Vol 4 No. 2 October 2024
Solo Journal of Anesthesi, Pain and Critical Care

E-ISSN : 2797-0035
P- ISSN : 2776-1770

CASE REPORT

Effectiveness of Atropine Sulfate and Diazepam in Organophosphate Poisoning in Remote Area: A Case Report

I Kadek Ludi Junapati✉*, Fabianus Anugrah Pratama**

Article Info :
Submitted :
14-08-2023
Accepted :
06-09-2024
Published :
31-10-2024
https://doi.org/10.20961/sojaV4i2.77914

Authors' affiliations:
*Boawae Primary Health Care Center, Nagekeo, Nusa Tenggara Timur, Indonesia.
**Bukit Lewoleba Hospital, Lembata, Nusa Tenggara Timur, Indonesia.

✉Correspondence:
ludijunapati@gmail.com

ABSTRACT

Background: Organophosphate poisoning is a significant public health concern in developing countries, including Indonesia, largely due to the widespread use of pesticides and insecticides. These chemicals, while effective for agricultural purposes, have been linked to severe health issues, including acute poisoning. One of the major health risks associated with organophosphate exposure is its potential link to suicide attempts. The toxic effects of organophosphates primarily stem from their inhibition of acetylcholinesterase, an enzyme crucial for the proper functioning of the nervous system. This inhibition leads to the accumulation of acetylcholine, resulting in overstimulation of the nervous system. Managing organophosphate poisoning poses a considerable challenge, particularly in remote areas where access to specific antidotes is limited.

Case Illustration: A 17-year-old female high school student presented to the emergency room of the Boawae Primary Health Care Center with a major complaint of decreased consciousness, as evidenced by a Glasgow Coma Scale (GCS) score of 9/15. The patient had no prior history of neurological or psychiatric disorders. It was suspected that the patient had attempted suicide by ingesting pesticides approximately 60 minutes prior to admission. At the time of admission, she exhibited symptoms including nausea and vomiting, which had progressively worsened. Upon examination in the emergency room, the patient displayed increased saliva production and pinpoint pupils. In response to these symptoms, the medical team administered intravenous Diazepam and Atropine Sulfate, continuing treatment until atropinization was achieved.

Conclusion: In managing organophosphate poisoning, particularly in remote regions with limited access to specific antidotes, Atropine Sulfate and Diazepam represent viable alternative treatment modalities. These treatments can effectively counteract the toxic effects of organophosphates and achieve necessary atropinized conditions to stabilize the patient's condition.

Keywords: Atropine Sulfate; Diazepam; Organophosphate Poisoning.

INTRODUCTION

Organophosphates are commonly used as pesticides in developing countries. Pesticides became an important component of worldwide agriculture systems during the last century, allowing for a noticeable increase in crop yields and food production.[1] Regulation of the Minister of Agriculture of the Republic of Indonesia Number 43 of 2019 explains that pesticides are all chemical substances and other materials, as well as microorganisms and viruses that are used to eradicate or prevent disease pests that damage plants, plant parts, or agricultural products and eradicate or prevent animals and micro-organisms in the house.

Approximately 3 million people worldwide are exposed to organophosphates yearly, causing an estimated 300,000 deaths. There are about 8000 exposures per year in the United States, with very few deaths reported[2]. Suicide using organophosphate and carbamate insecticides was prevalent, in which 10,303 cases are reported representing 42.02% of all suicide cases worldwide.[3] However, there are no official reports regarding the number of organophosphate poisonings in Indonesia.

Nagekeo Regency consists of 7 sub-districts, each with 1 Public Health Care. There is only 1 hospital in Nagekeo Regency, the Aeramo Regional General Hospital (RSUD), located in Aesesa District. Our Primary Health Care Center, Boawae Primary Health Care Center, is located in the Boawae District. The distance between the Boawae Primary Health Care and Aeramo Hospital is approximately 45 kilometers. Our Primary Health Care Center can be reached by ambulance within 1 hour and 15 minutes (40-50 km/h speed).

Organophosphate poisoning needs immediate response and proper management. Delaying time causes worsened clinical conditions of organophosphate poisoning patients. Thus, alternative management needs to be considered for organophosphate poisoning in remote areas[4,5]. We aim to share our experiences in organophosphate poisoning management by using diazepam and atropine sulfate as alternatives.

CASE ILLUSTRATION

A 17-year-old high school female student was admitted to the emergency room of the Boawae Health Center with a major complaint of decreased consciousness (GCS 9/15) and restlessness. No history of neurological and psychiatric disorders was found. Before her admission, the patient vomited 5 times a yellow-green liquid that smelled similar to pesticides. According to her family, they suspected that the patient consumed pesticides. 30 minutes before her admission, the patient experienced nausea and vomiting, which were getting worse when the patient arrived at the Primary Health Care Center. Arterial blood pressure 134/99 mmHg, a pulse rate of 104 beats per minute (bpm), a body temperature of 36.0 °C, with a body weight of 44 kg, height of 150 cm, an oxygen saturation level of 96% room and respiratory rate of 30 beats per minute. The laboratory examination consisted of urinalysis and complete blood count were within in normal limit.

The patient was profusely sweating and short of breath. In addition, her right and left eye both show pin-point pupils. Excessive mouth salivation with an impression of pesticide odor was observed. Right and left vesicular sounds were detected. Autonomous urination and defecation were found.

The patient received intranasal oxygenation (4 L per minute) and ringer lactate of 1500 ml daily. Additionally, the patient received 50 mg ranitidine intravenously once, 4 mg Ondansetron intravenously once, and 1.25 mg atropine sulfate every 15 minutes. 5 minutes after the 2nd atropine injection, the patient received diazepam 10 mg intravenously once. After receiving the 3rd injection of atropine, atropinization was achieved. After treatment for 1 hour 40 minutes, the patient's consciousness returned to normal. Eventually, the patient received 500 mg of activated charcoal and 1 tablet of antacids.

The patient’s physical examination showed that excessive salivation and sweating have significantly decreased. The patient's pupils have returned to mydriasis, and the patient’s vital signs have returned to normal (Figure 1). The patient was discharged 3 days afterward.

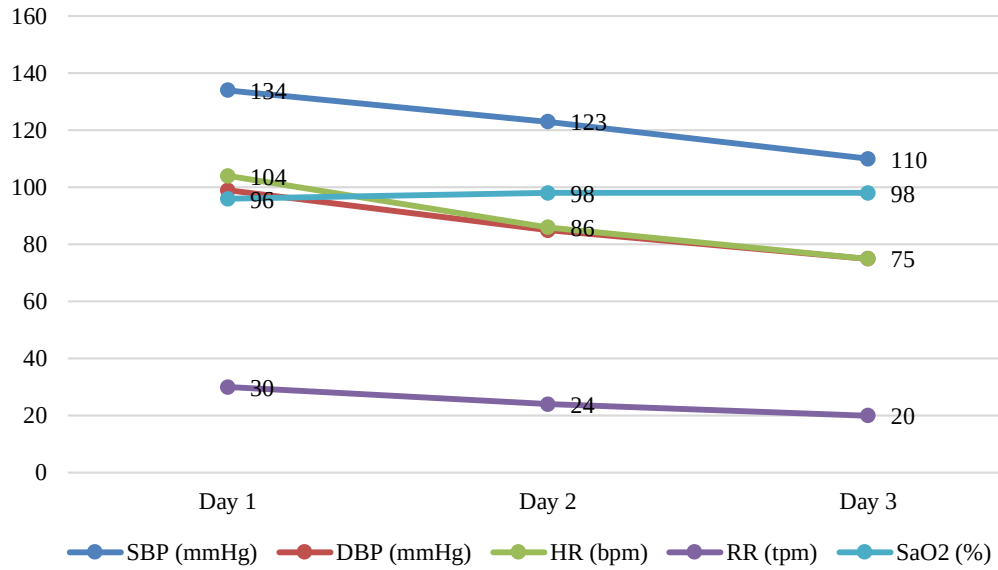

Figure 1. Vital Sign Changes of the Patient during Treatment
SBP: Systolic Blood Pressure; DPB: Diastolic Blood Pressure; HR: heart rate; bpm: beat per minute; RR: respiratory rate; tpm: time per minute; SaO2: oxygen saturation.

DISCUSSION

Organophosphates are commonly used as pesticides in developing countries. Pesticides became an important component of worldwide agriculture systems during the last century, allowing for a noticeable increase in crop yields and food production1. Regulation of the Minister of Agriculture of the Republic of Indonesia Number 43 of 2019 explains that pesticides are all chemical substances and other materials, as well as microorganisms and viruses that are used to eradicate or prevent disease pests that damage plants, plant parts, or agricultural products and eradicate or prevent animals and micro-organisms in the house.

Organophosphates are a group of chemicals that inhibit the activity of acetylcholinesterase (AChE), the enzyme responsible for transmitting synaptic nerve impulses in the central and peripheral nerves[4]. Organophosphate poisoning causes 3 types of primary syndrome: (i) acute cholinergic syndrome, (ii) intermediate syndrome, and (iii) delayed polyneuropathy5. The acute cholinergic syndrome is known as a cholinergic crisis, a condition in which acetylcholine receptors are overstimulated due to the accumulation of acetylcholine in the

synaptic spaces of neurons. The intermediate syndrome occurs 24-96 hours after organophosphate exposure, whereas delayed polyneuropathy appears 10-21 days after exposure[7].

Table 1. Peradeniya Organophosphorus Poisoning (POP) Scale[8]

	Clinical Criteria	Score
Pupil Size	>2mm	0
	<2mm	1
	Pin Point	2
Respiratory Rate	<20/min	0
	>20/min	1
	>20/min with central cyanosis	2
Heart Rate	>60/min	0
	41-60/min	1
	<40/min	2
Fasciculation	None	0
	Present, Generalized or Continous	1
	Both, Generalized or Continous	2
Level of Consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No Response to Verbal commands	2
Seizures	Absent	0
	Present	1

Organophosphate management generally includes 3 types, namely atropine, pralidoxime, and diazepam. Atropine acts as a competitive antagonist of acetylcholine which binds to muscarinic receptors. The muscarinic symptoms of organophosphate poisoning, such as sweating, salivation, lacrimation, nausea, rhinorrhea, vomiting and diarrhea, and cardiovascular problems, are counteracted by atropine sulfate. However, it is not effective on manifestations of nicotinic receptor[9,10]. Pralidoxime is one of the oxime class of drugs that are often used in the world. The oxime group works by reactivating the acetylcholinesterase, which Organophosphate Poisoning has inhibited. Pralidoxime is not yet available in Indonesia. Diazepam works by enhancing the effects of gamma-aminobutyric acid (GABA). GABA functions as the main inhibitory neurotransmitter in the central nervous system, functioning to reduce nerve excitability by inhibiting nerve transmission. GABA is a ligand-gated chloride ion channel and contributes to nicotinic acetylcholine and glycine receptors[11].

Table 2. Severity grading of organophosphorus poisoning based on the POP scale and atropine dose required for atropinization[7]

Grade	POP Scale	Atropine dose for atropinization
Mild	0 – 3	< 2 mg
Moderate	4 – 7	< 2mg – 10 mg
Severe	8 – 11	> 10 mg

Based on the patient's signs and symptoms, the patient is in the moderate (total score 5) severity category of organophosphate poisoning (Table 1). The POP scale appeared helpful in assessing the severity of poisoning[8]. The dosage range for atropine sulfate is 2 - 10 mg (Table 2). In Indonesia, atropine sulfate is available in 0.25 mg intravenous preparations. This patient received 1.25 mg of intravenous atropine sulfate at an interval of 15 minutes, carried out 3 times until atropinization was achieved. For recommendations specifying a range of atropine doses, there was often marked variation in time to atropinization: e.g., using the regimen of Harrison's textbook (0.5-2 mg repeated every 5-15 min), 56 atropinization would have occurred after either 55 or 690 mins depending on whether the larger dose was given every 5 mins or, the smaller dose given every 15 mins. Atropinization was attained most rapidly with a regimen of increasing bolus doses after failure to respond to the previous bolus[13].

5 minutes after the 2nd atropine injection, the patient received Diazepam 10 mg Intravenous once, even though the patient was not in a convulsive condition. Reduction of the effects of organophosphate poisoning, such as increased concentrations of acetylcholine and choline, was achieved by the use of diazepam, while atropine could not weaken these concentrations.[14] Administration of atropine and diazepam simultaneously is more efficient in decreasing mortality in soman poisoning than atropine or oxime alone. Diazepam enhances the efficacy of low doses of atropine and decreases the synaptic release of acetylcholine in the cholinergic nervous system[15].

CONCLUSION

The Atropine Sulfate dosage based on the degree of severity can be based on the patient's signs and symptoms. Atropine Sulfate and Diazepam can be used as alternative modalities for managing organophosphate poisoning to achieve atropinized conditions, especially in remote areas where the availability of an antidote is limited.

REFERENCES

1. Carvalho FP. Pesticides, environment, and food safety. *Food and Energy Security* 2017; 6: 48–60.
2. Naughton SX, Terry A V. Neurotoxicity in acute and repeated organophosphate exposure. *Toxicology* 2018; 408: 101–112.
3. Wang B, Han L, Wen J, et al. Self-poisoning with pesticides in Jiangsu Province, China: a cross-sectional study on 24,602 subjects. *BMC Psychiatry*; 20. Epub ahead of print 1 December 2020. DOI: 10.1186/s12888-020-02882-9.
4. LUCERO RM, GOMEZ JF, CARRASCAL MD, et al. Acute Organophosphorate Poisoning: Clinical, Diagnostic and Therapeutic Approach. *Quantum Journal of Medical and Health Sciences* 2021; 1: 34–38.
5. Karunarathna I, Bandara S, Jayawardana A. *Comprehensive Management of Organophosphate Poisoning: Clinical management.* 2018.
6. Tsai YH, Lein PJ. Mechanisms of organophosphate neurotoxicity. *Current Opinion in Toxicology* 2021; 26: 49–60.
7. Bereda G. Poisoning by Organophosphate Pesticides: A Case Report. *Cureus*. Epub ahead of print 3 October 2022. DOI: 10.7759/cureus.29842.
8. Malaviya NB, Parikh R, Pancholi K, et al. Assessment of the Peradeniya Organophosphorus Poisoning Scale as a Severity and Prognostic Marker in Patients With Acute Organophosphorus Poisoning Presenting to an Emergency Medicine Department. *Cureus*. Epub ahead of print 12 June 2023. DOI: 10.7759/cureus.40277.
9. Kumar KR, Sinha SN. review of the clinical management of current organophosphate poisoning treatments in humans. *Int J Health Sci (Qassim)* 2022; 2394–2415.
10. Aroniadou-Anderjaska V, Figueiredo TH, de Araujo Furtado M, et al. Mechanisms of Organophosphate Toxicity

and the Role of Acetylcholinesterase Inhibition. *Toxics* 2023; 11: 866.

11. Ochoa-de la Paz LD, Gulias-Cañizo R, D´Abril Ruíz-Leyja E, et al. The role of GABA neurotransmitter in the human central nervous system, physiology, and pathophysiology. *Revista Mexicana de Neurociencia*; 22. Epub ahead of print 13 April 2021. DOI: 10.24875/RMN.20000050.

12. Rehiman S, Lohani SP, Bhattarai MD. Correlation of serum cholinesferase level, clinical score of presentation and severity of Organophosphorous Poisoning. *Journal of the Nepal Medical Association* 2008; 47: 47–52.

13. Eddleston M, Chowdhury FR. Pharmacological treatment of organophosphorus insecticide poisoning: the old and the (possible) new. *Br J Clin Pharmacol* 2016; 81: 462–470.

14. Wicaksono RI, Manunel ES, Pawitra AS, et al. Literature Review: Impact Of Organophosphate Pesticide Exposure On Cholinesterase Enzyme Activity And Associated Risk Factors For Poisoning, 2017-2020. *Jurnal Kesehatan Lingkungan* 2023; 15: 247–256.

15. Vanova N, Pejchal J, Herman D, et al. Oxidative stress in organophosphate poisoning: role of standard antidotal therapy. *Journal of Applied Toxicology* 2018; 38: 1058–1070.