, acute poisoning by arsenic or its derivatives may occur at the processing of arsenic-contaminated metal ores. Arsenic and arsenic compounds pose a potential hazard for workers in the tanning, pharmaceutical and dye industries as well as staining cotton fabrics and glass decolourizing. One of the common arsenic compounds, arsenic trioxide (As_2O_3), a component of a formerly used dental paste, dissolves very well in oils, fairly well in acids and alkaline solutions.

Over the last several years very few cases of acute arsenic trioxide poisoning have been reported. The course of intoxication is usually severe, with mortality reaching 50 – 75% of all the arsenic trioxide poisoning (7). Death often follows within the first 48 hours since the poisoning. The lethal oral dose for man ranges from 1 – 4 mg/kg (7). A single dose of 5 – 50 mg is considered to be the toxic dose (12).

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Arsenic inactivates enzymes sulfhydryl groups, such as lactic dehydrogenase in heart muscle, thereby producing an intoxication. Similar effects refer to the gastrointestinal tract and nervous tissues and they are later manifested as clinical symptoms (11).

Furthermore, arsenic exhibits toxic effect on the sympathetic nerve endings thus producing vasodilation.

Arsenic is deposited in the liver, kidney, nails and skin (7). Highly soluble arsenic compounds are much more easily absorbed than those which are insoluble in water. The highest rate of elimination of the absorbed arsenic can be observed within the first four days following the poisoning (24). Some amounts of arsenic can still be determined as late as ten days after. The elimination of a single arsenic dose reaches its peak 4–8 hours since the poisoning (10).

In oral overdosage the clinical symptoms develop within 30 min to 2 hours (7). At first they include vomiting, watery bloody diarrhea, severe abdominal pains, oesophalgia, sometimes a garlic odour in the expiratory air. In severe cases shock symptoms develop, aggravated by the direct vasodilating effect (7). This is followed by circulatory collapse, brain oedema, coma and convulsions. Death resulting usually from the circulatory failure follows within 24 hours (7).

In patients surviving the first stage of the poisoning, liver damage with jaundice as well as kidney damage develop. The peripheral polyneuropathy is the characteristic symptom. In view of the short half-life of arsenic in blood the quantitative determinations in urine seem to have a higher diagnostic value (14).

CASE HISTORY

A woman aged 33, body weight 62 kg, suffering from a toothache put 1/3 of a new, sealed package of arsenic paste on the aching tooth (the arsenic paste corresponds to 5.5 g arsenic trioxide; thus 1/3 of the package contains 1850 mg pure arsenic trioxide). After about 2 hours she accidentally swallowed the paste and rinsed her mouth as she felt the burning sensation of the oral mucosa. Within the next 3 hours, nausea, vomiting, diarrhoea developed as well as abdominal pains of varying intensity which made the patient seek medical advice.

On admission, 100 hours after ingestion, the patient was conscious, in logical verbal contact and presented symptoms of gastroenteritis. BP of 110/70 and heart rate increase to 98/min could be observed. The subjective examination revealed traces of oral mucosa burn, abdominal tenderness and intensified peristalsis. The skin was pale and dry.

Gastric lavage was not undertaken owing to a long period of time between the poisoning and admission. The patient was given orally 62 g (1 g/kg b.w.) of activated charcoal. Biochemical testing did not reveal any abnormalities, except low potassium and chloride concentrations (3.2 mmol/l and 90 mmol/l, respectively). Arsenic was detected using the chelation method by Vasak and Sedevic, and then determined by atomic absorption spectrophotometry (14).

Considering the data from the history and the amount of poison ingested, which exceeded the dose reported as lethal, haemodialysis and simultaneous administration of DMPS were applied (24). Haemodialysis was carried out for 12 hours with no complications (Hemoflow E4, eff. surface area 1.6 m^2, Fresenius AG, Blood flow 150 ml/min). On the next days of the treatment, the patient received

conservative therapy. She was given 250 mg Unithiol (DMPS) i.v. every six hours for the first 48 hours. For the next 48 hours 250 mg 3 times a day. From day 5 to 28 i.e. till the end of hospitalization she received 250 mg DMPS every 12 hours. On day 2 of the treatment the patient's condition improved largely. Only the painfulness due to oral mucosa burn persisted. The burns healed up completely within 5 days of the treatment.

During the treatment, the neurological examination was repeated several times. The only neurological symptoms were transient 'pins and needles' and tingling sensation in the limbs which appeared on day 10 and receded within the next two days.

No other significant symptoms of the nervous system dysfunction were found. Also no symptoms of the liver and kidney damage could be observed. The patient was discharged from hospital in a good health condition after 28 days of treatment. The follow-up examination after 3 and 6 months did not reveal any abnormalities with respect to the function of the liver, kidney and the nervous system.

Arsenic excretion during the consecutive days of treatment is displayed in Fig. 1. Within the first week 84% of the total amount of arsenic determined over the period of 21 days was excreted with urine. The highest arsenic concentrations were noted on days 1, 2 and 3. From day 8 to 21 the arsenic concentrations remained low and varied from 113 to 472 μg/l (mean 296 μg/l).

On day 2 of the treatment, blood concentrations of zinc, copper and magnesium were determined. The deficits were corrected with Geriavit (Pharmaton). The concentrations of the essential metals regained normal values on day 6 and maintained at the same level till the end of hospitalization. Geriavit at the maintenance dose (1 capsule every 12 hours) was continued during that period.

DISCUSSION

The case discussed presently was a typical arsenic trioxide poisoning which was manifested by abdominal pains, vomiting, diarrhoea and oral mucosa burns. Probably thanks to the early haemodialysis and Unithiol administration no symptoms from the circulatory or the nervous systems developed. Positive effects of Unithiol in the treatment of arsenic poisoning in humans have been reported only by a few authors, mainly Russian ones (5,6,21,23). However, there are publications reporting inefficacy or even adverse effects of Unithiol in this kind of therapy (16,20).

In Western European countries 2,3 dimercapto-1-propanesulphonate started to be used for treatment of mercury and lead poisoning in the 70s. The compound is a derivative of dimercaprol (BAL), highly soluble in water, less in methanol and ethanol, and completely insoluble in organic solvents (7,17). Apart from the complex with cadmium (13), DMPS binds heavy metals due to the presence of sulfhydryl groups.

In the former Soviet Union DMPS was admitted for use in 1950, under the trade name of Unithiol. From 1956 it was used as a heavy metal chelator. For the next several years some research studies on the preparation were carried out in China, Soviet Union and Japan. Since 1975 Unithiol has been used for the treatment of mercury and lead poisoning in the US and some European countries (13).

There is a tendency to manage metal poisoning with the least toxic chelators (1,2,3,8,9,19,22). Experimental animal studies proved the low toxicity of DMPS (15,18). The recent studies with dogs revealed that the side effects of DMPS are dose-dependent (16). The doses from 15 to 75 mg/kg produced either no side effects or statistically insignificant number of weakly pronounced side effects. Evident circulatory and respiratory impairments which may have been the immediate cause of death were observed after the administration of 150 mg/kg DMPS. Comparative studies in animals intoxicated with arsenic revealed that DMPS had been the most effective chelator (4). It has to be stressed that the DMPS doses administered to humans do not exceed the lowest doses in animal studies reported by Klimmek et al. (16). Following the literature, in humans the side effects include allergic reactions after a long-term treatment. Furthermore, nausea, vomiting, weakness and vertigo may develop (13).

In the case described presently, the patient most probably consumed the lethal dose of arsenic. However, the amount of absorbed arsenic is difficult to estimate due to intense gastroenteritis and resulting self-elimination of the poison. Urinary excretion exceeded several times the levels recorded in other patients with similar poisoning hospitalized so far in our clinic. The dosage applied was that recommended by the manufacturer. It seems that the positive results, we have obtained, may be attributed to the early application of haemodialysis, and simultaneous Unithiol administration. No side effects of Unithiol therapy were observed. The decreased levels of magnesium, zinc and copper, on day 2 of the treatment, may have been the effect of the chelating activity of DMPS, which correlates with the reported results of animal studies (16).

According to the literature data, DMPS appears to be an effective chelator of arsenic in experimental animals and in humans. Contrary to BAL, it makes a water-soluble complexes, which prevent redistribution of arsenic to the brain. The case described presently confirmed the high efficacy of DMPS in the treatment of arsenic intoxication. The fact that prolonged DMPS therapy did not bring about any side-effects, and produced high rate of elimination may indicate the usefulness of DMPS for the treatment of occupational poisoning by arsenic and other DMPS--chelated metals. However, further studies would be desirable in order to investigate the applicability od DMPS for the management of arsenic poisoning.

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