CASE REPORT

Extracorporeal Methods in The Treatment of Poisoning

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ABSTRACT

Among the various ways of managing poisoning, haemodialysis may help in enhancing excretion of the toxic substance. We report a case, a Russian male, 35 years old, who was rushed to the Gleneagles Hospital Medan from the airport after being evacuated from Banda Aceh together with another older Russian who died as they arrived at the admission and Emergency Department. From the result of intensive allo anamnesis and the high anion gap metabolic acidosis, in the absence of disturbed renal and liver function, we presumed this patient was suffering from methanol intoxication. The time of exposure was approximately 70 hours before.

The exact length of dialysis time to excrete the noxious substance from the blood without plasma methanol determination was difficult. Moreover the time elapsed from exposure to treatment had been approximately 70 hours, which means the optic nerve had been so long exposed to formic acid, the toxic metabolite of methanol, that the damage should have been very severe. Ethanol is also known to be an antidote of methanol, which can be given orally by nasogastric tube, or i.v. It should be given early, and plasma ethanol level should be closely monitored to make it effective and safe. This was also unavailable. Another antidote is fomepizole which is also as yet unavailable in Medan. Folic acid, thiamin, and i.v. folinic acid are also recommended by the literature, as well as oral steroid.

Key words: methanol poisoning, hemodialysis, ethanol, fomepizole, methyl-prednisolon.

INTRODUCTION

General principles of the treatment of poisoning are to identify the poison, route and amount of exposure, the time of presentation relative to the time of exposure and the severity of poisoning. Knowledge of pharmacokinetic and pharmacodynamic of the toxin is essential. Treatment goals include support of vital sins, prevention of further poison absorption, enhancement of poison elimination, administration of specific antidotes and prevention of re-exposure. We report a case of poisoning, suspected to be from methanol, where in the absence of blood assay of the poison we managed to save the patient’s life and to some extent, his vision as well.

CASE ILLUSTRATION

A 35 year old Russian man was rushed to The Gleneagles Hospital Medan on December 27 2005 late in the afternoon together with a compatriot of his, another Russian, from Polonia, the airport of Medan. They had been flown in from Banda Aceh where they were found to be severely ill after what was believed as bouts of drinking alcoholic cocktail, on the previous Saturday night, about 72 hours before. Both patients were accompanied by their comrades who acted as an translator and also brought a letter from a foreign doctor in Banda Aceh mentioning his suspicion of methanol poisoning. On their arrival at the Admission and Emergency Department the older patient, a man of 57, died before proper clinical management could take place. The survivor presented, himself as lethargic, shortness of breath, extremely blurred vision. Blood pressure was 150/90 mmHG, heart rate 90 beats/minute, respiration was shallow, 28 times/minute and temperature 37.2°C. Both pupils were nearly in maximal mydriasis. Otherwise all physical signs were normal.

Laboratory work-up showed Hb 14.9 g/dl, Ht 49.9%, WBC 16.3x10⁹/L, blood glucose 92 mg/dl, liver function tests were normal, with total bilirubin 0.97 mg/dl, AST 16 U/L, ALT 23 U/L, ALP 113 U/L, gamma GT 23, U/L. Blood urea was 27 mg/dl, creatinin
Continuous renal replacement therapy (CRRT) such as continuous arterio-venous haemodialysis (CAVHD) or filtration (CAVH), or with dialysis (CAVHDF), continuous veno-venous haemodialysis (CVVHD) or filtration (CVVH) or with dialysis (CVVHDF) can be used to detoxify cases with unstable hemodynamics where conventional haemodialysis, hemofiltration or hemodiafiltration are not applicable. CRRT has also been used to remove tissue-bound substances, such as paraquat, in which the offending agent is released slowly from its reservoir, which might result in rebound phenomenon. But overall the amount of toxic materials removed with these methods is limited due to the slow nature of the process.

Hemoperfusion is a method using a cartridge with activated charcoal, coated with a thin, relatively porous semi-permeable membrane, through which blood is passed. Absorption occurs because the hydrophobic properties of charcoal. For removal of more lipid soluble intoxicants, hemoperfusion using non-ionic resins, such as Polystyrene co-polymer resin had been developed. Anyhow, the total amount of drug removed is usually small and is not of great clinical consequence.

Slow low efficiency dialysis (SLED) is a method using conventional hemodialyzers but with a slow blood flow, 100-200 ml/minute with also a slower than normal dialysate flow rate. Each treatment can last up to 10-12 hours everyday. This method is usually applied to critically ill patients. This procedure may also be used as an adjunct to conventional extracorporeal measures in the treatment of poisoning.

Peritoneal dialysis (PD) is considered to be ineffective in removing toxins and is seldom used except in circumstances under which no other more effective extracorporeal removal of toxins are applicable. This is due to the fact that removal by the peritoneal membrane is no better than that provided by the native kidney; thus, this method is only used in cases with significant renal function impairment.2

**Methanol Poisoning**

Methanol is an alcohol derivative, originally obtained from destructive distillation of hardwood, is widely used as an industrial solvent, antifreeze fluid, windshield wiper fluid, and windshield deicer, and also as alternative fuel. Because of its inebriating properties similar to ethanol, and because it is inexpensive and widely available, it has been responsible for many intoxications in the United States and many other countries. Methanol poisoning can be due to accidents or as a suicide attempt, but can also be due to inhaled evaporations as well as dermal
absorption. Methanol is rapidly and completely absorbed from the intestinal tract and metabolized by alcohol dehydrogenase and forms formaldehyde, which is further converted to formic acid. The ingestion is associated with acute inebriation, followed by asymptomatic period lasting 24-36 hours. At this point abdominal pain, caused by pancreatitis, seizures, blindness, and coma may develop. The blindness is due to the direct toxicity of formic acid on the retina. Methanol intoxication is also associated with hemorrhage in the white matter and putamen which can lead to the delayed onset of Parkinson-like syndrome. The lethal dose is between 60 and 250 ml. Lactic acidosis is also a feature of methanol poisoning (as well as that of ethylene glycol poisoning) and contributes to the elevated anion gap. Together with the appearance of the anion gap, an osmolar gap also becomes manifest and is an important clue to the diagnosis. The osmolar gap is the difference between the measured and calculated osmolality.\(^3\) The equation is as follows:

\[
\text{Calculated osmolality} = 2 (\text{Na}^+) (\text{mmol/L}) + \text{BUN} (\text{mg/dl}) / 2.8 + \text{glucose} (\text{mg/ml}) / 18
\]

In addition to supportive measures, therapy is centered on reducing the metabolism of methanol and accelerating the removal of the alcohol from the body. Decreasing metabolism is important since the metabolites rather than the parent compound are responsible for the toxic effect.\(^5\) Inhibiting the alcohol dehydrogenase, playing important role in the metabolic pathway, is one of the methods recommended, achieved by the administration of competitive agent, i.e. ethanol solution. However there are problems in administering this agent for treatment purpose. Intravenous preparations are often not available, and the pharmacokinetic characteristics of ethanol are erratic, making it difficult to maintain adequate plasma concentration. Thus plasma ethanol must be measured often and appropriate dose adjustment made. Patients must be monitored closely because they are intoxicated and at risk for liver injury and hypoglycemia. The efficacy of this method has never been studied prospectively and all clinical data are from case reports and retrospective case series.\(^4\) Fomepizole (4-methyl pyrazole) is an inhibitor of alcohol dehydrogenase that appears to have few of the adverse effects of ethanol and had been shown, in a prospective multicentre study involving 11 patients, to be effective and safe in the treatment of methanol poisoning.\(^5\)

Haemodialysis is a method of taking the toxin out of the body by way of diffusion and convection from the blood compartment to the dialysate compartment and to the drain.

The estimated time required for dialyzing poisoned patients to aim at the toxic concentration and their metabolites 5 mmol/L or less had been calculated by Hirsch et al\(^6\) and re-validated later by Youssef and Hirsch.\(^7\) They develop this formula:

\[
\text{Time Estimate} = \frac{-V \ln (5/A)}{0.06 k}
\]

\(V\) = Total body water in liters
\(A\) = initial plasma concentration of the offending agent in mmol/L
\(k\) = 80% of the manufacturer's specified dialyzers urea clearance in ml/minute

The use of fomepizole and/or ethanol and haemodialysis had also been applied to patients and are believed to reduce the dialysis required time. The use of an ethanol- and phosphate-enriched dialysate to maintain stable serum ethanol levels during haemodialysis for methanol intoxication had also been applied. In this method the authors mixed 475 ml of 65% ethanol to the acid portion of the bicarbonate based dialysate, and add one bottle of 45 ml of Fleet Phospho Soda and mixed rigorously into 4.5 liters of acid concentrate.\(^8\) Haemodialysis with high-flux polysulfone membrane and continuous hemodia-filtration had also been used to remove the offending agent in methanol poisoning.\(^9,10\)

**DISCUSSION**

Intoxication with methanol has been very rarely reported in Indonesian medical journals. Recently we read reports in the press on methanol poisoning due to consumption of local beverages like in North Sulawesi, but no medical publication on this occasion is available. Our patient was one of the many foreigners working for the many NGOs in Aceh after the Tsunami December 2004. The implementation of the Islamic Syariah makes it difficult to find alcoholic beverages in that region, and being Russian our patient was happy to be treated by his colleague to a Saturday night drink of self made cocktail, made from spirit and coke. They had their party of two in his friends room and after he thought he had enough, and that means several glasses, he went to his room to sleep. He might have had a tight sleep due to the inebriating properties of the methanol. Where his friend got the methanol from was not very clear, but most probably by buying some spirit from the many pharmacies or drug stores in town.

The next day they were quite comfortable, that they went to the local beach, together with comrades and had swimming in the sea. Only in the afternoon they, the two men, felt uncomfortable in their body and vision began to blur. It seemed that they had experienced an
asymptomatic episode of the usual course of methanol intoxication mentioned in the literature. The second day the uncomfortable feeling and blurred vision continued but only the next day that they decided to see a doctor, who was also a foreigner working in Aceh, and the doctor suspected methanol intoxication, and prepared evacuation to Medan. They reached the hospital late in the afternoon, which was approximately 70 hours after the time of consumption. The “host of the party” died soon after arrival. This probably was due to the greater amount of the toxic material consumed than our patient did. We were confident with the diagnosis of methanol intoxication, due to several reasons, i.e:

- the history of consuming inebriating alcoholic self made cocktail
- lethargy and shortness of breath
- near maximal dilated pupillae and severely blurred vision, with minimal reflex to light.
- acidosis in the absence of kidney and liver function disturbances with a high anion gap, of approximately 38 mmol/L.

Calculated serum osmolality in our patient was 289.5 mOsm/kg. This was not significantly different from normal.

Blood methanol determination is not available in the hospital, as well as in Medan. The only Laboratory who does the service is the Police Forensic Laboratory which would send samples to Jakarta and the result would be expected in 1-2 weeks time. So we directly gave 300 meq Bicarbonate solution, and put a blood access for dialysis. The dialysis started approximately 2 hours after the patient arrived in the hospital. The duration was 2½ hours, when normal respiration was restored, and the pupil was back to normal size with normal reflex to light. Post-haemodialysis laboratory investigation showed significant improvement of the metabolic acidosis, as well as reduction of the anion gap. pH: 7.41, pCO2: 24.9 mmHg, pO2: 125.2 mmHg, bicarbonate: 15.5 mMol/l, TCO2: 16.3 mMol/l, Base Excess: - 7.0 mMol/l, O2 saturation: 99%. Sodium: 133 mMol/l, Potassium: 3.1 mMol/L, Chloride: 92 mMol/l.

The next day when the patient had been able to communicate it was apparent that his vision was still very bad, near to the total blindness. We decided to dialyze him and this lasted 7 hours, and the next day on for 5 hours. On day 6 of admission he reported that his sight was much better, that he was able to dial his mobile phone. We decided to dialyze him further every day and until the 12th day of admission. Also much to our surprise he reported that each day brought improvement to his sight, although some times proved to be subjective, but this boosted his optimism, which seemed to increase his quality of life. Methanol has a low molecular weight, water soluble, and the metabolite formic acid which affect the optic nerve to be released through haemodialysis. The extraction should be complete, due to the chemical properties of the substance, but there had been reports where this extraction took prolonged time by hemodialysis, and even rebound on stopping dialysis.

The rather grim condition of the eyes really would not be too surprising because this is influenced by the time elapse between ingestion and haemodialysis. In this case it was approximately 72 hours. It is very interesting to know further what will the outcome of the eyes be, because permanent damage with complete blindness had been reported quite extensively. But the exact cause of the improvement of his vision, which he reported happened after each day of haemodialysis until day 12, was not sure.

CONCLUSION

There are some points which could be involved in, among others are the daily haemodialysis, the prescription of N-acetyl cystein and folic acid, the infusion of folinic acid and the prescription of steroid.

He was discharged from the hospital, to be flown to Jakarta and then to Moscow, accompanied by an intensivist doctor from Russia.
REFERENCES


