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**Original Research Article**

# A comparative study of atropine and atropine plus pralidoxime in the management of organo-phosphorous poisoning

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## ABSTRACT

**Background:** Poisoning with organophosphorus compounds (OP) is a common problem throughout the world particularly in developing countries. Standard treatment involves resuscitation, administration of the anti-muscarinic agent atropine, an acetylcholinesterase reactivator (pralidoxime) and assisted ventilation if necessary. In this study we compared the efficacy of add-on pralidoxime therapy over therapy with atropine alone in OP poisoning.
**Methods:** The study included 103 patients, out of 103 OP poisoning cases, 54 patients received both atropine and PAM (group A) and 49 received only atropine (group B). Main outcome parameters of the study were total hospital stay and mortality. The data was compared using 't' test while mortality was compared using Fisher's exact test. Data was tabulated, analysed, reviewed and evaluated.
**Results:** There was no difference in duration of hospital stay between the two group. The mean hospital stay in group A was 3.71±1.92 days and in group B was 3.14±2.01 days (p value >0.05). No difference in mortality was seen between the two group. Out of 54 in group A, 8 died and in group B out of 49, 7 died (p value >0.05). Importantly cost burden is very high in the pralidoxime added group.
**Conclusions:** There is no significant difference in use of atropine alone or atropine-pralidoxime combination in terms of morbidity and mortality in OP poisoning rather the later incurs more economic burden which may not be practicable in poor countries like India. However, a larger multicentric prospective study needs to be conducted, to be able to draw a definitive conclusion.

**Keywords:** Organophosphorus, Atropine, Pralidoxime

## INTRODUCTION

In India, organophosphates (OP) are the most common pesticides and they are also the most common cause of accidental/intentional poisoning in India.[1] India is a predominantly agrarian country where pesticides are routinely used for farming and as such, a huge proportion has access to the OPs and it is the most common modality of poisoning. Worldwide, the number of intoxications with organophosphorus pesticides (OPs) is estimated at about 3 000 000 per year, and the number of deaths and casualties about 3,00,000 per year.[2]

Data on the pattern of poisoning in North India accumulated at National Poison Information Center (NPIC) located in All India Institute of Medical Sciences, New Delhi suggest that suicidal poisoning with household agents (OPs, carbamates, and pyrethrinoids) is the most common modality of poisoning.[3]

Medical management is difficult, with case fatality generally more than 15%.[4] In many rural areas of Asia, organophosphorus pesticide self-poisoning is a serious clinical and public health issue.[5,6] About 60% of the estimated 5,00,000 self-harm deaths in the area each year

are brought on by pesticide poisoning.[7] A doctor will frequently encounter cases of OP poisoning in his or her practice, thus understanding how to treat such patients is crucial.

The OPs work by blocking the acetylcholinesterase enzyme, which raises the levels of acetylcholine in nerve terminals, sympathetic ganglia, neuromuscular endplates, and specific CNS regions, causing extensive cholinergic effects. Respiratory failure and lung injury are the primary causes of mortality in patients exposed to toxic compounds. However, the clinical presentation and symptoms can vary widely based on factors such as the specific nature of the substances encountered, the quantity ingested or inhaled, the degree of toxicity, and the duration between exposure and hospital admission.[8] Standard treatment involves resuscitation, administration of the anti-muscarinic agent atropine, an acetylcholinesterase reactivator such as pralidoxime, and assisted ventilation if necessary.[9] While the effectiveness of atropine in treating OP poisoning is well-established and widely accepted, the use of pralidoxime has generated significant debate within the medical community regarding its efficacy. The precise role of oximes in the treatment of OP poisoning remains unclear, with suggestions that they may provide benefits primarily to patients exposed to certain pesticides or individuals with moderate levels of poisoning. The use of oximes is also complicated by the need for it to be given before the aging of the acetylcholinesterase enzymes, failing which it is ineffective. It is often noted that patients reach very late to a tertiary health care centre, due to many reasons, and hence the use of oximes is non-productive in such cases. Even Cochrane reviews concluded that current evidence is insufficient to indicate whether oximes are harmful or beneficial in the management of acute organophosphorus pesticide poisoning.[10]

Since OP poisoning accounts for a high incidence of mortality in rural India, it was essential to evaluate the relative advantage of add-on pralidoxime therapy over treatment with parenteral atropine sulphate alone in OP poisoning.

### *Objective*

The aim of the study was to compare the efficacy of add-on pralidoxime therapy over therapy with atropine alone in OP poisoning.

## METHODS

### *Duration of study*

The duration of the study was one year (December 2017 – November 2018).

### *Design of the study*

It was a hospital based retrospective study.

### *Study population*

All consecutive patients admitted in the department of medicine, AMCH during the study period, with history and clinical evidence of OP poisoning.

### *Inclusion and exclusion criteria*

The study included 103 patients with history and clinical evidence of OP poisoning, 24 cases were excluded due to paucity of clinical signs, presentation after 24 hours of ingestion and because of lost follow up. Of 103 OP poisoning cases, 54 patients received both atropine and PAM (group A) and 49 received only atropine (group B). Baseline parameters like age, sex, time of presentation, severity-determined by Peradeniya organophosphorus poisoning (POP) scale were evaluated in both the group. Main outcome parameters of the study were total hospital stay and mortality.

### *Statistical methods*

The data was compared using unpaired ‘t’ test while mortality was compared using Fisher’s exact test. Data was tabulated, analysed, reviewed and evaluated. Ethical clearance was obtained from the Institutional Ethics Committee.

### *POP scale*

Pupil size: >2 mm (0), <2 mm (1), pinpoint (2); respiratory rate: <20/minute (0), >20/minute (1), >20/minute and central cyanosis (2); heart rate: >60/minute (0), 41-60/minute (1), <40/minute (2); fasciculation: none (0), present, generalized or continuous (1), present, generalized and continuous (2); level of consciousness: conscious and rationale (0), impaired response to verbal commands (1), no response to verbal commands (2); seizures: absent (0), present (1).

### *Statistical analysis*

The data was compared using unpaired ‘t’ test while mortality was compared using Fisher’s exact test. Data was tabulated, analysed, reviewed and evaluated.

## RESULTS

The majority number of patients were seen in the 21-30-years age in both the group with 21 patients in group A and 22 patients in group B respectively. The mean age was 31.16±13.97 in group A and 30.92±12.02 in group B respectively (Table 1).

Out of 54 patients, 21 were male and 33 were female in group A and out of 49 patients, 19 were male and 30 were female in group B respectively (Table 2).

The majority of the patients were presented within 6 hours of duration in both the groups with 26 patients in group A

and 24 patients in group B. The mean duration were 8.6±7.6 hours in group A and 8.3±7.3 hours in group B respectively (Table 3).

**Table 1: Age distribution.**

| Age (years) | Group A (no. of patients) | Group B (no. of patients) | P value |
|---|---|---|---|
| **12-20** | 12 | 11 | 0.92 |
| **21-30** | 21 | 22 | |
| **31-40** | 6 | 6 | |
| **>40** | 15 | 10 | |
| **Mean±SD** | 31.16±13.97 | 30.92±12.02 | |

**Table 2: Gender distribution.**

| Age (years) | Group A (no. of patients) | Group B (no. of patients) |
|---|---|---|
| **Male** | 21 | 19 |
| **Female** | 33 | 30 |

**Table 3: Duration at presentation.**

| Time (hours) | Group A (no. of patients) | Group B (no. of patients) | P value |
|---|---|---|---|
| **<6** | 26 | 24 | 0.83 |
| **6-12** | 14 | 11 | |
| **>12** | 14 | 14 | |
| **Mean±SD** | 8.6±7.6 | 8.3±7.3 | |

Severity (by POP score)- majority of the patients were mildly severe with 22 patients in group A and 20 patients in group B respectively (Table 4).

**Table 4: Severity.**

| Severity | Group A (no. of patients) | Group B (no. of patients) | P value |
|---|---|---|---|
| **Mild (0-3)** | 22 | 20 | 0.36 |
| **Moderate (4-7)** | 15 | 13 | |
| **Severe (8-11)** | 17 | 16 | |
| **Mean±SD** | 5.66±2.89 | 6.15±2.59 | |

The mean duration of hospital stay was 3.71±1.92 days in group A and 3.14±2.01 days in group B. Mortality rate were 14.8% in group A and 14.2% in group B respectively (Table 5).

For cost analysis, the cost of 1 ampule of pralidoxime (PAM) which contain 500 mg of pralidoxime is approximately 166 rupees while 1 ampule of atropine which contain 0.6 mg atropine is only 11 rupees (Table 6).

Both the groups were similar in baseline parameters like age, sex, time of presentation and severity.

There was no difference in duration of hospital stay between the two group. The mean hospital stay in group A was 3.71±1.92 days and in group B was 3.14±2.01 days (p value >0.05).

No difference in mortality was seen between the two group. Out of 54 in group A, 8 died and in group B out of 49, 7 died (p value >0.05).

Importantly cost burden is very high in the pralidoxime added group.

**Table 5: Outcome.**

| Outcome | Group A | Group B | P value |
|---|---|---|---|
| **Duration of hospital stay, mean±SD (in days)** | 3.71±1.92 | 3.14±2.01 | 0.14 |
| **Mortality** | 8 (14.8%) | 7 (14.2%) | |

**Table 6: Cost analysis.**

| Cost in each patient | Group A | Group B |
|---|---|---|
| **Approximate** | Atropine price + 5000-6000/- | Atropine price only |

## DISCUSSION

Organophosphates are one of the frequently used pesticides which can result in serious morbidity and mortality. In our study, the mean age were 31.16±13.97 in group A and 30.92±12.02 in group B respectively and the incidence were maximum in the 21-30 years age in both the group with 21 patients in group A and 22 patients in group B respectively which was consistent with studies done by Salame et al and Raddi et al.[11,12]

The incidence of female patients were more in both the groups with 33 female patients out of 54 patients in group A and 30 female patients out of 49 patients in group B respectively which was consistent with the study done by Chaturvedi et al.[13] The majority of the patients were presented within 6 hours of duration in both the groups. The mean duration was 8.6±7.6 hours in group A and 8.3±7.3 hours in group B respectively.

The severity of the symptoms of the two groups were comparable with majority of the patients belonging to the mild subgroup according to the severity as per Peradeniya OP (POP) scale. Hospital stay was not significantly different between the two treatment groups. De Silva et al who conducted a similar study, came to the conclusion that the clinically assessed outcome was comparable between the two groups.[14]

Since its discovery in 1956 by Wilson and his colleagues, pralidoxime has remained an integral part in management of organophosphorus poisoning. Our study suggests that

add-on pralidoxime therapy did not add any appreciable benefit in regard to mortality and duration of hospital stays, when compared with atropine monotherapy. Our study is in congruence with results observed in studies reported by Duval et al, De Silva et al, and Chabra et al.[14-16]

### *Limitations*

Duration of the study was short, only for 1 year and it was a single centered hospital based study. Existing co-morbidities of the study participants were not evaluated.

## CONCLUSION

There is no significant difference in use of atropine alone or atropine-pralidoxime combination in terms of morbidity and mortality in OP poisoning rather the later incurs more economic burden which may not be practicable in poor countries like India. However, a larger multicentric prospective study needs to be conducted, to be able to draw a definitive conclusion.

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