

THE SPECTRUM OF INTERMEDIATE SYNDROME FOLLOWING ACUTE ORGANOPHOSPHORUS POISONING: A RETROSPECTIVE COHORT STUDY FROM A TEACHING HOSPITAL OF CHHATTISGARHM. Murthy¹, D. Kosam², R. Nigam³, S. Chatterjee⁴, R. Murthy⁵, Sachin Pandey⁶**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Intermediate syndrome is a common complication found in patients with organophosphorus poisoning. The aim of this study was to find its incidence in this tribal dominated area of Chhattisgarh state. This is a retrospective study carried out at the ICU of a teaching Medical College hospital. In a period of one year, 720 cases of acute poisoning were admitted in the medical ICU ward, out of which, 682 cases (94.7%) were of organo-phosphorus poisoning. 64 cases (9.3%) had signs & symptoms of intermediate syndrome, which included inability to flex the neck, respiratory difficulty, convulsions and other features. All the 64 cases of intermediate syndrome required ventilatory support. Male: female ratio was 8:10. The commonest compound implicated in poisoning was Fenthion. Mortality was 18%. Patients with respiratory muscle weakness & proximal muscle paresis were the definitive predictors for the development of intermediate syndrome. Early recognition & prompt treatment has often proved successful, but, in mixed poisoning, recovery is variable and unpredictable.

KEYWORDS: Insecticide, Intermediate syndrome, Organo-phosphorus poisoning.

INTRODUCTION: Organophosphorus compounds are the commonest pesticides used for agricultural purposes in India. Being economical & readily available, these compounds are a household commodity. Therefore, they are incriminated as suicidal poison in cases of crop failure or socio-cultural disharmony. Nowadays, newer varieties of pesticides that have come into the market are often a mixture of conventionally known agents, differing in mode of action & their antagonism, resulting in enhanced morbidity & mortality. WHO estimated 3 million cases of poisoning and 2.5 million deaths worldwide annually.¹ Chemically, pesticides can be organo phosphorus compounds, organo chlorines, carbamates & pyrethenoids, which produce varied clinical manifestations, differing in severity & management protocol.

Organophosphorus poisoning presents in 3 well defined clinical phases:

1. Acute cholinergic crisis.
2. Intermediate syndrome.
3. Organophosphorus induced delayed neuropathy (OPIDN).

Acute Cholinergic Crisis: Occurs immediately after the ingestion of poison. Mainly the muscarinic symptoms predominate, like nausea, vomiting, diarrhea, urinary incontinence, miosis, salivation, lacrimation, bronchorrhea, bradycardia and hypotension etc. Nicotinic symptoms like fasciculations, muscle-weakness even muscle paralysis can occur; CNS symptoms include dizziness, confusion and coma.

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Intermediate Syndrome- Occurs within 48-96 hrs. After ingesting organo-phosphorus insecticide. Wadia in 1974 called it "Type II paralysis".² Senanayake in 1987 coined the term "Intermediate syndrome" because it occurs after the acute phase & before OPIDN. It is characterized by respiratory difficulty, weakness of proximal limb muscles, developing 2-3 days after ingestion of poison, difficulty in shoulder abduction & hip flexion, inability to flex the neck & ultimately respiratory paralysis. Motor cranial nerves - III, IV & X are usually involved with no sensory nerve involvement. Recovery is in reverse order.³

OPIDN- (Organophosphorus Poisoning Induced Delayed Neuropathy): develops 2-3 weeks later. Predominantly, the motor neuropathy, manifesting primarily as numbness and weakness of lower extremities with progressive ascending weakness of limb muscles occurs. OPIDN may persist for months to years.³

MATERIAL & METHODS: In this retrospective study of one year duration, a total of 720 cases of acute poisoning, admitted in ICU of a teaching hospital were included. Of these, 682 patients had the history of ingestion of organo-phosphorus poisoning and among total cases, 64 patients went into intermediate syndrome during the course of treatment. Clearance was obtained from the hospital ethical committee. All data regarding incidence, age, sex, type of compound, signs and symptoms, outcome etc. were collected from the medical record department of our hospital.

The data were analyzed following SPSS i.e. statistical package of social sciences 11.5 version. Suspected patients of organophosphorus poisoning with a particular smell of organophosphorus compound on naso-gastric suction, or insecticide containers brought by the relatives with strong suspicion were included in the study.

Exclusion criteria employed were, unconscious patient with history of fever, past history of epilepsy or weakness of muscles without history of poison ingestion. Diagnosis of Intermediate syndrome was made in patients, who developed muscle weakness, inability to flex shoulders, hips, proximal limb and neck after becoming conscious following acute phase of poisoning.

RESULTS: In a study period of one year, a total of 684 cases of acute poisoning were analysed. 64 cases were diagnosed to have intermediate syndrome. M: F ratio was found to be 8:10. Maximum number of patients (56.25%) belonged to the age group of 21-30 yrs. The Organo-phosphorus compound mostly predisposing to intermediate syndrome was, Fenthion (35%). In all 64 cases, incidence of respiratory muscle weakness & shoulder muscle paresis was 100%.

These patients required respiratory support, atropine & pralidoxime medication with continuous monitoring apart from other supportive measures. Average recovery time was between 4-30 days, while the case fatality rate was 18%. The important risk factors for intermediate syndrome were dose of poison ingested, or respiratory muscle paralysis developing 24 to 96 hours after taking the insecticide.

The predictors of outcome of intermediate syndrome can be standard neurological tests for function of the extra-ocular, facial, neck, flexor and proximal limb muscles. Significant muscle weakness in at least 3 of these muscle groups observed 24 hours after organo-phosphorus poisoning is diagnostic of classical intermediate syndrome. Electrophysiological measurements are more useful

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in predicting progression rather than recovery. Further research into this mechanism is further required.

DISCUSSION: Organo phosphorus poisoning is the commonest type of self- poisoning presenting and admitted in ICU in our set-up. WHO estimated it to be 3 million cases of poisoning worldwide, while it kills an estimated 2, 50, 000 people every year.¹ Organophosphorus compounds phosphorylates the esteratic site of the enzyme cholinesterase (ACHE), due which, it is unable to hydrolyse acetylcholine.⁴ This leads to accumulation of huge amount of acetylcholine at synapses causing immediate cholinergic symptoms. Overstimulation of nicotinic cholinergic receptors at neuromuscular junction results in depolarization blockade.

The resultant clinical features are muscle fasciculations & followed by generalized muscle weakness. There is another specific pattern of muscle weakness- first of proximal limbs, followed by neck muscles, muscles innervated by cranial nerves, accessory respiratory muscles & diaphragm. Wadia et al in 1974 first reported it as type II paralysis following OP poisoning.² It was termed as "intermediate syndrome" (IMS) by Senanayake & Karalliede in 1987.³

Organophosphorus compounds causing IMS include chlorpiriphos, diazinon, diamethoate, ethyl parathion, fenthion, malathion, methamidophos and parathion.⁵ Not all organophosphorus compounds produce IMS. Identifying the severity of OP poisoning is more significant than the specific compound in determining the development of IMS.⁶ Onset of IMS is within 1 to 4 days after ingestion. It lasts for 2-3 weeks.³ In our case series it took 4-30 days to recover. The exact pathophysiology underlying the development of IMS is still unclear.

Necrotizing myopathy or muscle injury, earlier thought as the probable cause, fails to explain the clinical scenario.^{5, 6, 7} Electromyography & repetitive nerve stimulation have shown IMS might be caused due to a combination of pre & post synaptic impairment of neuromuscular transmission at junction.^{5, 6} In our study, all 64 patients presented with respiratory & proximal muscle weakness. Infact, it is difficult to wean such patient off the ventilator, even when the cholinergic symptoms are well controlled.^{8, 9} 14 patients (87.5%) had difficulty in lifting their neck. Cranial N palsy was not noted in any of our patients.

Earlier, it was thought early & adequate oxime therapy may prevent the development of IMS.^{10, 11} But subsequent studies have failed to support it or prove conclusively, the merits of oxime therapy in managing organophosphorus insecticide poisoning¹²⁻¹⁵

Close observation of the patients for ventilatory & supportive care after the cholinergic crisis is over, remains the cornerstone treatment of this syndrome. Extubation of E T tube should be considered with precaution. Incidence of IMS is 7-60% worldwide.^{5, 6, 14}

In our study the survival was 82% & mortality 18%. In this retrospective study, we have focused on the incidence, clinical presentation & outcome of patient with IMS syndrome so that early recognition & prompt treatment can save lives of patients of organo-phosphorus insecticide poisoning, in our area. Our limitations being we could not do electrophysiological studies on our patients.

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Sr. No.	CHARACETRISTIC			PATIENTS WITH IMS		PATIENTS WITHOUT IMS	
				A	%	B	%
1	Age		16-30yrs	43	7.52	432	7.78
			30-50yrs	17	2.97	186	3.35
2	Gender		Male	24	4.20	212	3.82
			Female	40	6.99	406	7.31
3	Intent of exposure	Suicidal	yes	62	10.84	525	9.46
			No	2	0.35	93	1.68
		accidental	Yes	4	0.70	93	1.68
			No	60	10.49	525	9.46
4	amount of exposure		yes	64	11.19	20	0.35
			No	0	0.00	588	10.59
5	co-ingestant alcohol		yes	5	0.87	124	2.23
			No	59	10.31	494	8.90
6	Initial treatment with atropine 30amp in 15 minute		yes	51	8.92	185	3.33
			No	13	2.27	433	7.80
7	Initial treatment with initial PAM 1gm/8hour		Yes	54	9.44	216	3.89
			No	10	1.75	402	7.24
8	Abnormal Lab data - ARF		Yes	55	9.62	62	1.12
			No	9	1.57	556	10.01
Mean S.D.				(31.78, 24.37)		(308.44, 93.36)	

TABLE 1: Comparison of characteristics between patients with IMS & without IMS

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Sr. No.	Characteristic	Died	%	Survived	%	
1	Age	18-30yrs	12	9.23	42	8.4
2	Gender	male	8	6.15	24	4.8
		female	4	3.08	28	5.6
3	Intent of exposure	suicidal	12	9.23	40	8
		Accidental	0	0.00	12	2.4
4	Amount of exposure heavy		12	9.23	42	8.4
5	Co-ingestant alcohol	yes	0	0.00	20	4
		no	12	9.23	32	6.4
6	Initial treatment with atropine	30amp in 15 min.	12	9.23	24	4.8
		30amp in 30 min	0	0.00	28	5.6
7	Initial treatment with PAM	1gm/8hr.	12	9.23	24	4.8
		500mg/8hr.	0	0.00	28	5.6
8	Abnormal Lab data ARF		12	9.23	16	3.2
			0	0.00	36	7.2
9	Convulsions	yes	4	3.08	8	1.6
		no	8	6.15	44	8.8
10	ARDS	yes	8	6.15	8	1.6
		no	14	10.77	44	8.8
Mean S.D. (7.22, 5.36)			(27.78, 13.39)			

TABLE 2: Comparison of characteristics between Patients with intermediate syndrome who died & who survived

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