

## Clinical Report

# Acute renal failure due to the inhalation of organophosphates: successful treatment with haemodialysis

Consolación Rosado Rubio, Carmen Felipe Fernández, Rosario Manzanedo Bueno, Begoña Alaguero del Pozo and Jesús Martín García

Department of Nephrology, Complejo Hospitalario de Ávila, Ávila, Spain

Correspondence and offprint requests to: Consolación Rosado Rubio; E-mail: crosadorubio@hotmail.com

### Abstract

Organophosphate intoxication is a very infrequent cause of acute deterioration of renal function but, when it does occur, it seriously aggravates the clinical status and prognosis. The pathogenesis of renal injury in this context remains unknown, although it is suspected that direct damage occurs at renal tubules. It has not been demonstrated that substitutive kidney treatment and specific antidotes provide any clear benefit. Here, we report a 58-year-old patient who underwent an accidental organophosphate intoxication, who suffered acute anuric renal failure and severe metabolic acidosis and who was successfully treated with conventional haemodialysis. The patient recovered with no sequelae and no need for other therapeutic measures.

**Keywords:** acute renal failure; haemodialysis; organophosphate poisoning

### Background

In acute organophosphate poisoning, acetylcholinesterase is inhibited and there is an increase in acetylcholine in the synaptic junctions, leading to an overstimulation and disturbance of neurotransmission in the central and peripheral nervous systems [1]. The most frequent clinical findings are cholinergic crises and the intermediate syndrome, which may be life-threatening. However, there can be different disorders, which, although infrequent, worsen the prognosis.

Here, we report a case of a man who developed oliguric acute renal failure and severe metabolic acidosis due to the accidental inhalation of organophosphate insecticides, and who was successfully treated with three sessions of conventional haemodialysis and vasoactive support with noradrenalin, without the need for specific antidotes.

### Case report

A 58-year-old farmer attended the emergency unit complaining of temporal and spatial confusion and psychomotor disturbances. He suffered from Stage III chronic renal failure, with basal creatinine of 265.2  $\mu\text{mol/L}$  (3 mg/dL) secondary to diabetic nephropathy, and was receiving insulin, atenolol (50 mg/day) and furosemide (40 mg/day).

He was very aggressive, with tearing, salivation, hypothermia (32.6°C), hypotension (95/70 mmHg) and

anuria, without respiratory failure. The clinical situation had become increasingly severe over the preceding 72 h, without any specific cause. The laboratory findings showed: glucose 7.44 mmol/L (134 mg/100 mL), urea 46.48 mmol/L (280 mg/100 mL), creatinine 1428.54  $\mu\text{mol/L}$  (16.16 mg/100 mL), sodium 141 mmol/L (141 mEq/L), potassium 7.6 mmol/L (7.6 mEq/L), chloride 113 mmol/L (113 mEq/L), albumin 42 g/L (4.2 g/100 mL), pH 6.86,  $\text{HCO}_3^-$  44 mmol/L (44 mEq/L),  $\text{pCO}_2$  3.32 kPa (25 mmHg), lactate 1.2 mmol/L (10.8 mg/100 mL), ionic calcium 1.1 mmol/L (4.5 mg/100 mL), ethanol <0.1 mmol/L (<0.1 mg/100 mL), ammonia 46  $\mu\text{mol/L}$  (78.4  $\mu\text{g}/100\text{ mL}$ ), prothrombin time 110 seg, prothrombin activity 7%, myoglobin 352.4  $\mu\text{g/L}$ , haemoglobin 99 g/L (9900 mg/100 mL), normocytic and normochromic, leucocytes  $12.7 \times 10^9/\text{L}$  ( $12.7 \times 10^3/\text{mm}^3$ ) (neutrophils 86%) and platelets  $205 \times 10^9/\text{L}$  ( $205 \times 10^3/\text{mL}$ ). Serum amylase and the liver function test were normal.

The patient was admitted to the nephrology unit, where a temporary catheter was inserted in the femoral vein and he underwent three sessions of high-flux dialysis with a PEPA™ membrane, of 2 h each to 200 mL/min blood flux. He had to receive noradrenalin because of haemodynamic instability. He then showed a gradual recovery of diuresis and an improvement in general health, with the disappearance of the other symptoms. He was discharged 12 days later with a plasma creatinine level of 257.24  $\mu\text{mol/L}$  (2.91 mg/100 mL; Figure 1). Shortly after, the patient's wife admitted to have been using Zoovec™ (Diazinon)—the same agent her husband used at work—to disinfect the upholstery of a sofa (in a room used primarily by her husband for relaxation) several times during the previous month. This agent is used as a

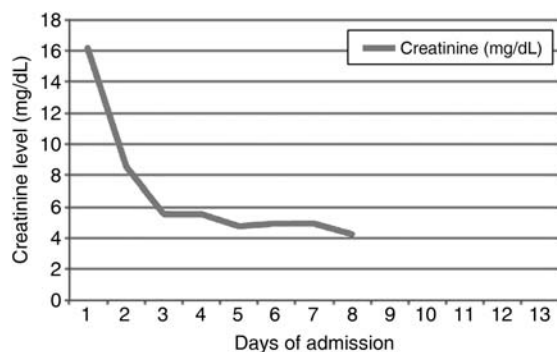


Fig. 1. Changes in creatinine levels during the patient's hospitalization.

pesticide against fly larvae, lice, ticks and mites. It is an irreversible inhibitor of the enzyme acetylcholinesterase, which hydrolyses acetylcholine permitting its reuptake from the synaptic cleft. This inhibition provokes the accumulation of acetylcholine in the neural network. Thus, the insect's nervous system is continuously stimulated and this, ultimately, leads to death. Because of the suspicion of poisoning due to that agent, blood acetylcholinesterase levels were determined, proving to be 3714 kU/L (3714 U/mL; normal range: 4–9 kU/L) at that time and 8432 kU/L (8432 U/mL) 5 months later.

These results seem to confirm the diagnosis of delayed organophosphate poisoning as the cause of the patient's acute renal failure and the rest of the symptoms, since he was in contact with a small amount of the agent for a long time.

Due to the later finding of exposure to the agent, it was not possible to start any specific treatment, despite what the patient recovered with only supportive treatment, with no long-term sequelae.

## Discussion

Acute organophosphate poisoning may occur through the skin, gastrointestinal tract or through the inhalatory pathway and is the result of the inhibition of acetylcholinesterase enzyme [1].

The toxicity of organophosphates causes adverse effects in many organs owing to haematological and biochemical changes due to the direct effects of the agent, acetylcholine and oxidative stress. The main damage occurs in the immune, reproductive and endocrine systems and in the liver, pancreas and lungs [2]. Some patients may suffer rhabdomyolysis [3].

These agents are an extremely rare cause of renal failure and <10 cases have been described [4]. This type of injury is more frequent in severe poisoning, although the effects do not seem to be related to the degree of acetylcholinesterase inhibition. There have been reports of oliguric and non-oliguric acute renal failure, proteinuria and acute tubular necrosis. The pathogenesis is unknown because of the lack of experimental data. In laboratory animals, an increase in low-osmolarity urinary flow has been reported, suggesting a direct influence on tubular

function, so several mechanisms have been advanced: direct damage to the distal convoluted tubule, an increase in oxidative stress, rhabdomyolysis and hypovolaemia due to dehydration [5].

Determination of serum acetylcholinesterase activity is useful for diagnostic purposes but not for the determination of the involved agent and prognosis.

Treatment consists of general measures, decontamination and prevention of absorption, although sometimes intensive measures are required such as ventilatory support. Specific treatments with antidotes do not significantly reduce morbidity or mortality. Acute administration of atropine blocks the muscarinic effects and pralidoxime reactivates the acetylcholinesterase inhibited by the toxic agent. Interleukin-10 has been shown to be efficient in preventing and decreasing the organic damage, particularly hepatic, pulmonary and renal, since it is a cytoprotective and a potent anti-inflammatory agent that inhibits proinflammatory cytokine production by activated macrophages and oxygen-reactive species [6].

Kidney failure may be fatal, since substitutive renal treatments have proved unsatisfactory and do not appear to improve survival. This could be due to the particular toxicokinetics of the agents: a high distribution volume, with a low blood level, tissue accumulation and slow release; however, there is a report of successful treatment with haemofiltration [5].

Our patient had oliguric acute renal failure, with severe metabolic acidosis and hypotension, with mild rhabdomyolysis, which could only be attributed to organophosphate poisoning. He recovered completely after conventional haemodialysis despite his haemodynamic instability. This is the first reported case of recovery from acute renal failure after conventional haemodialysis. This one supports, together with the previously reported use of haemofiltration in a similar case, the effectiveness of renal substitutive therapies in acute renal failure secondary to organophosphate poisoning.

*Conflict of interest statement.* None declared.

## References

1. Rovasio L, Framarini S, Baccaro F. Multiple organ dysfunction in acute organophosphate poisoning. *Med Intensiva* 2011; 35: 450–452
2. Betrosian A, Balla M, Kafiri G *et al.* Multiple systems organ failure from organophosphate poisoning. *J Toxicol Clin Toxicol* 1995; 33: 257–260
3. Gokel Y. Subarachnoid hemorrhage and rhabdomyolysis induced acute renal failure complicating organophosphate intoxication. *Ren Fail* 2002; 24: 867–871
4. Abend Y, Golland S, Evron E *et al.* Acute renal failure complicating organophosphate intoxication. *Ren Fail* 1994; 16: 415–417
5. Agostini M, Bianchin A. Acute renal failure from organophosphate poisoning a case of success with haemofiltration. *Hum Exp Toxicol* 2003; 22: 165–167
6. Yurumez Y, Ikizceli I, Sozuer EM *et al.* Effect of interleukin-10 on tissue damage caused by organophosphate poisoning. *Basic Clin Pharmacol Toxicol* 2007; 100: 323–327

*Received for publication:* 9.6.12; *Accepted in revised form:* 4.9.12