pISSN 2349-3925 | eISSN 2349-3933

Original Research Article

DOI: http://dx.doi.org/10.18203/2349-3933.ijam20175561

Clinical profile and outcome of intermediate syndrome in acute organophosphate poisoning

Rajendran Velayudham*, Senthilkumar S., Viswanathan Pandurangan

Institute of Internal Medicine, Madras Medical College, Chennai, Tamil Nadu, India

Received: 05 December 2017 **Accepted:** 11 December 2017

*Correspondence:

Dr. Rajendran Velayudham, E-mail: rsvr2003@hotmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Deaths by acute organ phosphorus poisoning is very common in rural India especially in people associated with agriculture sector. The present study was aimed to study the clinical characteristics of organ phosphorus compound (OPC) poisoning and to assess the associated factors related to the outcome (recovery/death) of intermediate syndrome (IMS).

Methods: This is an observational study conducted on 40 patients showing features of intermediate syndrome at Poison center, Institute of internal medicine, Rajiv Gandhi Government General Hospital, Chennai. Detailed clinical examination was done on the day of admission and daily with close monitoring. All patients included under study will be treated with pralidoxime as per protocol, atropine as required and other supportive measures was provided. Mechanical ventilatory support was provided for patients in respiratory failure. Patients are followed up till the end point of outcome (recovered and discharged/death) that was correlated with type of compound, quantum of exposure, duration of IMS, serum cholinesterase and creatinine kinase levels and respiratory failure.

Results: Patients of age group between 30-40 years are more affected. Males outnumbered the females and most of them are from agriculture sector (65%). Out of 40, on treatment and follow up 34 patients were recovered and 6 were died. Onset of intermediate syndrome ranges between days 2-4 following exposure and duration of symptoms was observed for 5–16 days. Methylparathion was the frequent compound associated with IMS in about 9 cases. Out of 40, 16 had respiratory failure and given ventilator support. Proximal muscle weakness was seen in about 38 patients as common symptom.

Conclusions: The results of the present study concludes that factors such as mode of poisoning, onset of IMS, type of compound, PChE level are not correlated with the outcome of study. Duration of IMS, respiratory failure, ventilator associated pneumonia (VAP), ventilator support duration were associated with outcome of the study. Hence, early recognition of IMS and its associated respiratory paralysis is very important in patients affected with OPC toxicity to prevent morbidity and mortality rate.

Keywords: Organophospate compounds, Intermediate syndrome, Mortality

INTRODUCTION

In this modern era of Industrialization, humans are continuously exposed to varied number of environmental pollutants. Of which, pesticides such as organophosphorus compounds (OPC) forms a major significant group posing a potential threat.¹ India being an agriculture based

country, OPC have made their run successfully into agriculture sector but at a cost of many lives. In developing country like India, pesticide self-poisoning is responsible in killing many people of rural areas as these compounds are easily available at cheaper cost and the mortality rate was as higher as 70%.²⁻⁴ OPC shows their action in humans in three phases namely acute cholinergic crisis,

intermediate syndrome (IMS) and delayed neuropathy. Among them IMS is the major contributing factor of OPC related toxic effects and mortality. IMS is characterized by cranial nerve paralysis, proximal and neck muscle weakness and respiratory paralysis.⁵

Many studies are conducted on OPC to recognize their etiology, incidence, risk factors associated and treatment.^{4,6,7} But still there is a lack of exact information related to pathophysiology and information regarding clinical profile and outcome of patients that causes IMS. Hence, this study was conducted with the aim to study the clinical profile of IMS in patients with OPC poisoning, to evaluate the frequency IMS in relation to various types of OPC, to study the outcome of IMS in terms of recovery or death and to correlate the outcome of IMS with type of compound, duration of IMS, respiratory failure, serum cholinesterase and serum creatinine kinase levels.

METHODS

This observational study was conducted between July 2013 to November 2013 at Poison centre, Institute of internal medicine, Rajiv Gandhi Government General Hospital, Chennai. 40. patients showing features of Intermediate syndrome are analysed comprehensively and included in the study.

Selection criteria

Inclusion criteria

Patients with symptoms of intermediate syndrome caused due to acute OP with characteristics of muscle and neck flexor weakness, respiratory failure, extra ocular movements restriction and consumption time of OPC of >24 hours and <7 days.

Exclusion criteria

Patients who have ingested mixture of pesticide or organocarbamate compounds, cholinergic crisis, hypokalemia and consumption time of OPC of >7 days.

Patients admitted with OP poisoning and meeting the requirements of inclusion criteria were selected and detailed history of the patients was collected. Complete clinical examination was done after obtaining informed consent. Type of compound, quantum of exposure, day of onset of IMS, duration of IMS, clinical features of IMS are recorded in detail. Routine blood investigations like complete hemogram, renal function tests, serum electrolytes are done. Serum cholinesterase levels two samples were taken (one during onset of IMS and the other during clinical recovery) and serum creatine kinase was done for all patients included under study. Detailed clinical examination was done daily with close monitoring. Clinical progression over the days was observed in terms of recovery, deterioration of illness and development of any secondary complications. Respiratory failure and the need for mechanical ventilation among the study group was noted. All patients included under study will be treated with pralidoxime (P2AM) as per protocol, atropine as required and other supportive measures was provided. Mechanical ventilatory support was provided for patients in respiratory failure. P2AM will be continued for all patients on ventilator. Patients on ventilator support are assessed for the duration on ventilator and development of ventilator associated pneumonia (VAP). Patients are followed up till the end point of outcome (recovered and discharged/death). Outcome of IMS were correlated with type of compound, quantum of exposure, duration of IMS, serum cholinesterase levels and respiratory failure.

Statistical analysis

Statistical analysis was carried out for 40 patients after categorizing each variable- age, sex, type of compound, quantum of exposure, duration of IMS, serum cholinesterase levels, respiratory failure and other clinical features, and finally outcome. Data were analysed using Statistical package- SPSS software. The values were presented as mean, standard deviation, and frequency of occurrence. Percentages were used to express the proportions of discrete variables. The statistical significance was calculated by the Chi square test, Fisher exact test. Variables were considered to be significant if P<0.05.

RESULTS

A total of 40 patients meeting the inclusion criteria were included in the study. Maximum number (37.5%) of cases was seen in the age group between 30-40 years (Figure 1). Males (75%) are more affected than females (25%) (Figure 2). 65% of cases were from agricultural sector while remaining 35% were unskilled laborers and others (Figure 3).

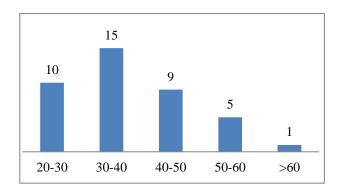


Figure 1: Age group of study participants.

Table 1 presents the relation of patient demographic characteristics with outcome of IMS. Out of 40 OPC exposed patients, about 34 were recovered and 10 were died. Of them most of the patients were under the age group of 30-40 years. Out of 65% of agricultural and 35% of non-agricultural people, 23 and 11 patients were recovered respectively.

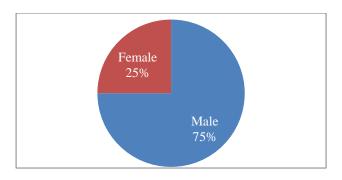


Figure 2: Gender distribution of the study participants.

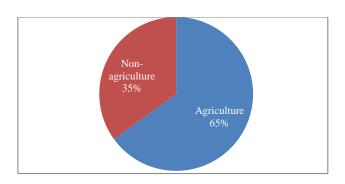


Figure 3: Occupation of the study participants.

Table 1: Relation of demographic characteristics of the patients with the outcome.

Characteristics Age group (in years)	Frequency (n=40 Sex))	Ou	tcome
	Male	Female	Recovery	Death
20-30	7	3	9	1
30-40	11	4	13	2
40-50	7	2	8	1
50-60	4	1	3	2
>60	1	0	1	0
Occupation				
Agriculture	26		23	3
Non-agriculture	14		11	3

Majority of cases 35 (87.5%) accounted ingestion as the route of exposure of them 29 are recovered whereas remaining 5 cases had inhalational exposure and all of them had recovered Almost 90% of patients consumed the compound intentionally and 10% consumed accidentally. On follow up 30 patients recovered. The difference between consumption and recovery is statistically not significant (p=0.376) (Table 2).

Occurrence of intermediate syndrome happened due to consumption of OPC of quantity varying from 60-120 ml. Out of 40, 15 patients consumed >120 ml of OPC. Of them on treatment, 9 are recovered and 6 were died and

this difference was significant statistically (P=0.008) as shown in Table 3.

Table 2: Exposure of OPC and its outcome.

	Frequency (n=40)	Recovery	Death
Route of expos	sure		
Ingestion	35	29	6
Inhalational	5	5	0
Intentional exposure			
Yes	36	30	6
No	4	4	0

Table 3: Quantum of exposure versus outcome.

Quantity (ml)	Frequency (n=40)	Recovery	Death	Total
60-80	7	7	0	7
80-100	12	12	0	12
100-120	6	6	0	6
>120	15	9	6	15

In our study population, onset of intermediate syndrome ranges between days 2-4 following exposure. But the day

of onset does not correlate with outcome (P>0.05). Duration of IMS was seen for 5-16 days. Death was

reported in the group of patients with duration more than 9 days. Duration of IMs was correlated well with outcome (P=0.003) as shown in Table 4.

Table 4: Onset and duration of IMS versus outcome.

	Frequency (n=40)	Recovery	Death
Onset of IM	S		
Day 2	12	9	3
Day 3	21	19	2
Day 4	7	6	1
Duration of 1	IMS		
4-8 days	22	22	0
9-12 days	12	10	4
>12 days	6	4	2

In our study, methylparathion (n=9) was the frequent compound associated with IMS. But the association between the type of compound consumed and outcome was statistically insignificant (P=0.498) (Table 5).

Table 5: Type of Compound consumed and outcome.

Compound	Frequency	Outcome	
	(n=40)	Recovery	Death
Chlorpyrifos	5	5	0
Diazinon	4	3	1
Dimethioate	5	4	1
Ethylparathion	5	5	0
Fenthion	1	1	0
Malathion	1	1	0
Methamidaphos	1	0	1
Methylparathion	9	8	1
Monocrotophos	5	4	1
Phosphamidon	1	1	0
Prophenophos	3	2	1

Table 6 presents the clinical symptoms of IMS. About 38 patients had proximal muscle weakness followed by neck muscle weakness (n=31). Out of 40, 16 had respiratory failure and given ventilator support. Respiratory failure caused statistically significant number of mortality (P=0.001). Of them 10 recovered and 6 died. Respiratory failure caused statistically significant number of mortality (P=0.001).

Table 6: Frequency of occurrence of individual clinical parameter.

Clinical parameters	Frequency	%
Bulbar palsy	15	37.5
EOM restriction	17	42.5
Neck muscle weakness	31	77.5
Proximal muscle weakness	38	95

Prolonged ventilator support was associated with VAP. Correlation between VAP and outcome was not statistically significant (P=0.08) (Table 7).

Table 7: Respiratory failure and outcome.

Respiratory failure	Frequency (n=40)	Recovery	Death
Yes	16	10	6
No	24	24	0

16 patients required ventilator support. Of this, 8 patients were on ventilator support for more than 9 days and out of these 5 patients died. Association between duration of mechanical ventilation and outcome of intermediate syndrome was statistically insignificant (P=0.08) (Table 8).

Table 8: Comparison of outcome with development of VAP.

Ventilator support duration	VAP	Recovery	Death
4-6 days	1	1	0
7-9 days	1	0	1
>9 days	7	2	5

Table 9 shows the categorization of PChE levels and the number of patients affected. It was categorized into severe, moderate and mild and normal. The association between PChE level and survival status was not significant (P=0.936).

Table 9: PChE activity and outcome.

PChE %during IMS	Frequency (n=40)	Recovery	Death
Mild	6	5	1
Moderate	16	14	2
Severe	18	15	3

Out of 40 patients, 15 cases had CK values in the normal range. 14 cases had values in the range of 300-600 U/L, 11 cases had values >600 U/L (Table 10).

Table 10: Creatine kinase levels and IMS.

Ck (U/L)	Frequency (n=40)
<300	15
300-600	14
>600	11

DISCUSSION

The present study was conducted in 40 patients with intermediate syndrome following acute organophosphate poisoning. All 40 cases were followed up, outcome in terms of either recovery or death is noted. All patients in our study independent of ventilatory support was treated with high dose P2AM (>4gm/day) as per standardized protocol. Maximum number of cases 15 (37.5%) was observed in the age group between 30-40 years. Similar observation was made by Goel et al.⁸ Males are more affected (75%) than the females (25%). This might be due

to the reason that males at this age group feels more stress towards their education, stress in jobs, settlement, and most of them are unable to cope up emotional conflicts and pressures of tough situations. Similar observation was also made by Kanagaraj et al in his study.⁹

In our study, 65% of cases were from agricultural sector while remaining 35% were unskilled labourers and others. This result was in accordance with the study of Kanagaraj et al.⁹ These findings explain that the increase number of cases reported from rural parts where agriculture is the sole occupation. Mortality was equally distributed in agriculture and non-agriculture group. In Rural areas, access to health care providers is minimal as well as awareness about preventive measures during handling of pesticides are lacking among the people. So, our study also highlights the matter of providing medical facility and health education among the people living in rural parts to bring down the number of cases being reported from agricultural sector.

Out of 40 patients included for study, majority i.e. 35 cases (87.5%) accounted for ingestion as the route of exposure to toxic OP compound. 5 patients had inhalational exposure. Of them 36 were affected themselves intentionally. On treatment and follow up, all 5 patients in inhalational group recovered whereas in the other group (ingestion) 6 deaths reported. Similar findings were done by Goel et al.⁸

In our study, occurrence of intermediate syndrome arised due to consumption of OPC of quantity varying from 60-120 ml. All 6 patients who died following intermediate syndrome had consumed >120 ml. From this it can be inferred that consuming a higher quantity of OPC leads significantly to death.

In our study, methylparathion was the common compound observed resulting in IMS constituted to about 9 cases. Similar finding was also made by Wadia et al.¹⁰

From the observations of the study it is inferred that onset of IMS ranges between day 2-4 following exposure and duration of IMS was between 5–16 days. Death occured in patients remaining in IMS for more than 9 days. Similar observation was also done by Kanagaraj et al.⁹

In our study group, most commonly observed clinical feature was proximal muscle weakness (95%) followed by neck muscle weakness (77.5%). Extra-ocular movement restriction was noted in 17 cases; like-wise bulbar palsy was seen in 15 patients. Wadia et al and Shaileesh et al in their observation also noted proximal muscle weakness as most common clinical presentation in intermediate syndrome. ^{10,11}

Among them, 16 patients had respiratory failure. All 16 patients required mechanical ventilator support either CMV or SIMV. Out of 16 patients who were put on mechanical ventilation, 8 patients (50%) was on ventilator support for more than 9 days and out of these 5 patients

died. Similarly, in majority of studies, mortality in IMS is attributed due to respiratory failure. ^{10,11}

In this study, out of 16 patients on mechanical ventilation, 9 patients who were on ventilator for more than 4 days developed VAP. Similar findings are also observed in study of Kanagraj et al.⁹

In our study, PChE levels at the onset of IMS was analysed for association with outcome and found the correlation was statistically insignificant (P= 0.936). Aygun et al in his study conducted conducted in Chennai also concluded that serum cholinesterase levels had no association with IMS.¹²

CONCLUSION

In the present study, the findings of the study highlights that the incidence of IMS in organophosphorus poisoning should be identified in early stages and careful treatment, monitoring and follow up of affected patients are needed to reduce the demises. Mortality occurred due to respiratory paralysis can be minimized by early identification of IMS and by providing prompt ventilator support. It should be given till the muscles of respiration recovered completely as they are the last to convalesce.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

institutional ethics committee

REFERENCES

- Upadhyay S, Sharma MK, Rao VK, Bhattacharya BK, Sharda D, Vijayaraghavan R. Organophosphorous Compounds-Toxicity and Detection Approach, Pesticides -Strategies for Pesticides Analysis. In: Margarita Stoytcheva M, Editor. 2011:315-33.
- 2. Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. Q J Med. 2000;93:715-31.
- 3. Eddleston M, Phillips MR. Self poisoning with pesticides. BMJ. 2004;328:42-4.
- 4. Ahmed SM, Das B, Nadeem A, Samal RK. Survival pattern in patients with acute organophosphate poisoning on mechanical ventilation: A retrospective intensive care unit-based study in a tertiary care teaching hospital. Indian J Anaesth. 2014;58(1):11-7.
- 5. Palimar V, Arun M, Mohan Kumar TS, Saralaya KM. Intermediate Syndrome In Organophosphorous Poisoning. JIAFM. 2005:27(1):28-30.
- Karalliedde L, Baker D, Marrs TC. Organophosphate-induced intermediate syndrome: aetiology and relationships with myopathy. Toxicol Rev. 2006;25(1):1-14.
- 7. Yang CC, Deng JF. Intermediate syndrome following organophosphate insecticide poisoning. J Chin Med Assoc. 2007;70(11):467-72.

- 8. Goel A, Joseph S, Dutta TK. Organophosphorus poisoning: Predicting the need for ventilator support. J Assoc Physicians India. 1998;46:786-90.
- Kanagaraj D, Senthilvelan M, Kosalram J. A Study On Clinical Profile And Outcome Of Intermediate Syndrome In Patients With Acute Organophosphate Poisoning. Int J Modn Res Revs. 2017;5(8):1603-7.
- Wadia RS, Sadagopan C, Amin RB, Sardesai HV. Neurological manifestations of organophosphorous insecticide poisoning. J Neurol Neurosurg Psychiatry. 1974;37(7):841-7.
- 11. Shailesh KK, Pais P, Vengamma V, Muthane U. 1994. Clinical and Electrophysiological study of

- Intermediate Syndrome in patients with organophosphorous poisoning. JAPI. 1994;42(6):451-3.
- 12. Aygun D, Doganay Z, Altintop L. Serum cholinesterase and prognosis of acute organophosphate poisoning. J Toxicol Clin Toxicol. 2002;40:903-10.

Cite this article as: Velayudham R, Senthilkumar S, Pandurangan V. Clinical profile and outcome of intermediate syndrome in acute organophosphate poisoning. Int J Adv Med 2018;5:62-7.