

CHARACTERISTICS OF PATIENTS WITH ORGANOPHOSPHORUS POISONING AND ITS MANAGEMENT: PHARMACOEPIDEMIOLOGICAL EVALUATION

MADHURI KULKARNI^{1*}, ANANT PATIL²

¹Department of Pharmacology, Government Medical College, Aurangabad, Maharashtra, India. ²Department of Pharmacology, Dr. DY Patil Medical College, Nerul, Navi Mumbai, Maharashtra, India. Email: anantdpatil@gmail.com

Received: 04 September 2018, Revised and Accepted: 19 September 2018

ABSTRACT

Objective: The objective of this study was to analyze demographics, management pattern, and clinical outcomes in patients with organophosphorus poisoning.

Methods: In this subgroup analysis of retrospective data of patients admitted in intensive care unit (ICU) with a diagnosis of acute organophosphorus poisoning, demographic details, pattern of use of medicines, dose of atropine and pralidoxime (PRAM), duration of ICU stay, and clinical outcomes were analyzed.

Results: A total of 92 patients with organophosphorus poisoning (mean age 34.7 years; male 69 [75%]) were included. The age of male patients was more than female patients (36.2 vs. 30.0 years; $p=0.047$). Atropine and PRAM were given to all patients. Ondansetron was used in all patients, whereas ranitidine was used in 91 (98.9%) patients. The mean total dose of atropine in male and female population was 99.5 mg and 89.0 mg, respectively ($p=0.298$). The mean total dose of PRAM in male and female population was 12.2 mg and 12.0 mg, respectively ($p=0.772$). There was no difference in the mean (standard deviation) duration of stay in ICU between male patients and female patients (7.6 [4.5] vs. 6.4 [3.9] days; $p=0.249$). A total of 61 (66.3%) patients were transferred to the ward, whereas 30 (32.6%) died.

Conclusion: Atropine and PRAM are the primary drugs for the treatment of organophosphorus poisoning. Ondansetron and ranitidine are useful drugs for the treatment of vomiting and gastric irritation, respectively, in these patients.

Keywords: Atropine, Intensive care unit, Organophosphorus poisoning.

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INTRODUCTION

Acute poisoning with organophosphorus compounds is one of the major concerns, especially in developing countries [1] including India [2-4] because of its high mortality rate [2,3]. A study from India has reported a mortality rate of 22.6% among hospitalized patients with pesticide poisoning [5].

Organophosphorus poisoning is not a single entity [6]. Organophosphorus compounds are the group of compounds with strong anticholinesterase activity. These are often used as insecticides and pesticides [7].

The symptoms of organophosphorus poisoning include those because of muscarinic and nicotinic receptor stimulation [7]. Patients with organophosphorus poisoning often require admission in the intensive care unit (ICU) [8]. The goals of the treatment of acute organophosphorus poisoning include limiting absorption of the toxin, increasing excretion of poison, and neutralizing the effects of organophosphorus compound by giving antagonist [9].

Overall treatment strategy of acute organophosphorus poisoning includes resuscitation, oxygen, intravenous fluids, antimuscarinic agent, acetylcholinesterase reactivator, and gastric lavage [10]. Atropine, a muscarinic antagonist, is a mainstay of treatment in acute organophosphorus poisoning [9]. Pralidoxime (PRAM) is another important compound in the treatment of acute organophosphorus poisoning [3].

Although poisoning with organophosphorus compounds is common, there are no large, systematic epidemiological studies from India [7]. Similarly, there are limited pharmacoepidemiological data related to organophosphorus compound poisoning from Maharashtra.

Objective

The objective of this study was to analyze demographics, management pattern, and clinical outcomes of patients with organophosphorus poisoning admitted in the medical ICU.

METHODS

Recently, a retrospective study among patients admitted in medical ICU with a diagnosis of acute poisoning was published [11]. In this article, we analyzed the subgroup of patients with organophosphorus poisoning admitted in medicine ICU from January 2017 to July 2017. Demographic details (age and gender) were collected. Different medicines used for the treatment of organophosphorus poisoning, dose of atropine, and PRAM were calculated. The difference in the dosage of these two medicines was analyzed. Duration of ICU stay was calculated. Clinical outcomes of male and female patients were compared. Approval from the institutional ethics committee was taken for the main study. As this is a subgroup analysis of larger data set, a separate approval from ethics committee was not obtained.

Statistical analysis

Continuous data are presented as mean and standard deviation (SD), whereas categorical data are presented as number and percentages. Unpaired t-test was used to compare the difference in the means between two groups. Categorical data were compared using Chi-square test. $p<0.05$ was considered as statistically significant.

RESULTS

A total of 92 patients with organophosphorus poisoning were included in this study. The mean age of patients in the study was 34.7 years. The study population was predominated by male population (75% vs.

25%). There was a significant difference in the age of male and female patients (36.2 vs. 30.0 years; $p=0.047$; Table 1).

Table 2 shows a list of medicines used in the treatment of patients with organophosphorus poisoning. The drugs were classified into four types based on their usage; those used as primary treatment, drugs for gastrointestinal disturbances, antimicrobial agents, and hypnotic/sedatives. Primary treatment in the form of atropine and PRAM was given to all patients with organophosphorus poisoning. Drugs used for the treatment of gastrointestinal disturbances included ondansetron and ranitidine. Ondansetron was used in all patients, whereas ranitidine was used in 91 (98.9%) patients. The antimicrobial agents used in patients with organophosphorus poisoning included ceftriaxone (70.7%), metronidazole (29.3%), cefotaxime (28.3%), amoxicillin-clavulanic acid (23.9%), amikacin (4.4%), meropenem (3.3%), and piperacillin plus tazobactam combination (3.3%). Hypnotic/sedatives used were midazolam (20.7%) and lorazepam (7.6%).

The mean total dose of atropine used in overall patient population, male population, and female population was 96.8, 99.5, and 89.0 mg, respectively (Table 3). There was no difference in the dose of atropine between male and female patients with organophosphorus poisoning ($p=0.298$). The mean total dose of PRAM in overall patient population, male population, and female population was 12.1, 12.2, and 12.0 mg, respectively (Table 3). There was no difference in the dose of PRAM between male and female patients with organophosphorus poisoning ($p=0.772$).

The mean (SD) duration of stay in ICU for overall patient population, male patients, and female patients was 7.3 (4.7), 7.6 (4.5), and 6.4 (3.9), respectively (Fig. 1). There was no difference in the duration of hospital stay between male and female patients ($p=0.249$).

A total of 61 (66.3%) patients were transferred to the ward, whereas 30 (32.6%) died. One patient was discharged against medical advice (Table 4). There was no significant difference in male and female

Table 1: Baseline characteristics of study population (n=92)

Characteristics	Result
Mean (SD) age	34.7 (13.1) years
Mean (SD) age of male patients	36.2 (13.1) years
Mean (SD) age of female patients	30.0 (12.3) years
Male, n (%)	69 (75)
Female, n (%)	23 (25)

SD: Standard deviation

Table 2: Medicines used for the treatment of patients with organophosphorus poisoning (n=92)

Drug	n (%)
Primary medicines	
Atropine	92 (100)
PRAM	92 (100)
Drugs for gastrointestinal disturbance	
Ondansetron	92 (100)
Ranitidine	91 (98.9)
Antimicrobial agents	
Ceftriaxone	65 (70.7)
Metronidazole	27 (29.3)
Cefotaxime	26 (28.3)
Amoxicillin-clavulanic acid	22 (23.9)
Amikacin	4 (4.4)
Meropenem	3 (3.3)
Piperacillin and tazobactam	3 (3.3)
Hypnotic/sedative	
Midazolam	19 (20.7)
Lorazepam	7 (7.6)

PRAM: Pralidoxime

patients in terms of a number of patients transferred to the ward and those died ($p=0.765$).

DISCUSSION

Acute poisoning is an important cause of hospitalization [12,13]. Self-poisoning with pesticides is a concern, especially in rural areas, because of easy access to toxic pesticides [14] and high rate mortality [15].

Unlike a study from Nepal [2], in our study, male population was more affected because of organophosphorus poisoning. Our results are similar to other studies from India [16-18], showing more occurrence of poisoning in male population compared to female population. As reported in other studies [2,16], people from working population were more commonly affected in our study too. The results of our study suggest that working male population is more affected by organophosphorus poisoning. We did not record the occupation and marital status of people affected, but it may have some association with organophosphorus poisoning [2].

Mortality in acute organophosphorus poisoning is usually because of respiratory failure and cardiovascular collapse due to cholinergic effects of the poison [19]. Atropine is an essential medicine for the treatment of organophosphorus poisoning. Serious cases cannot be managed without atropine [14]. Atropine remains the choice of drug for the management of cholinergic crisis in acute organophosphorus poisoning [3]. However, there are variations in the recommendations for atropinization [19].

Table 3: Total dose of atropine and PRAM used in patients with organophosphorus poisoning

Patient population	Mean total dose of atropine (mg)	Mean total dose of PRAM (mg)
Overall patient population (n=92)	96.8 (41.5)	12.1 (3.3)
Male patients (n=69)	99.5 (41.5)	12.2 (3.4)
Female patients (n=23)	89.0 (41.2)	12.0 (3.0)

PRAM: Pralidoxime

Table 4: Outcomes of patients with organophosphorus poisoning

Outcome	Overall patient population n=92 (%)	Male n=69 (%)	Female n=23 (%)
Transferred to the ward	61 (66.3)	45 (65.2)	16 (69.6)
Mortality	30 (32.6)	23 (33.3)	7 (30.4)
Discharged against medical advice	1 (1.1)	1 (1.5)	0

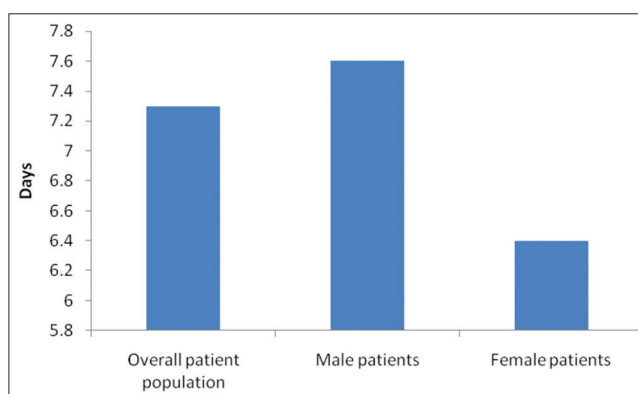


Fig. 1: Mean duration in intensive care unit stay of patients with organophosphorus poisoning

Glycopyrrolate is another anticholinergic drug that can be used for the treatment of organophosphorus poisoning [20]. In our study, all patients received atropine. In other studies too, all patients received atropine [18]. The mean total dose of atropine used in our study was 96.8 mg.

Atropine is ineffective at the nicotine-sensitive synapses. Reactivation of inhibited cholinesterase may be beneficial at both muscarinic and nicotinic receptors [21]. PRAM helps in restoring phosphorylated cholinesterase enzyme which is significantly inhibited in patients with organophosphorus poisoning. PRAM is useful for improving symptoms of muscle weakness and fasciculations [3]. In our study, all patients were treated with PRAM. High dose of PRAM has been shown to be associated with better survival as compared with lower dose [3]. In our study, mean total dose of PRAM used was 12.1 g. The requirement of PRAM in our study was similar to another study [20]. We did not find a significant difference in the dosing requirement of atropine and PRAM in male and female patients.

More than 5 days of stay in the hospital is common for patients with organophosphorus compound poisoning [16]. In our study, the mean duration of stay in ICU was 7.3 days. Our observation regarding hospital stay is similar to that reported by Kumar *et al.* [18].

Mortality rate due to organophosphorus poisoning in our study was similar to that of reported in another study from Gujarat [16].

Our study provides significant insights in terms of gender-wise comparison of characteristics in patients with organophosphorus poisoning. The results of our study underline the need and importance of education of the working population regarding harmful effects of organophosphorus compounds. Education and awareness may help to reduce the morbidity and mortality associated with acute organophosphorus poisoning.

Limitations of our study include retrospective study design, single-center study, and small sample size. Considering these limitations, the results of our study should be carefully interpreted and extrapolated.

CONCLUSION

Atropine and PRAM are the primary drugs used in the treatment of organophosphorus poisoning. There is no difference in the mean total dosage of these drugs and duration of stay in ICU between male and female population. Ondansetron and ranitidine are useful drugs for the treatment of vomiting and gastric irritation, respectively, in these patients.

ACKNOWLEDGMENT

Authors of this study wish to thank Dr. Siddharth Athawale for his contribution in data collection.

AUTHORS' CONTRIBUTIONS

Dr. Madhuri Kulkarni conceptualized the study. Dr. Anant Patil conducted statistical analysis. Both the authors contributed for the preparation of manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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