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ORIGINAL RESEARCH

Retrospective Study of Morbidity and Mortality in Organophosphorus Poisoning in and around Vijayawada, Andhra Pradesh

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ABSTRACT

Since India is an agriculture-based country, organophosphates (OP) still remain the main agent for crop protection and pest control and therefore harm people who are overexposed accidentally while handling the pesticides. Organophosphate compounds are widely used as pesticides in agricultural parts of the world. Organophosphorus pesticide self-poisoning is an important clinical problem in rural regions of the developing world, and kills an estimated 200 000 people every year. Due to their easy availability and low cost, organophosphates are one of the most common causes of poisoning in the world from agricultural, unintentional, or suicidal exposure. The initial management of acute OP poisoning includes cardio respiratory stabilization, decontamination (removal of clothes for possible source of continued exposure in occupational intoxication), irrigation of skin and eyes as well as gastric lavage and activated charcoal to minimize absorption of the OP compound.

Keywords: Accidentally, organophosphates, overexposed, pesticides, self-poisoning.

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INTRODUCTION

Since India is an agriculture-based country, organophosphates (OP) still remain the main agent for crop protection and pest control and therefore harm people who are overexposed accidentally while handling the pesticides.[1] Due to the low cost and easy availability; they have also become an agent of choice for suicide and self-poisoning. Frequently used OP includes Malathion, parathion, chlorpyrifos, diazinon, dichlorvos, fenitrothion, tetrachlorvinphos, and azinphos-methyl.[3-5] Organophosphate compounds are widely used as pesticides in agricultural parts of the world.[1] Toxicity of organophosphates is the result of excessive cholinergic stimulation through inhibition of acetylcholinesterase. Organophosphorus pesticide self-poisoning is an important clinical problem in rural regions of the developing world, and kills an estimated 200 000 people every year. Due to their easy availability and low cost, organophosphates are one of the most common causes of poisoning in the world from agricultural, unintentional, or suicidal exposure.[3] Serum cholinesterase level is depressed after organophosphorus (OP) poisoning, as reported by previous various studies. Confirmation of organophosphate poisoning is based on the measurement of cholinesterase activity. Although red blood cell (RBC) and plasma pseudocholinesterase

levels can both be used, RBC cholinesterase correlates better with central nervous system (CNS). Acetylcholinesterase is, therefore, a more useful marker for organophosphate poisoning.[4] The rapid accumulation of acetylcholine in the synaptic junctions of CNS and peripheral tissues results in a cholinergic crisis, characterized by range of muscarinic, nicotinic and central effects.[4]

Intermediate syndrome or type II paralysis usually occurs after 24-96 hours after acute cholinergic crisis. Incidence of Intermediate syndrome varies from 8-50%.[5] Chronic OP poisoning can cause organophosphate-induced delayed neuropathy and is seen mostly in agricultural workers.[6]

Gastric mucosa is permeable to organophosphates, and is a classical way of absorption in suicidal cases. Liver is the organ where activation and detoxification of organophosphate compound takes place, but they are eliminated primarily through kidneys.[7]

Clinical manifestations are broadly classified into muscarinic and nicotinic which include; bradycardia, hypotension (Muscarinic), tachycardia (nicotinic), increased salivation / lacrimation, excessive sweating, nausea, vomiting, diarrhea, pain abdomen, fecal and urinary incontinence.[8] CNS manifestations include anxiety, restlessness, convulsion, miosis, insomnia, coma, cheyne-stokes breathing, respiratory and cardiovascular failure.[9]

The initial management of acute OP poisoning includes cardio respiratory stabilization, decontamination (removal of clothes for possible source of continued exposure in occupational intoxication), irrigation of skin and eyes as well as gastric lavage and activated charcoal to minimize absorption of the OP compound.[10] The mainstay of treatment involves atropine — A central and peripheral muscarinic receptor antagonist and pralidoxime chloride, which reactivates inhibited acetyl cholinesterase.[11] In recent years new adjunct therapy and cheap medications such as sodium bicarbonate, magnesium sulfate as well as antioxidants have been considered for the management of OP poisoning.[12] Death is usually occurs due to cardiovascular and respiratory failure, paralysis of respiratory muscles and obstruction caused by bronchospasm and bronchial secretions.[12]

MATERIALS & METHODS

We enrolled 133 patients in a prospective study which was conducted in Department of Medicine, Nimra medical college, Ibrahimpatnam from May 2019 to June 2020. Institute ethical committee approved the study. All patients of OP poisoning were included in this study. However, we excluded those patients in whom OP poisoning was doubtful. Detailed clinical examination of the patients was done. Diagnosis of OP poisoning was based on clinical features, history of exposure to a known OP compound and was supported by low serum pseudocholinesterase levels. Patients were treated as per the standard protocol of organophosphate poisoning with respiratory support, atropine and pralidoxime. All patients were dealt up to recovery or death from poisoning. Psychiatric consultation was done in all the cases that recovered, before discharging them from the hospital. Baseline investigations included complete blood hemogram, urea, creatinine, arterial blood gas values, X-ray chest and serum pseudo-cholinesterase level. Data was retrieved from the files on a structured proforma. Studied variables included gender, age, amount of organophosphate consumed, mode of exposure, time lag in starting treatment, duration of ventilator support and hospital stay, acute complications and outcome of patients.

Types of Organ phosphorus Consumed:

We could identify the type OP compound in most of the cases, patient attenders would bring the bottle of OP compound, that patient would have consumed, to our Emergency department. The various types of OP substances consumed in the present study are as follows.

Diethomate (N = 33), chloropyrifos (N = 15), Quinalophos (N = 12), Acetamide (N = 1), dichlorrofos (N = 5), Dicofol (N = 1), Emamectin, endosulfan (N = 1), Ethiophos (N = 2), Glycophosate (N = 1), carbosulfan (N = 1), methylparathion (N = 3), Monocrotophos (N = 5), Phorate (N = 1), profens (N = 3), Profenofos (N = 2), Profenofos/cypromethrin (N = 1), Unknown OP compound (N = 45), Dermal exposure (N = 2).

Methodology:

Serum pseudocholinesterase level was estimated at the time of admission in all the patients by DGKC method (LiquiChek). The laboratory reference range of pseudocholinesterase used in the present study was Female = 3930-10800/l, male 4620-11500 u/l. Based on the serum pseudocholinesterase levels, the severity of poisoning was defined as per Kumar et al.[12] Mild poisoning: Pseudocholinesterase level 20-50% of normal or >1,401-3,500 IU/L. Moderate poisoning: Pseudocholinesterase level 10-20% of normal or 701-1, 400 IU/L. Severe poisoning: Pseudocholinesterase level is <10% of normal or < 700 IU/L.

RESULTS

In present study, 133 cases of OP poisoning were admitted during the study period , Table 1, One thirty one (98.5%) patients ingested the compound and only two patients (1.5%) had dermal/inhaled exposure while spraying pesticides in rice fields. One hundred two (76.7%) were males and 31 (23.3%) females. Most of the cases were young people 80% (< 40years) predominantly males. The overall mortality rate was 33.3% (42 out of 126 patients) and seven cases (5.2%) were discharged against medical advice. Delayed complications like mild sensory loss of lower limbs or weakness of limbs were uncommon in our patients on follow-up. In Table 2, there was wide variation in age ranging from a minimum of 13-68 years with mean age of 31.5 years. Forty-eight patients (36.1%) out of 133 were stable after gastric lavage. They were kept under observation for the next 3 days and finally discharged. The amount of OP compound consumed ranges from 10 ml to maximum 200 ml with mean 77.5. Mortality was higher in patients who required ventilator support >7 days [$P < 0.05$ statistically significant. Patients were on ventilator support for minimum 1 day to maximum 22 days with a mean 6.85 ± 4.32 days. The lag time for initiation of treatment was minimum 1.02 hours to maximum 9.57 hours with mean 4.65 ± 2.4. Diagram 3, shows the clinical presentation of acute poisoning was variable as shown. However, the most consistent feature was miosis (93.2%). Eighteen (13.5%) patients developed episodic convulsions. Transient elevation in liver enzymes was noticed in 13.5% patients. In Diagram 4, however, no significant increase in morbidity/mortality was seen in patients with hypokalaemia or deranged liver function test [$P > 0.05$]. Patient who developed single /multi-organ failure had increased mortality [$P < 0.0001$, statistically highly significant. Diagram 5 shows, 53 patients required ventilatory support, out of which only 11 patients survived. The mortality rate was directly proportional to the amount of poison consumed [$P < 0.00003$ statistically significant. Mortality rate was higher in patients with lag time > 6.5 hours [$P < 0.05$]. Twenty-one out of 133 (15.7%) developed derangement in renal function tests (defined as serum creatinine >1.4). In most of cases, derangement of the renal function was reversible and renal function tests improved within a week. However, increased mortality was seen in patients with serum creatinine >3.5 mg/dl [$P < 0.05$]. Out of three cases that had irreversible renal failure, one case had serum creatinine of 10.2 mg/dl on day of admission with severe metabolic acidosis and he died on the same day due to cardiac arrest. Rest of the two cases with Acute renal failure died within a week's time.

Table No 1: Gender, age and mode of poisoning

Total no. of patients n=133		Gender		Age		Mode of Poisoning	
		Male (N=102)	Female (N=31)	<40 years (%)	>40 years (%)	Suicidal (%)	Accidental (%)
survived	87(65.41 %)	73(54.8)	18(13.5)	79(59.3)	12(9.02)	89(66.9)	2(1.5)
expired	47(34.58 %)	29(21.8)	13(9.7)	27(20.3)	15(11.2)	42(31.6)	0(0)
total	133	102	31	106	27	131	2

Table No 2: Mean median and standard deviation

Parameter	Minimum	Maximum	Medial/Mean	SD
Age	13 years	68 years	28/31.5	12.98
Time between consumption and hospitalisation	1.02 hrs	9.57	4.05/4,65	2.433
Cholinesterase level	330	1890	700/905	450.23
Hospital stay	1 day	28 days	7.89/11.195	7.81
Amount of poison consumed	10 ml	200 ml	50/77.5	54.86
No of days on ventilator support	1 day	22 days	6.857	4.32

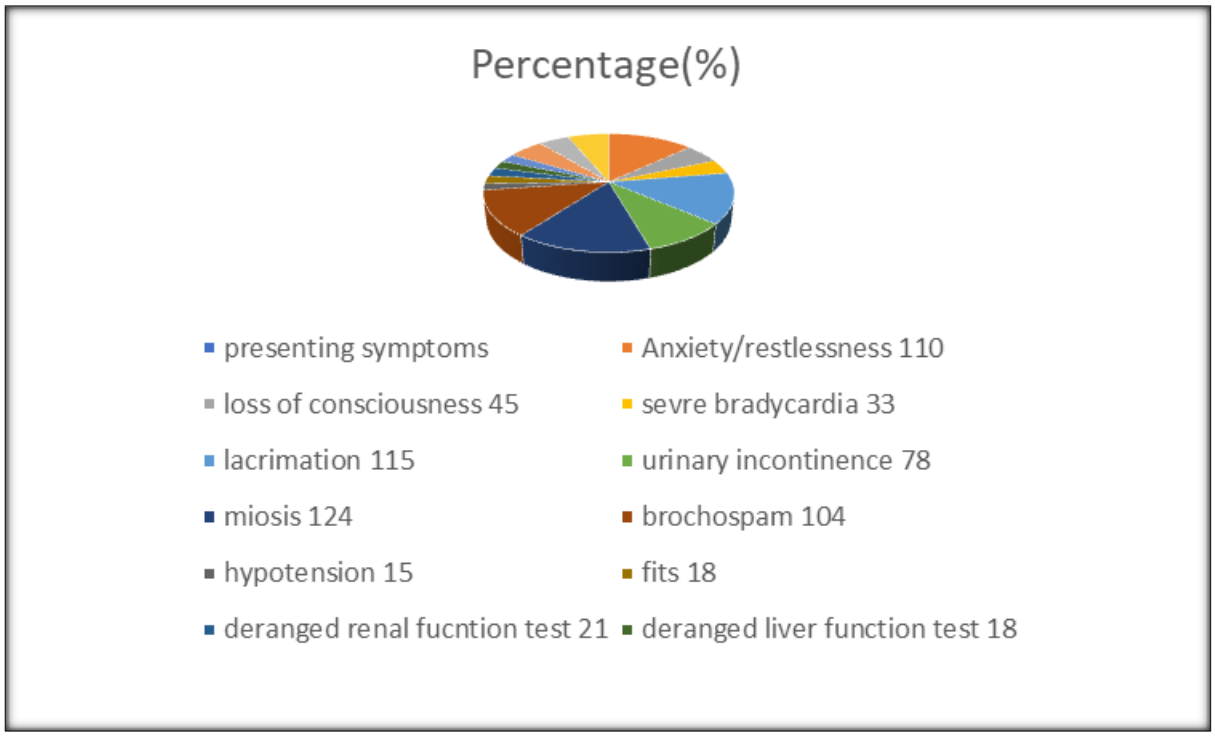

Figure No 1: Clinical manifestations and complications

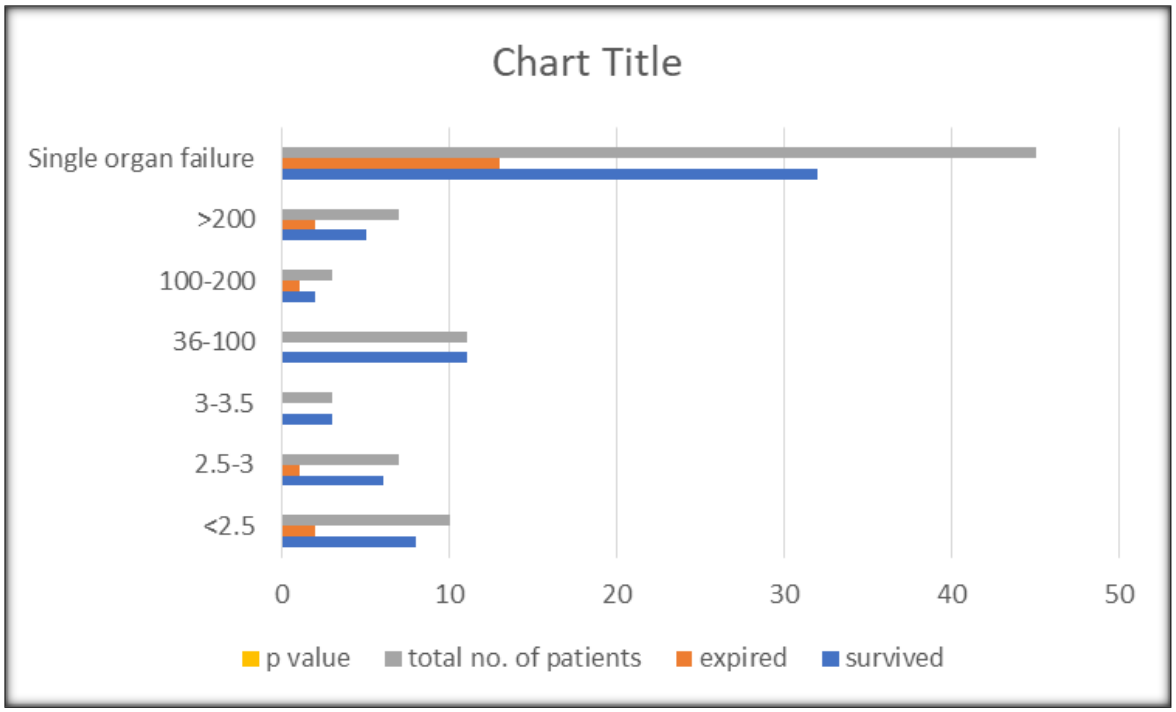

Figure No 2: Electrolyte imbalance and organ failure

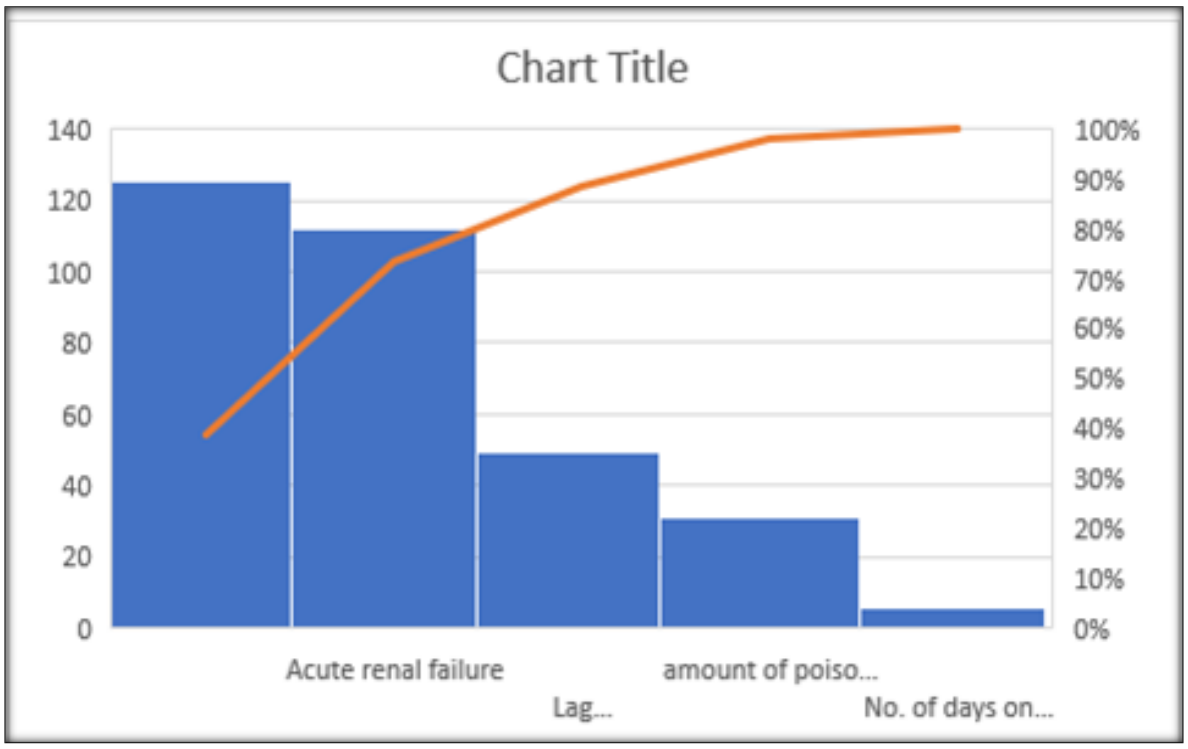

Figure 3: Outcome in patient's acute renal failure, lag, and amount of poisoning and no of days on ventilator.

DISCUSSION

OP compounds were synthesized by von Hoffman. OP pesticide poisoning is common in developing worlds.[14] The highest incidence is seen in India.[15] Suicidal and non-suicidal

organophosphate poisoning is a major problem in rural areas of India, with rapidly increasing incidence rate.[16]

In our study the female to male ratio is 1:3.2. In the present study, the incidence of poisoning was higher in males than in females (76.6% Vs. 23.3%). Similar trend was also observed by Safdar et al.,[15] and Aziza et al.[16] However, the female to male ratio given by Ather et al., is 1:1 and Tall et al., is 1:1.8 which is quite different from present study.[17,18]

The age ranged from 13-68 years with mean age was 31.5 years. However, Hayden et al.,[19] showed age range from 13-47 years with a mean age of 23 years. In the present study, the incidence of OP poisoning, was highest in patients aged less than 40 years. Majority of the cases (80%) were young people, predominantly males from the age group 13-40 years, this is comparable to other studies as done by Khan MN et al,[20] in which maximum number of patients were between 15-35 years of age. The people in this age group are described to be the most ambitious and more vulnerable to various emotional conflicts that may occur during this phase of life. Our observation was similar to the previous studies that showed the highest incidence of OP poisoning in people aged between 21-39 years.[21]

In our study, the incidence of suicidal poisoning is 98.6%, probably because it is cheap, easily available and used as a major pesticide in agricultural farming throughout India. This was in agreement with other studies,[22] which showed deliberate self-poisoning varying from 68-96%. In the study by Aziza et al.,[22] 76.92% cases were suicidal and 23.07% were accidental. Hypokalemia, hyperglycemia, acute renal failure, transient elevation of liver enzymes can occur in OP poisoning.[26] In our study, hypokalemia and transient elevation of liver enzymes were found in 15.03% and 13.5 % of cases respectively. Wang WZ et al.[22] observed that liver injury was seen in 9.8% and 5.17% of cases and control group, respectively in OP poisoning and mortality was higher in cases than controls (22.5% vs 6.32%). However, we failed to document a strict relationship between derangement of serum potassium and liver enzymes with the severity of OP poisoning and clinical outcome ($P > 0.05$). Acute renal failure was reported following exposure to OP poisoning in 15.03% of patients. Eighteen patients out of twenty one cases had transient reversible acute renal failure and three cases (2.2%) had irreversible renal failure. Mortality was higher in patients with acute irreversible renal failure (serum creatinine >3.5 mg/dl). Arefi M et al. in their study found 16.7% of OP poisoning had renal failure which is similar to our study. Similarly, S panda et al,[23] observed altered renal function between the survivors and non survivors suggesting their importance in predicting mortality. The transient renal injury may be due to both a direct action of the organophosphate, causing tubular cell necrosis or secondary mechanism that followed the cholinergic crisis, causing hypovolemic shock and rhabdomyolysis.

The most frequent signs noted in this study were miosis 93.2%, increased salivation 86.4%, anxiety and restlessness 82.7%, bronchospasm 78.2% and incontinence in 58.6%. Other frequent clinical features noted in this study are mentioned in [Table 3] with percentages, also comparable with other studies.[23] In the present study there were 33.8% cases of presented with altered sensorium or loss of conscious, in majority of cases it was subsequently followed by deep coma. Sequeira et al,[24] showed the frequency of deep coma to be 21%. Acute complications seen in this study were episodic convulsions in (13.5%) patients, severe bradycardia (24.8%), hypotension (11.3%) patients. Serious ventricular arrhythmias were not observed. Acute complications were bradycardia in 29 (93.5%), change in mental status in 10 (32.2%), low oxygen saturation (less than 90%) in 21 (67.8%) and subsequent convulsions in 3 (9.6%).

The duration of mechanical ventilation in our patients was 6.857 ± 4.32 days. In the present study, the mortality was highest in patients requiring mechanical ventilation for more than 7

days ($P < 0.05$), probably due to lung complications from prolonged mechanical ventilation and increased lag time. The high mortality in patients ventilated for <2 days and between 2-7days is most probably due to the severity of poisoning.[8] The mortality following OP poisoning varies from 4-30%.[25] In a study by Safdar et al.,[25] 4% of patients who received mechanical ventilator support ultimately expired. In another study, mortality was 50% in patients requiring mechanical ventilation.[26] In contrast to these observations; Aziza et al reported 8% mortality in patients who received mechanical ventilation.

In our study, it became evident also that most of patients who expired, there was a delay (maximum 9.57 hours) between consumption of OP substance and initiation of treatment, which is also supported by study done by Suleman MI et al.[28] Majority of the patients with a lag time less than 6.5 hrs recovered and survived, whereas the recovery and survival of patients decreased with the increase in lag time. Moreover, the patients with increased lag time required increased duration of mechanical ventilation.[28]

CONCLUSION

OP poisoning has become an agent of choice for self-poisoning because of its easy availability and low-cost factor especially in rural India. In OP poisonings, acute complications are seen more frequently than chronic complication. Mortality and morbidity are directly proportionate to the lag time in initiation of treatment and/or amount of OP substances consumed, clinical severity (single/multiorgan failure) and duration of ventilatory support. Mortality is also higher in patients who immediately develop acute complications like severe bradycardia and severe acute renal failure. Although each predictor (age, lag time, severity of poisoning, amount of organophosphate consumed, organ failure, acute kidney injury and duration of ventilation) is associated with mortality, death due to organophosphate poisoning results from overlapping contribution of these factors. No single factor is independently responsible for mortality in these patients. Therefore, the importance of rapid diagnosis, early and effective treatment should not be overlooked because patients who receive early and effective treatment generally do better and have less complications and decreased morbidity and mortality rate.

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