

Combined Hemoperfusion and Hemodialysis Treatment of Poisoning with Cholinesterase Inhibitors

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Three patients with cholinesterase inhibitor poisoning have been presented. The patients were in a deep coma and, in one of them, artificial mechanical respiration was instituted. All three cases were treated by a procedure combining hemodialysis and hemoperfusion with Amberlite resin (XAD-4), and the clinical picture improved over a short period of time. After the end of procedure, the platelet count was approximately 41% of normal. Some aspects of these intoxications are discussed.

Key Words: Cholinesterase, Inhibitors intoxication, Coma, Hemodialysis, Hemoperfusion.

INTRODUCTION

Diagnostic and therapeutic measures, especially against intoxication with cholinesterase inhibitors, require eliminating the toxic agents as rapidly as possible. The therapy consists of gastric lavage (in the case of oral intake), support of ventilation until respirator is introduced, administration of atropine and pralidoxime when necessary. In the early period of poisoning, inhibition is reversible and may be reactivated by oximes. Late reports contain data on the use of extracorporeal elimination of poisons in the management of these intoxications^{1,2}. We have recently treated successfully three patients suffering from severe poisoning with cholinesterase inhibitors by hemodialysis and hemoperfusion.

CASE REPORTS

1) A 28-year-old patient (S.K., male), because of a traffic accident with material loss, had swallowed about 100 ml of quinalfos (oral LD₅₀ for rats amounts to 66 mg/kg) in a suicidal attempt. Immediately after ingestion, he vomited. On the way to the hospital, the patient lost consciousness and was admitted to the department 50 minutes after poisoning.

On admission, he was cyanotic with white foam on his mouth, dyspneic, hypotonic, in deep coma

and was not responsive to stimulation. There was fecal and urinary incontinence. The patient had pinpoint pupils and they were not reactive to light. Diffuse rhonchi were heard at both lung bases. The heart rhythm was normal with mute sounds. The blood pressure was 18.7/10.7 kPa, and pulse rate 90/min. The abdomen was normal.

From the laboratory findings the following is emphasized: the serum glucose was 7.6/10.1/5.0 mmol/L, and the others were normal. The blood-cholinesterase on the fifth hospital day was 1000 U/L. The platelet count was 201; 126; 95; and 134 × 10⁹/L. Prothrombin time measured from 16s (50%) to 17s (44%), and from 15.5s (53%) to 12s (100%). Chest roentgenogram was normal and electrocardiogram showed an incomplete right bundle branch block.

Treatment was begun with gastric lavage, introduced subclavian catheter, inserted arteriovenous shunt on the left leg and extracorporeal hemodialysis administration with hemodialyzer of 1.4 m². Immediately after that, hemoperfusion over Amberlite resin (XAD-4) for 4 hours by means of general heparinization was started. The procedure began at 6.15 p.m., and at 7.30 p.m. the patient responded to verbal instructions. Blood flow through the hemoperfusion system was kept at 200 ml/min. At the end of the procedure, macrohematuria, with low platelet values (48.2% lower from the initial levels) and prolonged prothrombin time took place, and the hemoperfusion was stopped. On the next day, the patient's condition improved completely. Nasogastric tube and urethral catheter, instituted on admission, were removed. His convalescence was uneventful. The patient was treated with atropine and pralidoxime and his

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blood-cholinesterase activity on the 13th hospital day was 50% of normal. Three days after hospitalization, abstinence symptoms appeared and he was given clomethiazole and meprobamate. In 16 days the patient left the hospital. The psychiatric finding showed that the patient was critical towards the attempted suicide and it appears as a shortlasting affective reaction of an hysterical personality.

2) A 48 year-old patient (J.B., male) had a long history of ulcer disease. In 1971 the patient underwent surgical procedure because of duodenal ulcer perforation (suture) while, in 1974, a gastric resection was done. In 1979, however, the disease recurred and, since 1980, the patient is drinking greater quantities of alcohol every day.

The patient, while drunk, consumed an unknown quantity of quinalfos and, a few minutes after that, lost consciousness. On admission he was comatose, sweated, flushed, with plenty secretion in his mouth, with pinpoint pupils not reactive to light, shallow respiration and cyanotic extremities. Jugular veins were visible, and diffuse rhonchi were heard at the lungs. The heart rhythm was normal with muffled sounds. Pulse was 80/min, and the blood pressure 22.7/10.7 kPa. The liver was palpated for 4 cm. The presence of alcohol in the blood at the time of hospitalization was 1%. The white-cell count was $10.4-7.6 \times 10^9/L$ with 10-3 percent of nonsegmented cells. The serum glucose was 18.2-4.9 mmol/L, while the other "standard" laboratory tests were within the normal limits. The blood-cholinesterase was 68 U/L, and the platelet count was 372;166;146 and $126 \times 10^9/L$. After hospitalization, respiratory and metabolic decompensated acidosis and global respiratory insufficiency were found. Later, these findings were normal. An electrocardiogram was normal.

Minutes after arriving at the hospital the patient was treated with gastric lavage and, due to the progression of respiratory insufficiency, endotracheal intubation was done. Artificial mechanical ventilation was then instituted and subclavian catheter for dialysis was introduced. The hemodialysis, with a capillary hemodialyzer of 1.3 m², was immediately started and, after that, hemoperfusion over Amberlite resin (XAD-4) was performed. Heparin was administered. In the beginning of the procedure, blood pressure fell and it increased after the introduction of i.v. fluids. Blood flow through the apparatus was kept at 150 ml/min. The procedure lasted for 3 hours and 15 minutes. During the hemoperfusion the consciousness of the patient and blood pressure were restored. The patient's

respiration improved and eight hours later he was extubated. On the next morning, the patient regained consciousness. During the procedure, the platelets fell to 39.2% of normal. From the moment of admission he was treated with atropine and pralidoxime and, on the third day, with meprobamate as well, due to the development of abstinence syndrome. In 12 days the patient recovered completely and left the hospital.

3) The third case was a 29-year-old man (J.S.). It was discovered that, in 1982, the patient attempted suicide by cutting the blood vessels of his left forearm and, in March 1983, he again made an attempt to commit suicide by stabbing himself in the region near the heart. He underwent urgent surgery. In the same year, after having family problems, the patient consumed about 150 ml of quinalfos. After that, he was taken to a local health institution, where he was given 40 mg of atropine intravenously, and he was admitted to our Department of Medicine about 9 hours after poisoning. There are data that he was consuming about 1 liter of brandy per day.

On admission, the patient was comatose and afebrile. The pupils were narrow and not reactive to light. There were diffuse chest rhonchi. Heart rate was rhythmical with clear sounds. The blood pressure was 16.0/10.0 kPa, and pulse rate 96/min. The abdomen was normal. Hyperperistalsis was heard. Local contractions of muscles were present. The leukocytes were $11.0-4.0 \times 10^9/L$ with 10 percent nonsegmented cells. The platelet count was 145 and $60 \times 10^9/L$, and prothrombin time, after hemoperfusion, was 15s (46%). The blood-cholinesterase, taken at admission, was 68 U/L and the acid-base status presented as metabolic decompensated acidosis. Later, the finding of the acid-base status was normal. An ECG was normal.

Due to the serious clinical state of the patient, treatment was started immediately. A subclavian catheter was inserted and extracorporeal hemodialysis was attempted with a capillary hemodialyzer of 1.3 m². Shortly thereafter, hemoperfusion over resin (XAD-4) was initiated and it lasted for 2.5 hours. Heparin was administered and the blood flow held constant at 200 ml/minute. During, and immediately after, the procedure the patient regained consciousness and became somnolent. Atropine and pralidoxime continued to be administered and on the second hospital day, due to the development of abstinence symptoms, infusion of clomethiazole was given, followed by meprobamate. The patient's mental

and physical condition improved. He was afebrile and his blood pressure and pulse findings were normal. On the eight day after admission, he was transferred to the Department of Psychiatry for further treatment of psychogenic depressive reaction, the third suicidal attempt.

DISCUSSION

Today in the treatment of severe poisoning, various methods are used^{3,4,5)} including hemodialysis and hemoperfusion^{6,7,8)}. Hemoperfusion is the passage of blood through a column packed with granules of Amberlite resin which act as absorbents. In this procedure, physicochemical properties of an absorbent are used, while in hemodialysis there is a concentrational gradient between the blood and the solvent across the dialysis membrane. The method of hemoperfusion is effective in an experiment^{9,10)}, in which Amberlite resin is used for elimination of organophosphorus poisons. However, there is little experience with its use, particularly with the application of activated charcoal¹¹⁾ and dialysis in cholinesterase inhibitor poisoning. Hemoperfusion is when removing liposoluble substances which are bound to plasma proteins and have smaller molecular weight, as well as when the blood flow through the apparatus is greater. Molecules of 300-5000 daltons are most efficiently eliminated. However, this procedure has its disadvantages, including side-effects such as thrombocytopenia and, therefore, it is reserved for most severe poisoning. Three patients with methylparathion intoxication¹⁾, treated with plasma perfusion through activated charcoal, have been reported. One of these patients died from pneumonia. The method of hemoperfusion with activated charcoal has been described in the treatment of a 25-year-old patient⁹⁾ after an attempted suicide, and the procedure was undertaken 25.5 hours after intoxication. The patient died as the result of coma. In the comparison of in-vitro hemodialysis and hemoperfusion⁹⁾, analysing the clearance of organophosphorus compounds and nitrosthigmine proved to be nondialyzable, while its clearance values for hemoperfusion with activated charcoal amounted to 59.2 ml/min.

Demeton-S-methyl-sulfoxide and dimethoate had higher clearance rates by hemoperfusion than by dialysis (83.7:60.0 ml/min and 87.8:59.1 ml/min, respectively). Seyffart⁶⁾, in his publication, quoted malathion of organophosphorus poisons and reported that effective methods for its elimination are

forced diuresis (+), peritoneal dialysis (+), hemodialysis (++) and hemoperfusion over activated charcoal, while he gave no data on hemoperfusion with Amerlite resin. A 34-year-old female patient¹¹⁾, who ingested an organophosphorus poison intending to commit suicide, has been presented. She was successfully treated by a procedure combining hemoperfusion with activated charcoal and hemodialysis. Duration of treatment was 24 hours. There are also individual studies on the simultaneous use of these two methods: hemoperfusion with activated charcoal and hemodialysis. Fifteen patients intoxicated with various sedative-hypnotic agents treated with this combination have been reported¹²⁾. However, the use of combined hemoperfusion-hemodialysis therapy is a matter of debate in the treatment of organophosphorus poisoning, so, in the literature¹³⁾, this method is not discussed.

Our report describes three patients whose clinical picture was very severe. In one of the patients, mechanical ventilation was instituted and all three were in deep coma. In each case, the combined use of dialysis and hemoperfusion over Amberlite resin was effective, but this management is considered as yet an unproven form of therapy. All our three patients had completely resolved after a relatively short period of time: one regained full consciousness at the end of the procedure, the other became somnolent and the third, who was in a state of apnea, established spontaneous breathing followed by extubation, and his consciousness gradually restored. There are the studies carried out in-vitro²⁾ that speak in favour of hemoperfusion with Amberlite resin in intoxications: the clearance value for parathion with acrylhydrogel charcoal is 59.2 (relative clearance in percentage for a drug or pesticide at a blood flow rate of 1.25 ml/min) and 81.3 with Amberlite resin.

We conclude that each patient, poisoned with organophosphorus compounds, should be treated in an intensive care unit with monitoring of all vital functions, where the quoted therapeutic methods may be applied in the case of most serious poisoning.

REFERENCES

1. Lusknikov EA, Yaroslavsky AA, Shurkalin BK, Evseev NG, Barsukov UF: *Plasma perfusion through charcoal in methylparathion poisoning. Lancet* 1: 38, 1977
2. Okonek S: *Absorption kinetics of drugs and*

- pesticides as a function of the absorbent material, In: *Hemoperfusion*, eds. Sideman S, Chang TMS, McGraw-Hill, Washington, USA, pp 223-226, 1980
3. Berning TH, Krummenerl TH, Glaser J, Paulus H, Garlach U: *Die behandlung lebensbedroelicher exogener intoxicationen durch plasmaperfusion*. *Schweiz Med Wschr* 117:1368, 1987
 4. Garella S: *Extracorporeal techniques in the treatment of exogenous intoxications*. *Kidney Int* 33: 735, 1988
 5. Osterloch JD: *Utility and reliability of emergency toxicologic testing*. *Emerg Med Clin N Am* 8:693, 1990
 6. Seyffart G: *Poison index, dialysis and hemoperfusion in poisoning: Malathion*, II ed. Bad Homburg 1983
 7. Duraković Z, Plavšić F, Ivanović D, Gasparović V, Gjurasić M: *Resin hemoperfusion in the treatment of tricyclic antidepressant overdose*. *Artif Organs* 6:205, 1982
 8. Duraković Z, Duraković A, Duraković S, Ivanović D: *Poisoning with 2, 4-dichlorophenoxyacetic acid treated by hemodialysis*. *Arch Toxicol* 66:618, 1992
 9. Okonek S: *Probable progress in the therapy of organophosphate poisoning: Extracorporeal hemodialysis and hemoperfusion*. *Arch Toxicol* 35:221, 1976
 10. Okonek S, Thomas HJ, Baldamus CA, Hofmann A: *Hemoperfusion versus hemodialysis in the management of patients severely poisoned by organophosphorous insecticides and bipyridil herbicides*. *Artif Organs* 4:341, 1979
 11. Nagler J, Braeckman RA, Willems JL, Verpooten GA, DeBroe ME: *Combined hemoperfusion-hemodialysis in organophosphate poisoning*. *J Appl Toxicol* 1:119, 1981
 12. DeBroe ME, Verpooten GA, Christiansen MA, Rutsaert RJ, Halvoet J, Nagler J, Heydrickx A: *Clinical experience with prolonged combined hemoperfusion-hemodialysis treatment of severe poisoning*. *Artif Organs* 5:59, 1981
 13. Nicholson DP: *The immediate management of overdose*. *Med Clin N Am* 67:1289, 1983
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