Original Research Article

Study of clinical profile of inhalational organophosphate poisoning at tertiary health care center

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Abstract

Background: Organophosphorus (OP) compound poisoning is the commonest medico-toxic condition in developing countries. The easy and widespread availability of these compounds has increased the likelihood of poisoning. The present study was undertaken with the aim to study the factors affecting outcome of OP compound poisoning and implementing them in the current treatment protocols to prevent complications. **Material and Methods:** Present study was single-center, prospective, observational study, conducted in patients admitted with history of OP compound consumption or inhalation or accidental spill on clothing in contact with OP Compound OR patients with history of unknown poisoning with confirm clinical features of OP Compound Poisoning. **Results:** Majority of the patients (61.0%) were in the age group of 21 to 40 years. The age group of 41-60 years had 31 (31.0%) cases. Male patients (73.0%) were more than female patients (27.0%). DM was most commonly used OP agent in 37patients (37.0%) followed by CP 21 (21.0%) and MC among 10 (10.0%) of the cases. The commonest route of exposure was ingestion (96.0%) followed by inhalational route which was observed in 3 (3.0%) of the patients and least common was topical among 1(1.0%) of the cases. Maximum patients reported ICU stay of 5-6 days (68.0%) followed by 17 (17.0%). Fasciculations was the most common clinical feature (71.0%), followed by excess secretions and miosis in 65 (65.0%) each respectively, absent neck holding (22.0%), In present study 18 (18.0%) patients died and 82 (82.0%) of the patients survived. The quantity of OP compound consumed posed an 11 times higher risk of mortality. **Conclusion:** Mortality was higher cases, present late, delay in initiation of treatment and consumed larger amounts of Organophosphorus compounds. Lower serum cholinesterase levels correlated well with requirement of ventilatory support, increased duration of Intensive care unit stay and outcome.

Keywords: Organophosphorus compounds, serum cholinesterase levels, ventilatory support, intensive care unit, outcome.

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INTRODUCTION

Organophosphorus (OP) compound poisoning is the commonest medico-toxic condition in developing countries. It is the leading cause for emergency hospital admissions throughout India. The commonly used OP compounds are categorized as pesticides, herbicides, agents for chemical warfare when used in the form of nerve gases.[1,2] The easy and widespread availability of these compounds has increased thelikelihoodofpoisoning.[3] WHO estimates about three million people are being exposed to pesticide poisoning every year with about 2,00,000 death per year in developing countries.[3] Intentional use of OP compounds seems to be more common in regions where these pesticides are readily available. In hospital-based studies of India, mortality rates associated with pesticides have been reported to be as high as 50-70 %.[4] Organophosphate (OP) compounds are the most common

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culprits for deliberate self-poisoning deaths in Southern India. The mechanism of action of the OP poisoning is through the irreversible inhibition of the enzyme cholinesterase that accumulates at the synapses and myo-neural junction leading to cholinergic overactivity.[5] Direct cardiotoxic effects of OP compounds are also reported. However, the commonest complication leading to death is respiratory paralysis.[6,7] Early recognition and prompt ventilatory support may improve the prognosis and thus improve survival in cases of OP poisoning.[8] The present study was undertaken with the aim to study the factors affecting outcome of OP compound poisoning and implementing them in the current treatment protocols to prevent complications.

MATERIAL AND METHODS

Present study was single-center, prospective, observational study, conducted in Department of Medicine, Dr Shankarrao Chavan Government Medical College, Vishnupuri, Nanded, India. Study duration was of 18months (January2019-June2020). Study was approved by institutional ethical committee.

Inclusion criteria: Patients admitted with history of OP compound consumption or inhalation or accidental spill on clothing in contact with OP Compound. Patients with history of unknown poisoning with confirm clinical features of OP Compound Poisoning.

Exclusion criteria: Admitted patients with confirm history of non OP Compound Poisoning. Patients with history of unknown Poisoning without features of OP Compound Poisoning.

By using Convenience sampling the minimum sample size of 100 was arrived at. After approval from the Ethics Committee and with written informed consent, a pilot study was conducted. Based on the results of pilot study, sample size was calculated. All cases which satisfy inclusion criteria were included in study. Informed consent was taken. Cases were studied in reference to detail history and clinical examination, cases proforma sheet was completed with details about the time since exposure, dose of exposure, route of exposure, Gastric lavage and decontamination was done in all patients immediately after admission (preliminary treatment), serum Cholinesterase level on admission, time since exposure to start of medical treatment and clinical features assessment along with the following investigations like complete blood count, serum cholinesterase by spectrophotometry, blood urea level, serum creatinine and serum bilirubin were done. The outcome measure would be in hospital death and survival (defined as discharge of live patient from the hospital). Detailed evaluation of each patient was made. Each variable in the proforma was correlated with the outcome. The statistical software SPSS version 23.0 was used for the analysis of the data. Microsoft Word and Excel were used to generate graphs, figures and tables. Difference of proportions between qualitative variables was tested using chi-square test or Fisher exact test as applicable. Percentage, odds ratio and 95% confidence interval were estimated.

RESULTS

Majority of the patients (61.0%) were in the age group of 21 to 40 years. The age group of 41-60 years had 31 (31.0%) cases. Male patients (73.0%) were more than female patients (27.0%). Maximum number of patients were laborer (41.0%), followed by farmer (40.0%), housewives (13.0%), and only 6(6.0%) were students.

Table 1: General characteristic

Characteristic	Frequency	Percentage (%)
Age group (Years)		
≤20	4	4.0
21-30	32	32.0
31-40	29	29.0
41-50	17	17.0
51-60	14	14.0
>60	4	4.0
Gender		
Male	73	73.0
Female	27	27.0
Occupation		
Farmer	40	40.0
Housewife	13	13.0
Laborer	41	41.0
Student	6	6.0

DM was most commonly used OP agent in 37patients (37.0%) followed by CP 21 (21.0%) and MC among 10 (10.0%) of the cases.

Table 2: Distribution of patients according to OP agents used

OP Agent	Frequency	Percentage (%)
CP	21	21.0
DC	9	9.0
DM	37	37.0
MC	10	10.0
MP	5	5.0
MT	5	5.0
QP	3	3.0
TM	4	4.0
TZ	6	6.0
Total	**100**	**100.0**

The commonest route of exposure was ingestion (96.0%) followed by inhalational route which was observed in 3 (3.0%) of the patients and least common was topical among 1(1.0%) of the cases. Maximum patients reported ICU stay of 5-6 days (68.0%) followed by 17 (17.0%) patients who stayed at the ICU for over 6 days and 15.0% who stayed for less than 5 days. The mean duration of stay in the ICU was 5.49 ± 1.72days.

Table 3: Distribution of cases according to Route of Exposure and ICU stay

Characteristic	Frequency(n)	Percentage (%)
Route of Exposure		
Ingestion	96	96.0
Inhalation	3	3.0
Topical	1	1.0
Duration of Stay in ICU (in days)		
<5	15	15.0
5-6	68	68.0
>6	17	17

Fasciculations was the most common clinical feature (71.0%), followed by excess secretions and miosis in 65 (65.0%) each respectively, absent neck holding (22.0%), altered mental status (15.0%), bradycardia (12.0%) and hypotension (6.0%). Only 2 (2.0%) cases were observed to have Intermediate syndrome and both the cases died during the course of the treatment.

Table 4: Distribution of patients according to clinical features at presentation

Present Illness	Frequency	Percentage (%)
Fasciculations	71	71
Miosis	65	65
Excess secretions	65	65
Neck holding absent	22	22
Bradycardia (<60 beats/min)	12	12
Hypotension– BP ≤ 100/70 mm hg	6	6
Altered Mental Status	15	15.0

Maximum cases 34 (34.0%) suffered from respiratory failure as the main complication in the present study. IMS and convulsions each were observed among 4 (4.0%) of the cases respectively. There were 3 deaths among those with IMS, thus becoming the complication with highest mortality.

Table 5: Distribution of cases according to complications

Complication	Frequency(n)	Percentage (%)
Respiratory Failure	34	34.0
IMS	4	4.0
Convulsions	4	4.0

In present study 18 (18.0%) patients died and 82 (82.0%) of the patients survived.

Table 6: Distribution of patients according to Outcome

Outcome	Frequency	Percentage (%)
Death	18	18.0
Survival	82	82.0

The quantity of OP compound consumed (p=<0.0001) posed an 11 times higher risk of mortality (p=<0.0001). Similarly,

absence of neck holding posed a 7 times higher risk of mortality (p < 0.0001). Other factors that were significantly associated with a higher risk of mortality were low mean serum cholinesterase levels(p=0.003), later presentation at hospital (p=<0.0001) and absence of altered mental status at presentation (p=0.004). Conversely, greater duration of ICU stay was inversely associated with mortality as recovering cases tend to stay longer at the ICU.

Table 7: Predictors of mortality in OP poisoning cases (Univariate logistic regression)

Variables	Odds ratio	95%CI	p-value*
Age	1.03	(0.99,1.08)	0.136
Gender	1.05	(0.34,3.28)	0.935
Neck holding absent	7.29	(2.40-22.20)	<0.0001
Duration of ICU stay	0.58	(0.42,0.80)	0.001
Time interval between consumption and admission	1.56	(1.20,2.02)	<0.0001
Serum Cholinesterase	1.00	(0.99,1.00)	0.003
Quantity Consumed	11.42	(3.93,33.12)	<0.0001
Altered mental status	0.17	(0.05,0.56)	0.004

*p<0.05 was statistically significant

On multivariate logistic regression analysis, the factors that were independently associated with mortality in OP poisoning cases were age more than 40 years (p=0.038) and time interval between consumption and admission (p=0.044). Whereas, the higher mean duration of ICU stay (p=0.014) was found to be inversely related to mortality which might be due to the ventilator support and adequate treatment received by the patients who stayed for longer duration.

Table 8: Predictors of mortality in OP poisoning cases (Multivariate logistic regression)

Variables	Odds ratio	95 % CI	p-value
Age	1.09	(1.00,1.19)	0.038
Gender	1.52	(0.26,8.99)	0.643
Neck holding absent	0.93	(0.09,8.89)	0.937
Duration of ICU stay	0.62	(0.43,0.91)	0.014
Time interval between consumption and admission	1.71	(1.01,2.88)	0.044
Serum Cholinesterase	1	(0.99,1.00)	0.054
Altered mental status	2.03	(0.15,28.11)	0.598

*p<0.05 was statistically significant

DISCUSSION

The incidences of organophosphorus pesticide poisonings are common in the developing world.[9] Suicidal and non-suicidal organophosphate poisoning is one of the major problems in rural areas of India, with rapidly rising incidence rate.[10] Toxicity of these compounds may result insignificant mortality and morbidity. About 99% of fatal cases occur in developing countries, especially in agricultural workers.[11] Mortality rates have been reported ranging from 10 to 22%.[12] In the Kashmir valley Malik *et al.* revealed that 33.5% of the cases of Organophosphorus compound poisoning were under the age of 25 years.[13] In Mangalore, Karnataka the most common age group to be affected was between 20-30 (36.6%).[14] The age affliction reported by the present study was similar to that from the other studies as mentioned above.[15-16] The reason could be that this age group by all probability is vulnerable to various emotional conflicts that occur during this phase of life. Problems leading to psychological stress may induce the youths for taking the drastic steps to end their life by consuming toxic substances. Males were affected more than females (73.0% versus 23.0% respectively) in the present study. A similar pattern was observed by other studies by Padmanaba *et al.*,[17] and Joshi *et al.*,[18] Where the male to female ratio ranged from1.2:1 to 4:1. The reason behind this may be due to the fact that males constitute the main work force in the fields, as they are more involved in spraying crops and handling pesticides. There may be a regional difference in the gender association of Organophosphorus compound poisoning as in some Northern regions of India like Jammu that have a female preponderance in Organophosphorus compound poisoning due to their role in spraying pesticides in the apple orchards.[13] It was observed that nearly 80.0% of the affected population was farm labourers and farmers. This was also observed in several studies and may be attributed to their easy accessibility to the Organophosphorus as a part of their occupations. In the present study, Dimethoate was most commonly used OP agent (37.0%) followed by Chlorpyrifos (21.0%). Study by Gagarin *et al.*,[20] also reported Methyl parathion was the most common poison consumed (27%) followed by Chlorpyrifos (22%). It was also the most common poison detected in the study by Banerjee *et al.*,[21] Dimethoate was most commonly consumed OPC in the study of Banday *et al.*,[22] This variation in the type of poison consumed can be attributed

to the regional availability of pesticides in different regions. In the present study, fasciculations was the most common clinical feature (71.0%), followed by excess secretions and miosis in 65 (65.0%) each. This shows that muscarinic effects predominate and appear first as compared to the nicotinic effects. Similarly, the study by Emerson *et al.*[23] showed that muscarinic symptoms were found in 92% of the cases. Miosis as observed in our study was found to be a good clinical sign to diagnose Organophosphorus poisoning, which is also comparable with other studies that showed similar rates of miosis. We found that miosis was found in nearly two-third of the cases and in 91% cases in the study done by Banerjee *et al.*,[21] which was higher than that observed in our study. In the present study respiratory failure was observed among 34 % cases as the predominant complication. Respiratory failure was similarly reported by other studies as the main complication of Organophosphorus poisonining.[24] Other complications were Intermediate syndrome and convulsions each in 4.0% of the cases respectively. Intermediate syndrome and convulsions were observed in four cases, out of which three died eventually during the course of treatment. Similar complications were reported by previous studies.[24,2] In our study, mortality was 18 %, maximum in the age group of 41-50 years (41.2%). The deaths were slightly higher among females (18.5%) as compared to males (17.8%). Most of the deaths resulted from consumption of Monochrotophos and Chlorpyrifos. The commonest clinical feature observed on admission among the cases that died during the course of the study was hypotension (83.3%). Other studies have also reported similar mortality rates following OP poisoning varying from 4-30%.[24,26] In study by Safdar *et al.*[25] 4% of the patients died. Mortality was higher in those cases that had consumed large amount of OP substances (50-100 ml) and was highest in cases who consumed >100 ml ($p < 0.05$). As observed in the present study, morbidity and mortality was proportionately higher in majority of patients who developed single/mutli-organ failure and required prolonged ventilatory support. Frequency of mortality due to organophosphates given by Yamashita, *et al.* [27] varied between 4% and 30% and 5.5% in a study by Malik *et al.*[13] In our study, it became evident also that most of patients who expired, there was a delay between consumption of Organophosphorus substance and initiation of treatment of more than nine hours, which is also supported by study done by Suleman MI *et al.*[24] 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] The reason for higher mortality rates may be due to late arrival, not receiving any treatment at periphery before arrival to the hospital, poverty and illiteracy, unawareness regarding mortality rate of Organophosphorus poisoning and non-availability of intensive care unit (ICU) facilities.[29] In our study the mean Sr. cholinesterase level was higher among the survivors as compared to the deaths. This difference in the mean Sr. cholinesterase levels and outcome was statistically significant. According to Turabi A *et al.*,[30] out of 1999 patients, 899 (44.97%) showed lower levels of serum cholinesterase. Mortality in the present study was less as compared to study conducted by Agarwal S B *et al.*,[31] Lower serum cholinesterase levels were associated with higher requirement for ventilatory support ($p = 0.02$) as well as longer average duration of ICU stay($p<0.001$) among the cases that experienced mortality. Overall, in our study the factors that independently predicted mortality among the Organophosphorus poisoning patients included greater time interval from consumption to hospitalization ($p = 0.035$) and higher quantity of the OP compound consumed. New policies for educating the public especially of rural areas about the dangerous life-threatening effects of Organophosphorus compounds could help ameliorate the harmful effects of such poisoning and be an effective prevention strategy for reducing its incidence.

CONCLUSION

Mortality was higher cases, present late, delay in initiation of treatment and consumed larger amounts of Organophosphorus compounds. Lower serum cholinesterase levels correlated well with requirement of ventilatory support, increased duration of Intensive care unit stay and outcome.

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