

## Comparison of efficacy of atropine versus atropine with pralidoxime in organophosphorus poisoning

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### ABSTRACT

**Background:** Comparison of the efficacy of atropine alone against atropine with pralidoxime in the treatment of organophosphorus (OP) poisoning.

**Methods:** Forty two patients between the age group of 18 to 65 years, treated for OP poisoning and matched for baseline characteristics, were included in two groups based on treatment received as "Atropine only" or "Atropine plus pralidoxime(PAM)". Main outcomes of the study were ICU stay, total hospital stay and mortality. ICU and hospital stay were compared using 't' test while mortality was compared using Fisher's exact test.

**Results:** Total hospital stay was not significantly different between the treatment groups (95% CI of difference: -4.227, 0.784). Length of stay was also not significantly different between patients who received atropine plus PAM within 6 hours of consumption of poison and those who received 6 hours later (95% CI of difference: -4.154, 0.954; p value: 0.2).

**Conclusion:** Our data supports the use of only atropine over atropine plus PAM in patients with OP poisoning on account of no significant difference /reduction of hospital/ICU stay and mortality in the latter group. However, a study with a larger sample needs to be conducted, to be able to draw a definitive conclusion.

**Keywords:** Organophosphorus (OP) poisoning, Pralidoxime (PAM), Peradeniya OP scale

### INTRODUCTION

Organophosphates (OP) are the most common pesticides used in India, and unfortunately, they are also the most common cause of intentional/accidental poisoning in India.<sup>1</sup> Being an agrarian driven economy, India has a huge percentage of the population involved in agriculture, and as such, a huge proportion has access to the OPs, leading up to a large number of poisoning cases.

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.<sup>2</sup> Medical management is difficult, with case fatality generally more than 15%.<sup>3</sup> Organophosphorus pesticide self-poisoning is a major clinical and public-health problem across much of rural Asia.<sup>4,5</sup> Of the estimated 5,00,000 deaths from self-harm in the region each year, about 60% are due to pesticide poisoning.<sup>6</sup> It is very common for a physician to come

across many cases of OP poisoning in his practice, and thus knowledge of treatment of the same is quintessential.

The OPs act by inhibiting the enzyme acetylcholinesterase resulting in the increased levels of acetylcholine in the nerve terminals, sympathetic ganglia, neuromuscular endplates and certain CNS regions, causing widespread cholinergic effects. Drugs like atropine, oximes have long been discovered which are very useful in OP poisoning. Though atropine has been accepted for its role in the management of OP poisoning, controversy exists about role and usefulness of oximes. The role of oximes is not completely clear. They might benefit only patients poisoned by specific pesticides or patients with moderate poisoning.<sup>3</sup> 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.

Our study aims to compare the utility of atropine alone against atropine with oximes in the treatment of OP poisoning, as measured by the average duration of stay in ICU.

## METHODS

This is a retrospective, hospital based study, and data was collected from the medical records department, Father Muller medical college, Mangalore. The institutional ethics committee has approved the study before obtaining the data.

### Inclusion criteria

Patients suspected to have consumed OP and reported to the hospital within 24 hours.

### Exclusion Criteria

1. Patients presenting after 24 hours of intake of poison.
2. Patients with coexistent illness which can interfere with the treatment of OP poisoning.
3. Patients who have consumed other poison along with OP (if known).
4. Patients who have had treatment already initiated before reporting to the hospital.

Forty two OP poisoning cases between January 2011 to December 2012 were included in the study and data collected from them. The case record form consisted of details like demographic data, time since consumption of OP compound, severity as per Peradeniya OP scale (POP scale), treatment provided, duration of hospital stay and ICU stay, outcome of treatment.

Patients in the study were divided into two groups based on the treatment received, as "Atropine only" or "Atropine plus PAM". The latter were further grouped based on whether treatment was initiated within or more than 6 hours of consumption of poison.

Baseline characteristics like age, sex, severity of poisoning based on Peradeniya OP scale, time at presentation to the hospital etc. were compared between the two groups for comparability. Main outcomes of the study were ICU stay and total hospital stay and mortality.

Statistical Methods: The data was compared using 't' test while mortality was compared using Fisher's exact test. Data was tabulated, analysed, reviewed and evaluated.

## RESULTS

Table 1 shows that the baseline characteristics were comparable including severity of poisoning.

**Table 1: Comparison of baseline characteristics.**

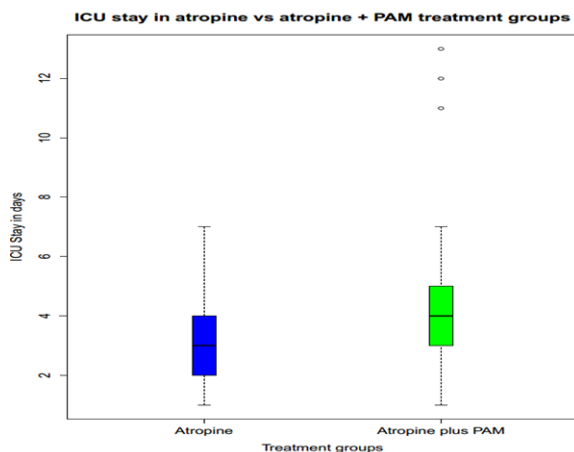
Baseline characteristics	Atropine group N=13	Atropine plus PAM group N=29	P value
Age (Mean $\pm$ SD in years)	31.3 $\pm$ 15.3	34.8 $\pm$ 16.1	n.s
Sex			
Male	8 (61.5%)	23 (79.3%)	n.s
Female	5 (38.5%)	6 (20.7%)	n.s
Time at presentation in hours (Mean $\pm$ SD)	8.1 $\pm$ 6.9	5.4 $\pm$ 3.7	n.s
Severity based on Peradeniya OP scale			
Mild	11 (85%)	23 (79.3%)	n.s
Moderate	2 (15%)	4 (13.8%)	n.s
Severe	0	2 (6.9%)	n.s

**Table 2: Comparison of main outcomes between atropine and atropine plus PAM treatment groups.**

	Atropine group n=13	Atropine plus PAM n=29	95% CI of the difference (LCI, UCI)	P value (significant if <0.05)
ICU stay in days (Mean $\pm$ SD)	3.2 $\pm$ 1.8	4.6 $\pm$ 3.1	(-3.241, 0.461)	0.137
Total Hospital Stay in days (Mean $\pm$ SD)	5.7 $\pm$ 2.3	7.4 $\pm$ 4.1	(-4.227, 0.784)	0.173
Death	1	1	-	0.528
Survival at discharge	12	28	-	
Discharge against medical advice*	2	7	-	-

\*taken as alive at the time of discharge and part of survival at discharge data shown

ICU stay was not significantly different between the two treatment groups (95% CI of the difference: -3.241, 0.461; Figure 1). Total hospital stay was also not significantly different between the treatment groups (95% CI of difference: -4.227, 0.784).



**Figure 1: Boxplot showing no significant difference in ICU stay in OP patients treated with atropine vs. atropine plus PAM.**

Only two patients died, one in each of the treatment groups. However, survival status of 9 patients were only known till date of discharge (2 in atropine group and 7 in atropine plus PAM group) as these patients were discharged against medical advice.

Length of stay was not significantly different between patients who received atropine plus PAM within 6 hours of consumption of poison and those who received 6 hours later (95% CI of difference: -4.154, 0.954; p value: 0.2).

One patient who died in the atropine plus PAM group received treatment within 6 hours of consumption of OP poison.

## DISCUSSION

The demographic profile of the study population showed that the males were more in both the atropine group (61.5%) and the atropine plus PAM group (79.3%). This is because of the higher incidence of suicides due to consumption of OP compounds in the males when compared to females as established by Gunnell D<sup>7</sup> et al in their study on "The global distribution of fatal pesticide self-poisoning: Systematic review". Chugh SN<sup>8</sup> et al noted that a particular feature of self-poisoning in northern India is the frequent ingestion of aluminium phosphide, a fumigant used to protect grain stores, with an associated case fatality in excess of 70%.

The severity of the symptoms of the two groups was comparable with majority of the patients belonging to the mild subgroup according to the severity as per Peradeniya OP scale. ICU stay was not significantly different between the two treatment groups (95% CI of the difference: -3.241, 0.461; Figure 1). De Silva et al who did a similar study concluded that outcome, as assessed clinically, was similar in the two groups,<sup>9</sup> this questions the necessity of cholinesterase reactivators for treatment of acute OP poisoning.

Length of stay was not significantly different between patients who received atropine plus PAM within 6 hours of consumption of poison and those who received 6 hours later (95% CI of difference: -4.154, 0.954; p value: 0.2). Eddleston M et al in their double-blind randomised placebo-controlled trial demonstrated that there was no benefit from the administration of the WHO recommended regimen of pralidoxime chloride to patients with symptomatic OP insecticide poisoning.<sup>10</sup>

Comparative trials to definitively establish the non essentiality of the use of oximes are lacking and hold potential for future research.

## CONCLUSION

Our data supports the use of only atropine over atropine plus PAM in patients with OP poisoning on account of no significant difference /reduction of hospital/ICU stay and mortality. However, more studies with larger sample size need to be conducted, to be able to draw a definitive conclusion.

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