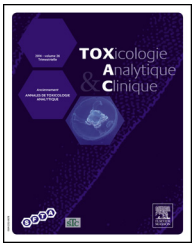
Toxicologie Analytique & Clinique 34 (2022) 121—126

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com



CASE REPORT

# A case report of acute kidney injury following organophosphate methidathion poisoning

Bilel Chefirat[a,b,c,*], Anissa Zergui[a,b,c], Haciba Rezk-Kallah[a,b,c]

[a] *Department of Pharmacy, Faculty of Medicine, University Oran1 Ahmed Ben Bella, Oran, Algeria*
[b] *Department of Pharmacology Toxicology, University Hospital Center of Oran, Oran, Algeria*
[c] *Environmental Health Research Laboratory, University Oran1 Ahmed Ben Bella, Oran, Algeria*

Received 20 October 2021; received in revised form 22 January 2022; accepted 11 March 2022
Available online 3 May 2022

**KEYWORDS**
Organophosphate;
Cholinesterase activity;
Acute Kidney Injury;
Pralidoxime;
Hemodialysis.

**Summary** Organophosphate pesticides (OPs) have a deleterious effect on the nervous system but they can also affect other systems and organs. Respiratory and cardiac complications are common, but the pathophysiology of nephrologic damage has not been fully studied.

We report a case of voluntary intoxication with Ultracide 40® (Methidathion at 420 g/L) presenting on admission a suggestive clinical picture of poisoning with a cholinesterase inhibitor. The assay for butyrylcholinesterase (BChE) activity confirmed the poisoning. In addition to symptomatic and evacuation treatment, the patient received antidotal treatment with atropine and pralidoxime. The patient presented on day 4 oligo-anuria with hyponatremia, hyperkalemia, hyperuremia and metabolic acidosis which evolved to Acute Kidney Injury (AKI) thus requiring daily hemodialysis sessions in combination with pralidoxime. This evolution was biologically and clinically favorable.

Sporadic case reports of AKI secondary to OPs poisoning have been described in the scientific literature. These cases were successfully treated with pralidoxime combined with hemoperfusion or hemodialysis.

Acute OPs poisoning can also induce AKI. Hemodialysis could counteract the toxic effects of OPs by maintaining the acid-base balance and minimizing the harmful effects of OPs on the kidneys. Randomized Controlled Trial (RCT) studies of dose adjustment of pralidoxime in cases of renal failure are needed to establish good management guidelines.



* Corresponding author.
*E-mail addresses:* chefirat.bilel@gmail.com, chefirat.bilel@univ-oran1.dz (B. Chefirat).

https://doi.org/10.1016/j.toxac.2022.03.002

## Introduction

According to the World Health Organization (WHO), 3 million cases of pesticide poisoning occur annually, leading to 250.000 fatalities annually. Out of the 2 million cases are suicidal poisonings [1]. These poisonings are a serious public health problem, especially in developing countries with high agricultural potential.

The deleterious health effects of OPs have been documented for decades and have become an increasing environmental concern. Four neurotoxic effects have been linked to poisoning by OPs: cholinergic syndrome (muscarinic, nicotinic and central syndrome), intermediate syndrome, organophosphate-induced delayed polyneuropathy (OPIDP) and chronic organophosphate-induced neuropsychiatric disorder (COPIND) [2]. Although OPs have deleterious effects on the nervous system, they can also affect other systems and organs. Respiratory, neurological and cardiac complications are common, while the pathophysiology of nephrological damage has not been studied in depth [3].

We report a case of acute poisoning with methidathion (MD), an organophosphate insecticide, in a patient who presented with cholinergic syndrome and Acute Kidney Injury (AKI), successfully treated with pralidoxime combined to daily sessions of hemodialysis.

## Case Presentation

A 25-year-old man farmer with no medical history, was found unconscious in his home after intentionally ingesting an unknown amount of a methidathion pesticide (Ultracide® 420 g/L). On admission to the medical emergency department of the University Hospital Center of Oran (UHCO), through an evacuation from a provincial health sector, the patient presented with coma (Glasgow coma scale 5/15), seizures, salivation, excessive sweating, miosis, bradycardia, hypotension, hypoxia and bronchospasm.

The initial management consisted of abundant gastric lavage which brought back a greenish-blue liquid, orotracheal intubation for mechanical ventilation in controlled mode, under sedation with Diazepam and analgesia with Fentanyl, and rehydration with 0.9% isotonic saline. The diagnosis of acute poisoning with cholinesterase inhibitors was made based on clinical findings. The patient therefore received antidotal treatment containing atropine (0.5 mg as a loading dose in slow IV, repeated until atropinisation, then maintenance dose of 0.02 mg/Kg/h, for 24 hours) and pralidoxime (400 mg then 1 g/8 h).

The patient was then transferred to the intensive care unit, where blood samples were taken to assaying plasma cholinesterase activity (butyrylcholinesterase or BuChE). The BuChE was collapsed, thus confirming the diagnosis (127 IU/L for usual values of 4620—11500 IU/L). In addition, a moderate electrolyte disorder was revealed by the admission ionogram (slight hypokalemia and hyponatremia) with no particularities in the hepatic and renal tests (Table 1).

The day after admission, there was a slight neurological improvement (reactive pupils, reactivation of the cough reflex) with a slight increase in BuChE to 1136 IU/L. Diuresis is less than 500 mL/24 h.

On day 4, the BChE level relapsed to 663 IU/L. The patient presented with oligo-anuria, hyponatremia, hyperkalemia, hyperuremia and metabolic acidosis (Table 1) which evolved to AKI. Daily hemodialysis sessions were thus instituted, with administration of pralidoxime at the same dose, 2 h after each dialysis session.

On day 5, the patient was conscious and showed clinical and biological improvement with a slight increase in the BuChE level to 1134 IU/L and then to 1362 IU/L on day 7.

On day 8, the patient was placed under medical supervision and benefited from daily hemodialysis sessions with pralidoxime. The general condition was still stationary and the BuChE levels were 1163 IU/L, 1378 IU/L on day 11, and 980 IU/L on day 12 (Fig. 1). Dialysis was continued until day 11 with a control renal assessment performed on day 13.

The evolution was marked by a resumption of renal function, the correction of the acid-base disorders with slight hyponatremia (Table 1) and by the complete disappearance of the muscarinic, nicotinic and central syndromes, with total recovery after 13 days despite a BuChE always below the usual values (980 IU/L on day 12). A control assay of BuChE was performed one week after the patient's discharge and returned slightly elevated compared to the last but still below the usual values (1994 IU/L).

## Discussion

Methidathion (MD) is a phosphorothioate-type organophosphate pesticide, marketed in different trade names: Advathion®, Dafathion®, Limacide®, Ultrathion® and Ultracide® (at a concentration of 420 mg/L). It is a highly toxic compound in view of its $LD_{50}$ which is 20 mg/kg in rats by the oral route [4]. The toxic dose in humans is 93 mg/kg [5]. For an average body weight of 70 Kg, the toxic dose of MD is 6.51 g, which represents only 1.55% of the vial, an amount that could easily have been reached by our patient.

MD is a cholinesterase inhibitor. Like its OPs analogs, MD can cause, in case of acute poisoning, the inhibition of cholinesterases, enzymes responsible for the degradation of acetylcholine, and leads to an excessive stimulation of the cholinergic receptors at the level of the autonomic nervous system, the central nervous system and the neuromuscular junction. This will leads to the appearance of a muscarinic syndrome, with a nicotinic syndrome and finally a central syndrome [1,6]. Our patient showed a pathognomonic clinical picture of cholinesterase inhibitor poisoning. The diagnosis, made according to the clinical signs and anamnesis, was confirmed by cholinesterase activity assays. A collapsed admission cholinesterase level (127 IU/L) confirmed acute cholinesterase inhibitor poisoning (Fig. 1). Cholinesterases constitute a biomarker of effect which is important for the diagnosis of this type of poisoning. In addition, it makes it possible to assess the severity of the poisoning, to validate the use of an antidotal treatment that regenerates cholinesterases as well as to determine the effectiveness of the antidotal treatment [7,8].

The antidotal treatment for OPs poisoning is twofold: atropine to overcome muscarinic stimulation by acetylcholine; and pralidoxime, a cholinesterase reactivator which hydrolysis the enzyme-pesticide bond. Pralidoxime also acts in synergy with atropine (atropine-like effect) thus

**Table 1** Biological assessment of the patient on admission, on the 4th and 13th day of hospitalization.

| Paramètres | Usual values | On admission | $D_4$ | $D_{13}$ |
|---|---|---|---|---|
| Kalemia (mmol/L) | 3.5—5.1 | **3.1** | **6.5** | 4.2 |
| Natremia (mmol/L) | 135—145 | **129** | **115** | **130** |
| Calcemia (mmol/L) | 2.25—2.50 | 2.3 | 2.3 | 2.4 |
| Arterial pH | 7.38—7.42 | 7.4 | **6.8** | 7.4 |
| Arterial $pCO_2$ (mmHg) | 38—42 | 40 | 27 | 38 |
| Arterial $HCO_3^-$ (mmol/L) | 25—27 | 25 | **21** | 26 |
| Plasma urea (mmol/L) | 2.5—7.5 | 4.5 | **44** | 6.2 |
| Serum creatinine (μmol/L) | 50—115 | 86 | **125** | 92 |
| Aspartate aminotransferase (IU/L) | 5—40 | 14.66 | NIP | NIP |
| Alanine aminotransferase (IU/L) | < 41 | 11.83 | NIP | NIP |

In bold: pathological values (outside the usual ranges) NIP: No Information Provided.

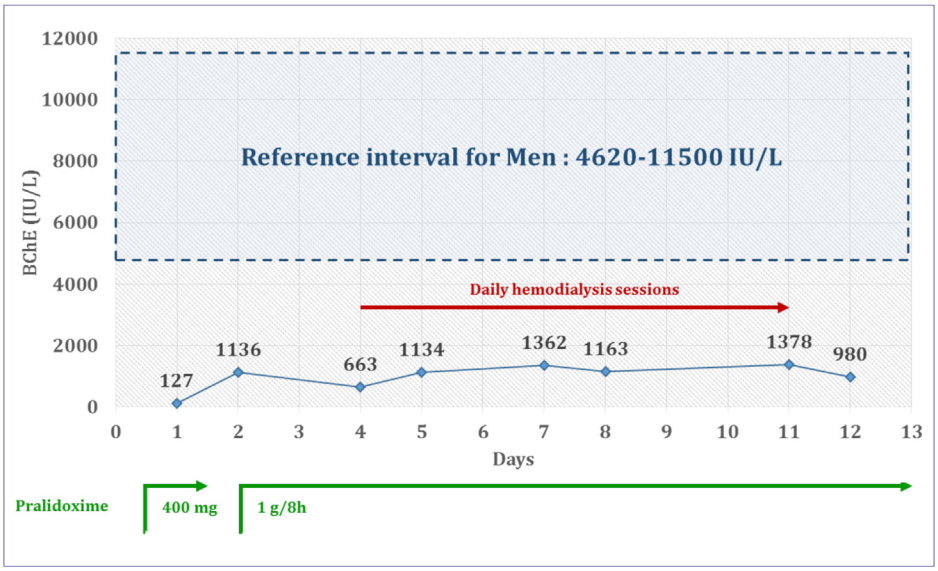



**Figure 1.** Treatments evolution and cholinesterase activity of the observation.

allowing the dose of the latter to be reduced [6]. According to the United States Environmental Protection Agency (US EPA), it is recommended to observe the patient, who has been poisoned with OPs, closely for at least 72 hours to ensure that symptoms (sweating, visual disturbances, vomiting, diarrhea, chest distress, and abdominal, and sometimes pulmonary edema) do not recur when atropinization is stopped. In very severe poisoning by ingested OPs, especially more lipophilic and slowly hydrolyzed compounds, metabolic elimination of the toxicant may require up to 5 to 14 days. In some cases, this slow elimination can combine with a profound inhibition of cholinesterase, requiring atropinization for several days or even weeks [9].

The muscarinic syndrome lasted 48 hours despite the administration of atropine. Prolonged atropinisation would have been necessary but this is not the case theoretically as MD is rapidly metabolised and eliminated from the body. Data on the biological elimination half-life of MD in humans are not available in the scientific literature. However, it is described that the activity of 14C-MD (MD labelled in the heterocyclic ring), administered to rats at a single dose of 4 mg/kg, is 80% excreted within 96 hours [10]. Therefore, the profound inhibition of cholinesterases could be explained by other factors.

Nicotinic syndrome has been treated with pralidoxime, a pharmacodynamic antidote that reactivates cholinesterases inhibited by the pesticide. However, OPs poisoning with two methoxy groups, such as malathion and dimethoate, is generally considered to be rather resistant to the oxime. In this case, dimethyl-BuChE is reactivated more slowly than dimethyl-AChE [11]. The chemical structure of MD with two methyl groups could explain the slow reactivation of BuChE by pralidoxime. The AChE assay would have been interesting for this case because it would have made it possible to compare the regeneration kinetics of the 2 types of enzymes and thus to see whether it is not a preferential inhibition of BuChE, a property recognized for some pesticides. This possibility remains very plausible because the patient has improved clinically in parallel with a low BuChE and it is known that AChEs are a better reflection of the neurological state during acute OPs poisoning. Indeed, *Worek and colleagues* report in their study that determining the

activity of BuChE for the diagnosis and therapeutic monitoring of this type of poisoning may not give reliable information on the status of AChE [11].

The success of oxime treatment is also conditioned by other factors: the continued presence of high concentrations of inhibitor in the plasma, ageing and the generation of phosphorylated oximes (POX) [12].

The first depends on the dose and pharmacokinetics of the inhibitor: the pharmacokinetics of MD do not present any particularity that could explain the oxime resistance. MD is well absorbed by all routes of exposure, oral, mucocutaneous and respiratory, due to its lipid-solubility. It is rapidly distributed throughout the body and crosses the blood-brain and placental barriers. To be active, MD, which is a sulphur derivative, undergoes oxidative desulphurisation to form an oxon, whose phosphoric ester functions are then hydrolysed by esterases. MD is rapidly excreted mainly in the form of carbon dioxide and urinary metabolites of low toxicity [13].

It could be suggested that MD, due to the fat-soluble character of OPs, has formed a deep compartment with a possible redistribution phenomenon described for some highly fat-soluble OPs, which consists in the re-circulation of OPs stored in the adipose tissue, which could explain the prolonged intoxication and clinical relapse after apparent recovery [14]. MD does not apparently belong to this group of highly fat-soluble pesticides, given the value of its low octanol-water partition coefficient, expressed in Log Pow, which is 2.42 (the fat-soluble qualification limit is 3) [15,16].

However, Zoppellari and colleagues, in their MD intoxication case report, referred to a probable redistribution of the pesticide from fat to blood, responsible for a deterioration of the patient's clinical condition on day 5 of the intoxication with an increase in plasma and urine levels of the pesticide [17]. This is also the opinion of Kim and colleagues, who report that MD has a relatively high solubility in fat and a very high apparent volume of distribution throughout all the body. Consequently, the redistribution of MD from fats to the blood can occur when plasma levels decrease [18].

In addition, it should be noted that the supposedly ingested dose is considered to be very high in our patient as indicated above and could lead to a variation in the kinetic profile (metabolites can be detected in the urine for several weeks) and thus limit the effectiveness of the antidotal treatment with 2-PAM [19].

The second factor is ageing, a phenomenon resulting from the monodealkylation of dialkoxyphosphorylated cholinesterases. The aged enzyme does not reactivate either spontaneously or under the action of oximes, and the recovery of the enzyme activity depends on the *de novo* synthesis of the enzyme [20].

Compounds with both methoxy side chains appear to age more rapidly than the corresponding ethoxy side chain inhibitors, and MD is one of these methoxy compounds [IUPAC name: n3-(dimethoxyphosphinothioylsulfanylmethyl)-5-methoxy-1,3,4-thiadiazol-2-one], which may counteract effective reactivation by oximes. Thus, the effect of MD on cholinesterase inhibition is long-lasting, especially at high doses [12,18].

This resistance to reactivation has been attributed to two possible mechanisms. The first is a change in the conformation of the inhibited enzyme induced by ageing, making it more stable. The second can be attributed in part to the electrostatic repulsion by the aged ChE of the oxime by the negatively charged oxygen of the P-O- and the adjacent negatively charged group Glu-199 [21].

The ability of oximes to reactivate inhibited cholinesterases is clearly limited by the inevitable formation of phosphorylated oximes (POXs) with strong anticholinesterase activity. However, POXs do not appear to be very stable in plasma and are rapidly destroyed by a POX-hydrolase. The variation in POX-hydrolase activity may also contribute to the variable response to oxime therapy in patients with OPs intoxication [22].

With regard to renal disorders caused by intoxication, the patient presented since admission early signs of acute functional renal failure (pre-renal) due to hypovolaemia caused by extracellular dehydration (salivation, excessive sweating). This resulted in hypotension associated with bradycardia and a moderate electrolyte disorder. There was also oliguria during the first 3 days of hospitalization (diuresis < 500 mL/24 h).

On day 4, the patient is oligo-anuric (diuresis < 100 mL/24 h), the blood is low in sodium (115 mmol/L), high in potassium (6.5 mmol/L), acidic (pH 6.8), and highly concentrated in urea (44 mmol/L). Salt and water reabsorption in the proximal tubule is accompanied by passive reabsorption of urea, which explains the greater increase in plasma urea than creatinine (125 μmol/L) during functional AKI. As a metabolic consequence, a metabolic acidosis has developed with a decrease in bicarbonate (21 mmol/L), associated with a compensatory decrease in carbon dioxide partial pressure (27 mmHg) and arterial pH (6.8). Daily haemodialysis sessions were then performed.

The pathophysiology of this OPs-induced AKI is hypothetical. Several mechanisms are assumed: (1) An accumulation of reactive oxygen species (ROS) induced by oxidative stress, generated by the metabolites of OPs in the kidneys and causing histopathological damages [23]. (2) Direct damage to the renal tubules due to high intratubular concentrations of OPs metabolites [24]. These concentrations have been demonstrated in subjects who died following acute OPs poisoning [25]. (3) Increased myoglobinuria due to rhabdomyolysis [26]. (4) Hypovolaemia due to dehydration [27].

Concerning the type of renal lesions, Sulak et al. performed a histopathological examination of kidney biopsies after oral administration of MD to adult male Wistar albino rats at a dose of 5 mg/kg body weight. Glomerular sclerosis, vascular congestion and fibrosis, and focal tubular necrosis were seen extensively. In addition, hydropic degeneration of tubular epithelial cells and severe interstitial infiltration of mononuclear cells were observed.

The suggested molecular mechanism of action was increased formation of malondialdehyde inducing lipid peroxidation or a possible increase in ROS induced by MD [28].

It is important to note that the effects of other components of the Ultracide® commercial product on the kidney have not been evaluated. These are phosphoric acid (<25%), sulphamic acid (<10%), fatty alcohol A 6 OE (<10%), alpha-isomethyl-ionone (<1%), diphenyl ether (<1%), benzyl salicylate (<1%), alpha-methyl ionone (<1%) and beta-methylionone.

According to scientific literature, AKI secondary to acute OPs poisoning has been successfully treated with

hemoperfusion and hemodialysis sessions combined with antidotal therapy, including pralidoxime. Early and repeated haemoperfusion is an effective treatment for OPs poisoning. It eliminates the fat-soluble poison bound to plasma proteins [29]. Hemodialysis is necessary for AKI due to acute OPs poisoning. It minimizes the harmful effects of OPs on the kidneys. However, *Kim and colleagues* found that hemoperfusion was not effective in removing MD from the body and does not provide real clinical benefit to the patient, due to its very high fat solubility and apparent volume of distribution [18].

Moreover, it has been suggested in this case that the kidney injuries are due to possible nephrotoxicity of pralidoxime, especially since high maintenance doses (1 g every 8 hours) were kept for 13 days. It is known that pralidoxime is a relatively non-toxic drug, and cases of its toxicity are rare. In healthy volunteers, dizziness, diplopia, headache, tachycardia and blurred vision may occur with overdose. No nephrotoxic effects have been described in the scientific literature [30]. The role of pralidoxime in the renal disorders occurring in the patient is therefore nil. However, pralidoxime should be used with caution in patients with renal impairment and dose reduction is necessary [31]. This is what was concluded in the experimental study by *Kayouka and colleagues* which was carried out in male Sprague Dawley rats. The elimination of pralidoxime in AKI, induced rats by administration of potassium dichromate, is significantly impaired with a doubling of the plasma elimination half-life, a tripling of the area under the curve ($AUC_{0\text{-}180\ mn}$) and a significant reduction in clearance. From a clinical point of view, these results suggested that the pralidoxime dosing regimen should be adjusted in patients with OPs poisoning and impaired renal function, particularly when the pralidoxime regimen is high [32] which was the case with our patient.

## Conclusion

OPs are known neurotoxics, they also remain redoubted for their nephrotoxic effects requiring adequate clinical and biological monitoring. This was shown in the present case, which developed an AKI following voluntary intoxication with methidathion.

Cases of AKI are described in the literature in relation to poisonings by different OPs (dimethoate, quinalphos, methamidophos, chlorpyrifos, diazinon, methyl-parathion) but the pathophysiology of this AKI remains poorly elucidated. In addition to symptomatic and basic antidotal treatment, extracorporeal purification techniques (plasmapheresis, haemodialysis, haemofiltration) seem to counteract the toxic effect of OPs on the kidneys by maintaining the acid-base balance. However, Randomized Controlled Trial (RCT) studies of dose adjustment of pralidoxime in situation of Kidney Injury are necessary to establish good management guidelines.

## Disclosure of interest

The authors declare that they have no competing interest.

## References


[1] Kumar A, Margekar SL, Margekar P, Margekar V. Recent advances in management of organophosphate and carbamate poisoning. Indian J Med Spec 2018;9(3):154—9, http://dx.doi.org/10.1016/j.injms.2018.06.007.

[2] Jokanović M, Kosanović M. Neurotoxic effects in patients poisoned with organophosphorus pesticides. Environ Toxicol Pharmacol 2010;29(3):195—201, http://dx.doi.org/10.1016/j.etap.2010.01.006.

[3] Zafar R, Munawar K, Nasrullah A, Haq S, Ghazanfar H, Sheikh A, et al. Acute renal failure due to organophosphate poisoning: a case report. Cureus 2017;9(7):e1523, http://dx.doi.org/10.7759/cureus.1523.

[4] Fisons Pest Control Ltd. Harston Eng: World review of pest control (Fisons Pest Control. ed.); 1970. Retrieved from https://books.google.dz/books?id=3f7zAAAAMAAJ. LCCN:.68005253.

[5] Milne GWA. CRC Handbook of Pesticides (1st). Boca Raton, Floride: CRC Press; 1994. ISBN:0-8493-52447.

[6] Braitberg G. Drugs and Antidotes in Acute Intoxication. Critical Care Nephrology 3rd ed. Elsevier; 2019. p. 574—88, http://dx.doi.org/10.1016/B978-0-323-44942-7.00098-4.

[7] Jalady AM, Dorandeu F. Intérêt du dosage des cholinestérases dans le cadre des intoxications aux organophosphorés. Annales Françaises d'Anesthésie et de Réanimation 2013;32(12):856—62, http://dx.doi.org/10.1016/j.annfar.2013.08.018.

[8] Chefirat B, Belabbaci N, Abourejal N, Rezk-Kallah H. Intérêt des oximes et du dosage de l'activité cholinestérasique dans les intoxications aiguës aux insecticides carbamates. Bulletin d'information toxicologique 2013;29(1):26—36. Available from: https://www.inspq.qc.ca/toxicologie-clinique/interet-des-oximes-et-du-dosage-de-l-activite-cholinesterasique-dans-les-intoxications-aigues-aux-insecticides-carbamates.

[9] EPA (U.S. Environmental Protection Agency/Office of Prevention, Pesticides, and Toxic Substances), Reigart, J.R., Roberts, J.R. Recognition and Management of Pesticide Poisonings. Fifth Edition. 1999 EPA Document No. EPA 735-R-98-003, and available in electronic format at: http://www.epa.gov/pesticides/safety/healthcare, 44.

[10] Esser HO, Müller PW. Metabolism of GS 13005, a new insecticide. Experientia 1966;22:36—8, http://dx.doi.org/10.1007/BF01897756.

[11] Worek F, Diepold C, Eyer P. Dimethylphosphoryl-inhibited human cholinesterases: inhibition, reactivation, and aging kinetics. Arch Toxicol 1999;73(1):7—14, http://dx.doi.org/10.1007/s002040050580.

[12] Gupta RC. Toxicology of organophosphate and carbamate compounds. 1st ed; 2006, http://dx.doi.org/10.1016/B978-0-12-088523-7.X5000-5. ISBN:978-0-12-088523-7.

[13] (Comité de Coordination de ToxicoVigilance) C.C.T.V. Expositions aux spécialités phytopharmaceutiques contenant du Méthidathion: cas signalés à la MSA et au réseau de toxicovigilance de 2000 à 2006; 2008. Available from: http://www.centres-antipoison.net/CCTV/rapport_CCTV_methidathion_2008.pdf.

[14] Vale JA. Toxicokinetic and toxicodynamic aspects of organophosphorus insecticide poisoning. Toxicology Letters 1998;102—103:649—52, http://dx.doi.org/10.1016/s0378-4274(98)00277-x.

[15] (Organisation des Nations Unies pour l'Alimentation et F.A.O. l'Agriculture)/OMS. (Organisation mondiale de la Santé). Résidus de pesticides dans les produits alimentaires Rapport. Réunion conjointe du groupe FAO d'experts des résidus de pesticides dans les produits alimentaires et l'environnement et

d'un groupe OMS d'experts des résidus de pesticides. Editeur Food & Agriculture Org; 1992. ISBN:92-5-203276-2.
[16] ILO (International Labour Organization). 2006. International Chemical Safety Cards (ICSC) 1659: Methidathion. Available from: https://www.Ilo.Org/Dyn/Icsc/Showcard.Display?P_Version=2&P_Card_Id=1659.
[17] Zoppellari R, Targa L, Tonini P, Zatelli R. Acute poisoning with Methidathion: a case. Hum Experiment Toxicol 1990;9(6):415—9, http://dx.doi.org/10.1177/096032719000900610.
[18] Kim KH, Kim SH, Her C. Methidathion poisoning. Korean J Crit Care Med 2017;32(4):363—9, http://dx.doi.org/10.4266/kjccm.2016.00073.
[19] Testud F, Grillet JP. Insecticides organophosphorés, carbamates, pyréthrinoïdes de synthèse et divers. EMC—Toicologie-Pathologie professionnelle 2007;2(2):1—24, http://dx.doi.org/10.1016/s1155-1925(07)71836-0, 16- 059-C-10.
[20] Vale JA, Bradberry SM. Organophosphorus and carbamate insecticides. Crit Care Toxicol 2016:1—26, http://dx.doi.org/10.1007/978-3-319-20790-2_52-1.
[21] Masson P, Fortier PL, Albaret C, Froment MT, Bartels FC, Lockridge O. Aging of di-isopropyl-phosphorylated human butyrylcholinesterase. Biochem J 1997;327(2):601—7, http://dx.doi.org/10.1042/bj3270601.
[22] Kiderlen D, Worek F, Klimmek R, Eyer P. The phosphoryl oxime-destroying activity of human plasma. Arch Toxicol 2000;74(1):27—32, http://dx.doi.org/10.1007/s002040050648.
[23] Kaya Y, Bas O, Hanci H, et al. Acute renal involvement in organophosphate poisoning: histological and immunochemical investigations. Ren Fail 2018;40(1):410—5, http://dx.doi.org/10.1080/0886022X.2018.1489289.
[24] Eid RA. Apoptosis of rat renal cells by organophosphate pesticide, quinalphos: ultrastructural study. Saudi J Kidney Dis Transpl 2017;28(4):725—36. Retrieved from: https://www.sjkdt.org/text.asp?2017/28/4/725/211330.
[25] Betrosian A, Balla M, Kafiri G, Kofinas G, Makri R, Kakouri A. Multiple systems organ failure from organophosphate poisoning. J Toxicol Clin Toxicol 1995;33(3):257—60, http://dx.doi.org/10.3109/15563659509017994.
[26] Rubio CR, Fernández CF, Bueno RM, Alaguero del Pozo B, García JM. Acute renal failure due to the inhalation of organophosphates: successful treatment with haemodialysis. Clin Kidney J 2012;5(6):582—3, http://dx.doi.org/10.1093/ckj/sfs138.
[27] Georgiadis G, Mavridis C, Belantis C, et al. Nephrotoxicity issues of organophosphates. Toxicology 2018;406—407:129—36, http://dx.doi.org/10.1016/j.tox.2018.07.019.
[28] Sulak O, Altuntas I, Karahan N, Yildirim B, Akturk O, Yilmaz HR, et al. Nephrotoxicity in rats induced by organophosphate insecticide methidathion and ameliorating effects of vitamins E and C. Pestic Biochem Physiol 2005;83(1):21—8, http://dx.doi.org/10.1016/j.pestbp.2005.03.008.
[29] Zhenhe LI, Guixia W, Guodong Z, Yuliang Z, Jiaqiang L, Shanmei L. Application of hemoperfusion in severe acute organophosphorus pesticide poisoning. Turk J Med Sci 2017;47(4):1277—81, http://dx.doi.org/10.3906/sag-1611-40.
[30] Gupta R, Parmar M. Pralidoxime. Treasure Island: StatPearls Publishing, Floride; 2020. Retrieved from: https://www.ncbi.nlm.nih.gov/books/NBK558908/.
[31] McEvoy GK, Snow EK, Miller J. Handbook on injectable drugs. 19th ed American Society of Health-System Pharmacists; 2017. Retrieved from: https://www-medicinescomplete-com.proxy.cc.uic.edu/#/browse/hid.
[32] Kayouka M, Houzé P, Risède P, Debray M, Baud FJ. Acute renal failure alters the kinetics of pralidoxime in rats. Toxicol Lett 2009;184(1):61—6, http://dx.doi.org/10.1016/j.toxlet.2008.10.022.