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Study of Clinical Profile of Intermediate Syndrome in Patients Admitted With Organophosphorus Poisoning At Tertiary Care Hospital in Rural India

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Abstract **Original Research Article**

Background: Poisoning with organophosphorus compounds (OPCs) is one of the commonest forms of poisonings in our country especially in rural areas especially due to easy availability. Intermediate syndrome (IS) appears after the acute cholinergic phase but before the expected onset of delayed neuropathy characterised by weakness of neck flexors & proximal muscle, cranial nerve palsies & respiratory muscle paralysis which usually develops between 24 to 96 hours of ingestion of the poison. ***Aim:*** To study the clinical profile of IS in patients admitted with OPCs Poisoning. ***Results:*** Out of 130 cases of OPCs poisoning, 36 (27.69%) cases were with intermediate syndrome. Proportion of poisoning was higher in males (67.6%) as compared to females. Artificial ventilation was required by 89% patients with IS for mean duration of 10 days. Out of 5 deaths, 2 attributed to patients with IS. Ventilator support significantly associated with development of IS. Presence of combination of altered sensorium, flaccid paralysis and respiratory insufficiency was statistically significantly associated with mortality. ***Conclusion:*** Early recognition of the intermediate syndrome, timely ventilator support and intensive follow ups are keys to reduce mortality in OPCs poisoning.

Keywords: Insecticide, Type 2 paralysis, Suicide, PAM, Ventilatory support.

INTRODUCTION

Poisoning with organophosphorus compounds (OPCs) is one of the commonest forms of poisonings in our country especially in rural areas [1]. Incidence of organophosphorus poisoning (OPP) is high because of easy availability of these compounds. Suicidal attempts in the form of consumption of toxic compounds are one of the major public health care issues in India [2].

In OPP, well defined clinical phases are seen: i). Acute cholinergic crisis characterised by muscarinic manifestations; ii). Intermediate syndrome; iii). Delayed neuropathy. Senanayake [3] from Srilanka in 1987 coined the term "Intermediate Syndrome (IS)". But IS was first described as 'Type II paralysis' by Wadia *et al*. [4] in 1974. Weakness of neck flexors & proximal muscle, cranial nerve palsies & respiratory muscle paralysis which usually develops between 24 to 96 hours of ingestion of the poison, are the cardinal features of IS.

In rural population around this hospital, being a farming community OPCs are used as pesticide. OPP is most common form of poisoning encountered in Pravara basin. This study was conducted to study the clinical profile of IS in patients admitted with OPP.

MATERIALS AND METHODS

This cross-sectional observational study was conducted at Pravara Rural Hospital, Loni in Department of Medicine for three years. The study was approved by Institutional Ethical Committee (IEC). All patients admitted with exposure to acute OP poisoning, irrespective of route & cause were enrolled. Patients who refused to give consent, less than 12 years of age, patients who were discharged against medical advice & with incomplete IPD sheets were excluded from study. One hundred & thirty (130) patients admitted with acute OP poisoning during above mention study period were enrolled in the study.

Information about sociodemographic profile, type & amount of poisoning, time of ingestion, time interval between consumption & arrival at hospital, mode & route of poisoning, intent of poisoning was obtained from the patients or accompanying close relative of patient. Symptoms and signs recorded after thorough clinical examination. The severity of poisoning was graded as mild, moderate & severe

according to 'modified Dreisbach'scriteria[5]'. Patients underwent daily standard general & systemic (esp. neurological) examination. Attention was paid to cholinergic, nicotinic and IS related symptoms & signs. Development of intermediate syndrome (IS), need for artificial ventilation, duration of stay and mortality were primary outcome variables. Amount of Atropine and Pralidoxime (PAM) given, and delay for starting PAM after consumption and development of various complications during hospitalization were secondary outcome variables.

Collected data was compiled using Microsoft Excel maintaining confidentiality. Data analysed using SPSS Software v.16. Descriptive statistics like frequencies and percentages for categorical data & mean and standard deviation for continuous data were used. Standard error of difference between two means (Z test) and Chi-square test used for analysis. A p-value<0.05 was considered to be statistically significant.

RESULTS

In the period from January 1999 to December 2001, about 150 cases of poisoning with different compounds were admitted to Pravara Rural Hospital, Loni. The analysis of nature of compounds revealed that poisoning with organophosphorus compounds (OPCs) was the commonest, and it accounted for 130 (86.67%) cases of this series. Out of 130 cases, 36 (27.69%) cases were with intermediate syndrome (IS).

Table no. 1 depicts sociodemographic profile of patients & causes of OPC poisoning. The proportion of poisoning was higher in males (67.6%) as compared to females. Highest proportion of cases was from age group 15- 25 years (41.54%). Mean age in years for males & females was 31.51 & 26.19 respectively. Total mean age was 26.92 years. The most common mode of poisoning was by ingestion & the commonest cause being suicide observed in 93.84% of patients [Table no.1].

Table no. 2 highlights comparison of clinical parameters at the time of admission in patients with & without IS. Out of 130 patients of OPP, 94 (72%) patients were without IS while 36(28%) patients developed IS. It was observed that duration of interval between ingestion of poison (dimethoate) & development of IS varied from 18 hours to 104 hours. In patients with IS, delay in admission was more 3.36 hrs as compare to 2.81 hrs in patients without IS. Most of the cases in this study were of mild grade 68 (52.31%) followed by moderate 49 (37.69%) & severe 13 (10%). At the time of admission regarding clinical severity, most patients with IS were having moderate grade (66.66%) while patients without IS were having mild grade severity (69.19%). The duration of time required for improvement of signs of IS varied from 2 days to 20 days with mean duration of 9 days. About 36% patients recovered within 10 days. Only 7 patients had prolonged IS with duration between 2-3 weeks. Maximum duration of IS (20 days) was seen in dimethoate poisoning [Table no.2].

Artificial ventilator required for 88 (68%). Artificial ventilation was required by 89% patients with IS for mean duration of 10 days. Out of 5 (3.84%) deaths, 3 attributed to Patients without IS & 2 attributed to patients with IS. Multiorgan failure associated with septicaemia and toxic effect of OPCs on different organ system was the main cause of death. No correlation found between dose of poison ingested; administration of treatment (PAM & atropine) & incidence of IS. Mean dose & duration of atropine therapy was more in patients with IS. PAM mean dose was slightly higher in patients with IS.

Table no. 3 highlights comparison of neurological parameters at the time of admission in patients with & without IS. About 67% patients with altered sensorium developed IS as against 33% with normal sensorium who developed IS. Out of 56 cases with flaccid paralysis, 32 cases (57.14%) developed IS. Out of 15 cases with pyramidal tract signs, 7 (46.66%) developed IS. About 97% & 64% patients with IS had fasciculation &miosis the time of admission, respectively [Table no.3].

Amongst patients poisoned with OPCs, the different compounds involved were Dimethoate, Dichlorovas, Parathion, Malathion, Monochrotophos, Chlorpyriphos&Diazinon. Out of 130 patients with OPCs poisoning (OPP), 83 (63.85%) had poisoning with Dimethoate. *Fig no. 1* displays distribution of patients of IS with regards to OPCs & clinical severity. Maximum incidence of IS was noted in patients poisoned with dimethoate. Twenty four out of 83 patients (29%) with dimethoate poisoning developed IS [Figure no.1].

Table-1: Sociodemographic profile of patients & causes of OP poisoning

Age (years) & Gender wise distribution		Male	Female	Total (%)
	15-25	33	21	54 (41.54)
	26-35	29	16	45 (34.61)
	36-45	16	5	21 (16.15)
	46 & above	10	0	10 (7.69)
	Total	88 (67.6%)	42 (32.31%)	130 (100%)
Occupation		No. cases		%
	Farmers	59		45.38
	Home maker	31		23.35
	Students	28		21.54
	Others	12		9.23
Causes	Suicide	122		93.84
	Accidental	7		5.39
	Homicidal	1		0.77

Table-2: Comparison of clinical parameters at the time of admission in patients with & without Intermediate syndrome (IS)

Clinical parameters		Patients without IS (n=94)	Patients with IS (n=36)
Delay in admission (Hrs.)		2.81 +/- 1.01	3.36 +/- 1.98
Clinical severity	Mild	65(69.15%)	3(8.34%)
	Moderate	25(26.6%)	24(66.66%)
	Severe	4(4.25%)	9(25%)
Respiratory Distress	Present	28(29.78%)	32(88.88%)
	Absent	66(70.22%)	4(11.12%)
Artificial Ventilation	Required	56(60%)	32(89%)
	Mean duration[#]	6.13 days	10.2 days
	Range	1-12 days	1-22 days
Atropine Therapy	Mean Dose (mg)	450.17	1032.22
	Mean duration (days)	2.13	4.81
PAM	Mean Dose (gms)	3.12	3.67
	Range(days)	1-6 days	1-8 days
Deaths		03(3.19%)	02(5.5%
# Difference between two means is statistically significant.			

Table-3: Comparison of Neurological parameters at the time of admission in patients with & without Intermediate syndrome (IS)

Neurological parameters		Patients without IS (n=94)	Patients with IS (n=36)
Flaccid paralysis		24 (25.53%)	32 (88.88%)
Pyramidal tract signs		8(8.51%)	7(19.44%)
Paralytic signs (Type I)	Present	35(34.05%)	36(100%)
	Absent	62(65.95%)	0
Sensorium	Normal	81(86.17%)	12(33.33%)
	Altered	13(13.83%)	24(66.67%)
Fasciculation	Present	78(82.98%)	35(97.22%)
	Absent	16(17.02%)	1(2.78%)
Miosis	Present	76(80.85%)	23(63.89%)
	Absent	18(19.15%)	13(36.11%)

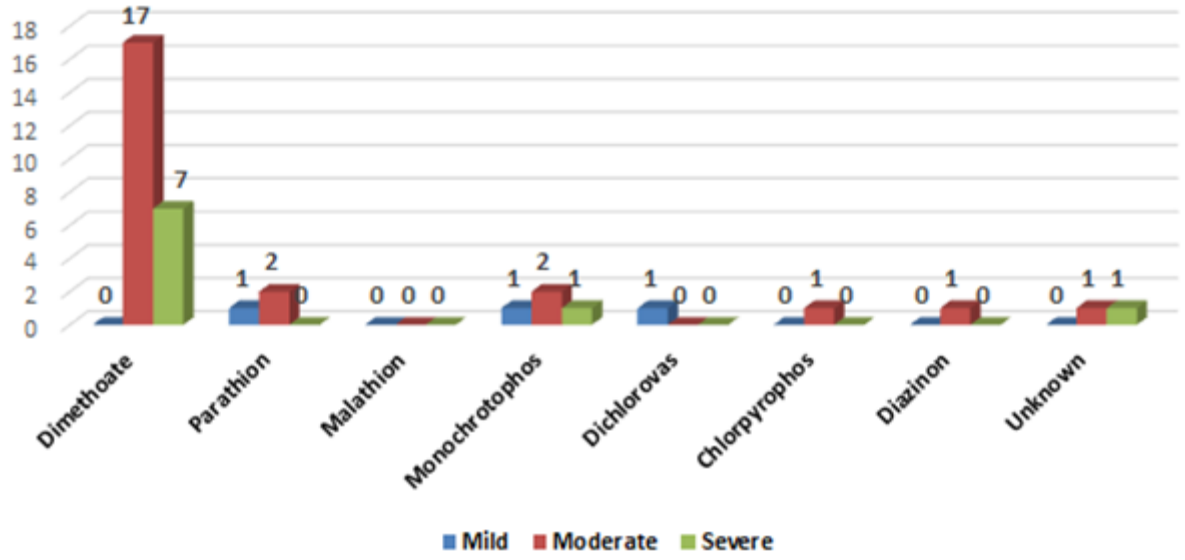

Fig-1: Distribution of patients of intermediate syndrome with regards to OPCs & clinical severity of poisoning

DISCUSSION

This study reports male domination in OPCs poisoning with male to female ratio 2.09:1. In every age group males outnumbered females. The proportion of poisoning was maximum in the age group of 15-25 years. This may be due to gender roles allocated to males & working age group. Similar observations were quoted by Mundhe *et al*. [6], Ahmed *et al.* [7]. Whereas female preponderance was reported by SC De *et al*. [8] (M: F= 1:1.5)65. SC De *et al*. [8] also reported 75% of their patients were from 15-29 years of age. Suicide (94%) was most common cause followed by accident (5.39%). Similar observations were made by AvinashShankar [9] who reported 97.69% cases of suicide & 1.73% cases of accident. Different trend was noted in study done by Mundhe *et al.* [6].

Duration of onset of IS from ingestion of poisoning reported by Wadia *et al*. [4] &Senanayake *et al*. [3] was 9-85 hours & 24-96 hours, respectively. Higher incidence of development of IS was reported by Wadia *et al*. [4] (49%), Bleecker *et al*. [10] (42%) & Coulson J [11]. Mundhe *et al*. [6] reported 13% development of IS. Delay in admission to hospital after poisoning was noted higher in patients with IS. It could be a precipitating factor but it was not statistically significant. According to modified Dreiscbach's classification of clinical severity [5], cases were classified into mild, moderate & severe grades of clinical severity. Least incidence of IS was observed in patients with mild grade severity (8.34%). This may suggest association between clinical severity & development of IS but it was not statistically significant. The duration of IS described by Wadia *et al*. [4] was of 72 hours. But similar observations were noted by Senanayake[3] (4-18 days), Bleecker[10] (5-33 days). Early administration of PAM did not help in prevention of IS. Similar observations role of PAM in IS have been made by other researcher [7, 12-15]. All our patients were given similar dosages of PAM hence we could not correlate the incidence of IS with dosage of PAM. Senanayake *et al*. [3] noted respiratory distress in 7/10 patients & 4 of them required ventilator support. Study done by Adlakha *et al*. [16], mean dose of atropine was 166.3 mg. Association between mortality & development of IS was statistically insignificant. Higher incidence of mortality was noted in study done by Senanayake *et al*. [3] (30%), Mundhe [6] (17%) & Gunnel D *et al.* [17]. Study carried out in India by Muley *et al*. [18], mortality was 11% while 34% cases required ventilator support.

Patients with altered sensorium at the time of admission had higher incidence of IS than those with normal sensorium. In study done by Wadia *et al.* [4], 5 out of 11 patients (45.45%) who had flaccid paralysis developed IS but none with pyramidal tract signs developed IS. The weakness was seen first in neck flexors & then other groups of muscles. At the time of recovery, depression of tendon reflexes was first to recover. Similar pattern of weakness was described by Wadia *et al*. [4], Senanayake *et al*. [3]. Presence of combination of altered sensorium, flaccid paralysis and respiratory insufficiency was statistically significantly associated with mortality.

Incidence of IS was reported to be higher with dimethoate & fenithion in some studies. Our study did not include any case of fenthion poisoning. Wadia *et al*. [4] & Senanayake *et al.* [3] reported OPCs involved in development of IS were dimethoate, fenthion, monochrotophos&methamidophos. The OPCs involved & incidence of IS reported by JD Bleecker *et al*. [10] are comparable with our study except fenthion. All these observations suggest that even though some OPCs (dimethoate & fenthion) are more likely to induce an IS, it is not confined to some distinct compounds only, and also that it is not a rare condition.

Need for careful monitoring of OPCs poisoning patients highlighted by significant incidence of intermediate syndrome in the present study. The respiratory muscles are the last to recover and this fact should be borne in mind while weaning the patient from the ventilator. Deaths due to respiratory paralysis can be prevented by early recognition of the intermediate syndrome; timely ventilator support and intensive follow up.

REFERENCES

1. Srivastava A, Peshin SS, Kaleekal T, Gupta SK. An epidemiological study of poisoning cases reported to the National Poisons Information Centre, All India Institute of Medical Sciences, New Delhi. Hum ExpToxicol. 2005;24:279-85.
2. Chowdhary AN, Banerjee S, Brahma A, Biswas M K. Pesticide poisoning in nonfatal, deliberate self-harm: A public health issue. Indian J Psychiatr. 2007;49:117-20.
3. Senanayake N and Karalliedde L. Neurotoxic effects of organophosphorus insecticides. An intermediate syndrome. New England Journal of Medicine. 1987: 316:761-3.
4. Wadia RS, Sadgopan C, Amin RS, and Sardesai HV. Neurological manifestations of organophosphorus poisoning. Journal of Neurology, NeuroSurgery and Psychiatry. 1974: 37: 841-7.
5. Dreisbach, Robery H. Hand book of poisoning diagnosis and treatment. Langemedical publications, Palo Altos, California (Publ) 1971; pp1-100.
6. Mundhe SA, Birajdar SV, Chavan SS. The clinico-demographic study of morbidity and mortality in patients with organophosphate compound poisoning at tertiary care hospital in rural India. Int J Adv Med 2017;4:809-18.
7. 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;58:11-7.
8. De SC, Chatterjee SC. Poisoning with OP insecticide. J OF Indian Med Assoc 1967; 48:153-157.
9. Avinash Shankar. Handbook of Poisoning. Bhalani Publishing House; 2ND edition. 2005; 20-100.
10. De Bleecker J. Intermediate syndrome in OPP, a prospective study. CRIT CARE MED 1993; 21(11):11.
11. Coulson J. Predicting the intermediate syndrome in organophosphorus poisoning. Indian J Crit Care Med. 2015; 19:377-8.
12. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet. 2008;371:597-607.
13. Narang U, Narang P, Gupta O. Organophosphorus poisoning: A social calamity. J Mahatma Gandhi Inst Med Sci. 2015;20:46-51.
14. Hulse E, Davies J, Simpson A, Sciuto A, Eddleston M. Respiratory complications of organophosphorus nerve agent and insecticide poisoning. Am J RespirCrit Care. 2014;190(12):1342-54.
15. Chaudhary SC, Singh K, Sawlani KK, Jain N, Vaish AK, Atam V, et al, Prognostic significance of estimation of pseudo cholinesterase activity and role of pralidoxime therapy in organophosphorus poisoning. Toxicol Int. 2013;20:214-7.
16. Adlakha A. OP &Carbamate poisoning in Punjab. JAPI 1988; 36:210-12.
17. Gunnell D, Eddleston M, Phillips MR, Konradsen F. The global distribution of fatal pesticide self-poisoning: systematic review. BMC Public Health. 2007;7:357.
18. Muley A, Shah C, Lakhani J, Bapna M, Mehta J. To identify morbidity and mortality predictors in acute organophosphate poisoning. Indian J Crit Care Med. 2014;18:297-300.