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A Study of Clinical Profile of Patients of Organophosphate Poisoning in a Teaching Hospital in Rural Maharashtra

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ABSTRACT

Background: *Organophosphates (OP) or phosphate esters are the most used compounds as pesticides in agriculture. Toxic exposure to these substances, accidental or intentional, is also not uncommon, especially in rural areas. Acute toxicity manifests as a cholinergic crisis, and the death is usually due to cardiovascular and respiratory failure.* ***Objectives:*** *This study was conducted to analyze the clinical profile of OP poisoning patients in a teaching hospital, where the majority of the clientele is from rural background.* ***Methods:*** *80 patients, above 16 years of age, admitted with OP poisoning were included in the study. The diagnosis was based on a history of exposure and characteristic clinical features and was supported by serum pseudocholinesterase (PChE) levels. The clinical features, management, complications, and outcome were analyzed.* ***Results:*** *Deliberate self-harm was the leading cause of exposure. The mean age of patients was 32.3 years. The male-to-female ratio was 1.4:1. Four patients developed the intermediate syndrome. The average dose of atropine required was 26.84 mg and pralidoxime 24 gm. The serum cholinesterase level was <10% in 5, 10%-20% in 7, 20%-50% in 16, and >50% in 52 cases. The mean ICU stay was 4 days. The mortality rate in our study was 3.75%.* ***Conclusions:*** *The mortality was directly proportional to the amount of OP consumed, clinical severity, PChE levels, and delay in seeking medical attention. This study highlights the importance of rapid diagnosis and initiation of early treatment.*

Keywords: Organophosphate, Muscarinic, Nicotinic, Acetylcholinesterase, Atropine, Pralidoxime

INTRODUCTION

Poisoning is a global health challenge. Organophosphates and Carbamates, or 'organophosphorus compounds' (OP) are responsible for the poisoning in the majority of cases, especially in agrarian countries like India [1]. About 385 million cases of unintentional exposure to pesticides occur every year among farmworkers (about 44% of the estimated 860 million agricultural population worldwide) leading to 11,000 deaths [2]. In India, mortality rate attributed to unintentional poisoning was 0.26 (0.16-0.36), males 0.34 (0.2-0.46), females 0.17 (0.12-0.24) per 100,000 population in 2019 [3]. OPs are commonly employed in farming as a pesticide. The commonly used OPs in India are Chlorpyriphos, Dimethoate, Dichlorvos, Parathion, Malathion, Monocrotophos, and Glyphosate [4,5]. These agents are readily available over the counter. Their easy availability makes them an instrument of choice for deliberate self-harm. An estimated 168,000 pesticide self-poisoning deaths take place annually in India, that is, 19.7% of global suicides [6]. OP compounds are easily absorbed through the skin and mucous membranes. Absorption through gastric mucosa is the most common mode of poisoning. OPs are metabolized by Cytochrome P450s in the liver, either by deacylation to create an inactive metabolite, or through a desulfuration to produce an active oxon metabolite, and are essentially eliminated by the kidneys [7]. The OPs inhibit Cholinesterase Acetylcholinesterase (AChE) and Butyrylcholinesterase (BChE) or Pseudocholinesterase or Plasma Cholinesterase (PChE). AChE hydrolyses Ach and is primarily found at postsynaptic neuromuscular junctions, especially in muscles and nerves, while PChE

is mainly found in plasma and liver. The ratio of PChE and AChE in human plasma is to the tune of 1000:1 [8]. The inhibition of AChE causes ACh accumulation at all nerve endings [9]. The excess ACh results in various signs and symptoms within minutes to hours; the common symptoms are Salivation, Lacrimation, Urination, Defecation, Gastric cramps, and Emesis (SLUDGE) [10,11]. OP poisoning (OPP) can manifest in three phases: acute cholinergic crisis, intermediate syndrome, and delayed neuropathy [11,12]. The OP-induced inhibition also causes low circulating PChE levels and is used for the diagnosis of OPP.

Atropine is an established specific antidote for the muscarinic effects of OPP. Atropine is a central and peripheral muscarinic receptor antagonist. However, atropine does not bind to nicotinic receptors and is ineffective in treating neuromuscular dysfunction. Pralidoxime (2-PAM) and other oximes, such as HI-6 and obidoxime, are cholinesterase reactivating agents that are effective in treating both muscarinic and nicotinic symptoms. Oximes may cause transient worsening of symptoms due to oxime-induced AChE inhibition and should not be administered without concurrent atropine. WHO recommends the use of pralidoxime (>30 mg/kg bolus followed by >8 mg/kg/hr infusion) along with atropine in the management of OPP [13].

AIM AND OBJECTIVE

This study was conducted to analyze the clinical profile and outcome of OP poisoning patients in a teaching hospital, where the majority of the clientele is from rural background.

METHODS

The study included 80 patients, admitted to medical ICU from July 2020 till July 2021.

Inclusion Criteria

All patients above 18 years of age, reporting a confirmed history of OP exposure/ingestion were included in the study.

Exclusion Criteria

The patients where the poison was not positively identified, had some pre-existing comorbidity, and those who received initial treatment from some other health care facility were excluded from the study.

The history of exposure, symptomatology, physical signs, and PCE levels were tabulated and analyzed. The diagnosis in each case was based on the history of exposure and clinical features and was confirmed by low serum PCE levels. The severity of poisoning was defined based on the POP scale and serum ChE level (latent poisoning serum ChE <50% of normal laboratory values, mild 20% to 50%, moderate 10% to 20%, and Severe <10% of normal laboratory value) [13]. Psychiatric consultation of each patient was carried out before discharge from the hospital (Table 1).

Table 1 Peradeniya Organophosphorus Poisoning (POP) scale

Parameters	Value	Points
Pupil size	>2 mm	0
	<2 mm	1
	Pinpoint	2
Respiratory rate	>20	0
	<20	1
	<20 with central cyanosis	2
Heart rate	>60	0
	41-60	1
	<40	2
Fasciculation	Absent	0
	Present-generalized/continuous	1

	Generalized and continuous	2
Level of consciousness	Conscious and coherent	0
	Impaired	1
	No response to verbal commands	2
Seizures	Absent	0
	Present	1

RESULTS

In the current study, data of 80 patients (58.75% male, 41.25% female) admitted with OPP were analyzed out of a total 151 cases of poisoning. All patients had consumed the compound with the motive of self-harm. The OP consumed was identified in most cases from the used bottles. 22 of 80 (27.5%) patients used chlorpyriphos, and 19 (23.75%) used dimethoate for self-harm (Table 2).

Table 2 Type of OP consumed

S. No.	Name of OP	Number	Percentage
1	Chlorpyriphos	22	27.5%
2	Dimethoate	19	23.75%
3	Profenophos	9	11.25%
4	Dichlorvos	8	10%
5	Glyphosate	7	8.75%
6	Monocrotophos	6	7.5%
7	Dicrotophos	3	3.75%
8	Azamethiphos	3	3.75%
9	Temephos	2	2.5%
10	Ethoprophos	1	1.25%

Most of the patients were young, 40% from the age group of 16 years to 25 years, 32.5% from 26 years to 35 years, 12.5% from 36 years to 45 years, and 7.5% patients from the age group of 46 years to 55 years (Figure 1). The average time of presentation was 5.16 hours after consumption of OP (Figure 2).

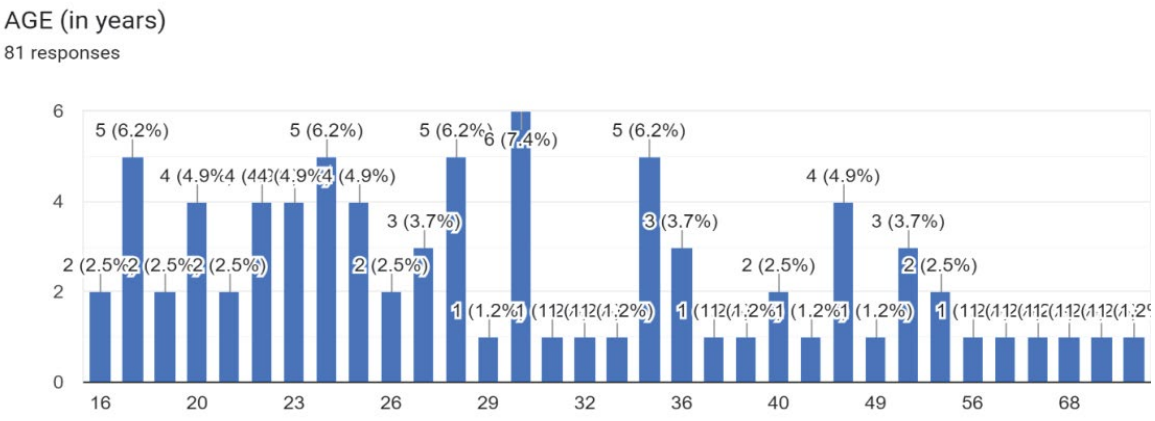

Figure 1 Age distribution of the patients

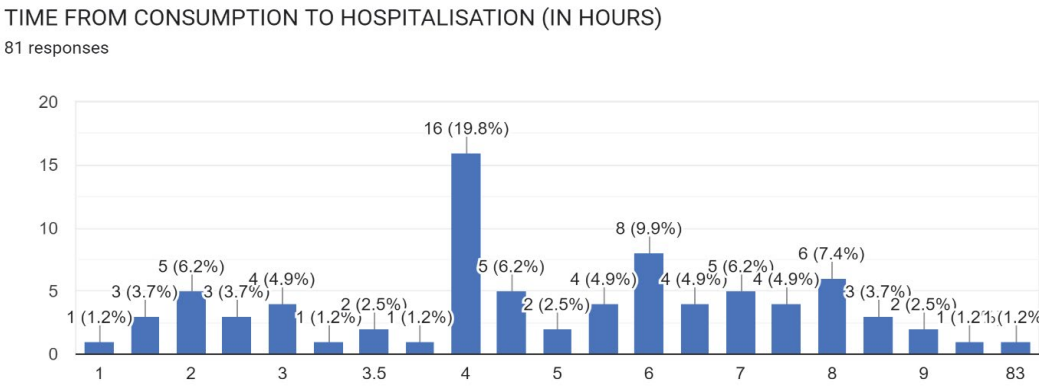

Figure 2 Interval from OP consumption to hospitalization

The most common signs and symptoms were salivation (38.3%), lacrimation (35.8%), and diaphoresis (16%) apart from nausea and vomiting that was present in all the patients. The other features in decreasing order occurrence were weakness, diarrhea, sweating, bradycardia, hypotension, bronchospasm, abdominal pain, miosis, fasciculations, cramps, and paralysis respectively (Figure 3 and Figure 4). Serum cholinesterase was <10% in 5, 10% to 20% in 7, 20% to 50% in 16, and >50% in 52 cases.

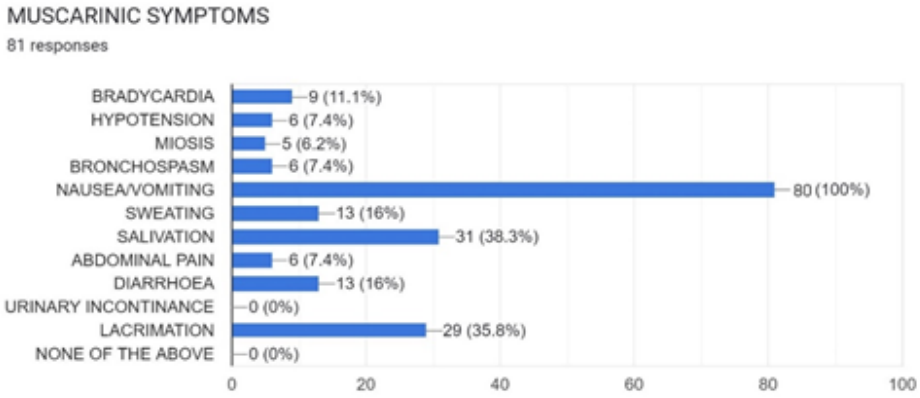

Figure 3 Frequency of muscarinic features

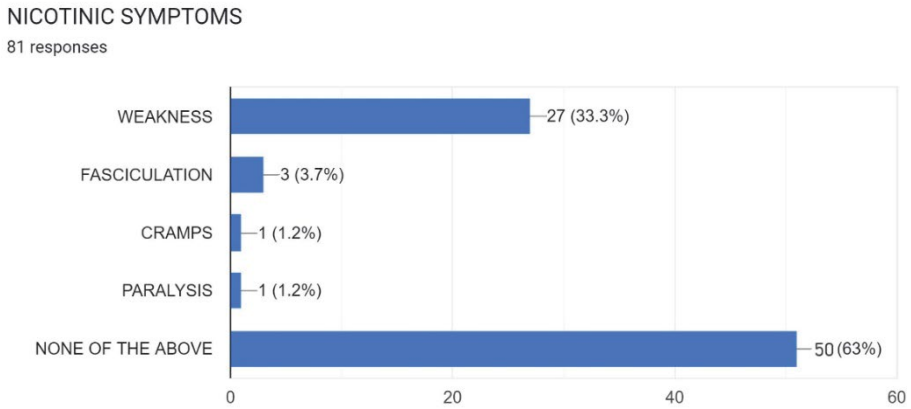

Figure 4 Frequency of nicotinic features

DISCUSSION

The OPs act by inhibiting Acetylcholinesterase (AChE) which causes Acetylcholine (ACh) accumulation at all the nerve endings in Central Nervous System (CNS), Autonomic Nervous System (ANS), and Neuromuscular Junction (NMJ) [9]. The excess synaptic ACh binds to muscarinic receptors in the CNS and the parasympathetic portion of the ANS, and nicotinic receptors in the CNS, sympathetic and parasympathetic ganglia, and NMJ. In approximately 20% of the patients, prolonged inhibition of AChE activity with pre and post-synaptic impairment of neuromuscular transmission, leads to development of Intermediate Syndrome. Its occurrence relates to the severity of the poisoning, not the specific OP [14-16]. It develops between 1 day to 4 days of exposure and may persist for 2 weeks to 3 weeks. The patient develops muscular weakness involving ocular muscles, head and neck, proximal limbs and the muscles of respiration resulting in ventilatory failure. The development of intermediate syndrome heralds a poor prognosis [17].

Poisoning due to OP is most common in developing countries like India because of its widespread use in agriculture and availability. Suicidal ingestion is more common than accidental poisoning. It is rampant in the rural population with rising incidence. All patients included in our study consumed OP with the intent to self-harm [18]. In our study male to female ratio was 1.4:1. Similar results were also found in other studies as well [5,14,19].

In India, the incidence of OPP is higher in the younger population. The average age in our study was 32.3 years (range 16 to 80). Only 10% of patients were >50 years of age. The mean age of the study population was 36.81 ± 14.9 years in a study of 441 patients by Reddy et al. According to Reddy, B. Shrikar, et al, people in the age group of 15 years to 35 years are described to be most ambitious and more vulnerable to various emotional conflicts that may occur during this phase of life [5, 20].

The most observed symptom was nausea and vomiting Figure 3 and 4 similar results were found in the study by Banerjee et al. Acute complications seen were bradycardia in 9 (11.25%), respiratory distress in 9 (11.25%), and hypotension in 6 (7.5%) patients [18]. Respiratory distress developed in these patients because of aspiration of gastric contents, secretions, and respiratory muscle weakness. In a study concluded by Prasad et al., lacrimation was present in 80% followed by vomiting in 78% of patients [21]. The mortality rate was 3.75% in the present study (Table 3). Mortality increases in ICU patients requiring ventilation. The average duration of mechanical ventilation in our study was 3 days. The mortality can be high in severe poisoning and prolonged of mechanical ventilation. In a study done by Hiremath P. et al, out of 18 intubated patients 14 had serum cholinesterase levels of <1000 IU/lt out of which 4 patients died. Patients with a value <1000 IU/lt had an average hospital stay of 21 days [22].

In our study serum, cholinesterase levels on the day of presentation were low in 28 (35%) patients. The need for oxygenation and intubation was more in moderate to severe cases with cholinesterase levels <1400 IU/lt. Mortality was higher in cases with cholinesterase levels <700 IU/lt. Similar results have been observed by other authors also (Table 3) [23,24].

We used pralidoxime in first 48 hours to 72 hours in our study, as is the current practice and, also recommended by WHO. The oximes are useful only if used early in the clinical course, as the OP undergoes 'aging'[25]. The efficacy of oximes has been questioned recently. A randomized, double-blinded, and placebo-controlled trial by Syed S, et al concluded that adding pralidoxime does not seem to be beneficial and at the same time does not result in increased mortality rates [25]. Pralidoxime was not shown to be beneficial in patients with acute OPP in another meta-analysis of six randomized trials [26]. However, the validity of these randomized trials has been questioned by Eddleston M, et al who recommend a large RCT to compare the current WHO-recommended pralidoxime regimen with a placebo to determine the role of oxime therapy in OPP [27]. Currently, the oximes enjoy the approval of WHO, USA, Asian and European countries for the treatment of acute OPP.

CONCLUSION

We have presented the clinical profile of 80 patients, who consumed OP compounds for self-harm. Chlorpyriphos was the most abused (27.5%) OP. Most patients were young (<45 years). Clinically 65 (81.25%) patients presented with mild, 9 (11.25) moderate, and 6 (7.5%) presented with severe poisoning. Four patients went on to develop the intermediate syndrome. Eleven patients needed ventilatory support, out of these three patients (3.75%) succumbed. PChE levels correlated well with clinical presentation. The mortality was directly proportional to the amount of OP

consumed, clinical severity, PChE levels, and delay in seeking medical attention. This study highlights the importance of rapid diagnosis and initiation of early treatment.

DECLARATIONS

Conflict of Interest

The author's declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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