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ORIGINAL ARTICLE

Outcome of treatment of OPC poisoning patients with atropine or atropine plus pralidoxime

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Abstract

Background: *Organophosphorus compound (OPC) poisoning is common in Bangladesh and management facility is not adequate in most hospitals. Both inj. Atropine and inj. Pralidoxime is used as antidote for the management of OPC poisoning, although there is controversy regarding benefit of inj. Pralidoxime.*

Objective: *This randomised clinical trial was conducted to compare the outcome of OPC poisoning patients treated by inj. Atropine along with supportive measures and by inj. Atropine plus inj. Pralidoxime along with supportive measures . This study also evaluated the clinical profile of OPC poisoning patients.*

Methods: *A total number of 109 patients, admitted in medicine ward in Khulna medical college hospital during one year period were included in this randomised clinical trial. The patients were divided into two groups according to alternate day of admission in the medicine wards. Forty nine patients of group A was treated by inj. atropine only along with other supportive measures required and group B of 60 patients was treated by inj. atropine plus inj. pralidoxime along with supportive measures.*

Results: *49 patients of group A was treated with atropine alone and 60 patients in group B was treated with atropine plus pralidoxime. Death rate was 14.28% in atropine treated group and 16.66% in atropine plus pralidoxime treated group (p=0.733). The difference in death rate is not statistically significant. Four (8.18%) patients from atropine treated group and 4 (6.67%) patients from pralidoxime intervention group developed respiratory failure and ventilatory support was given in ICU. These 8 patients recovered. But this difference in development of respiratory failure is not statistically significant (p=0.766). The difference of death rate between male and female (12.5% Vs 18.87%) is not also significant (p=0.360).*

Conclusion: *This study reveals that pralidoxime provides no better outcome in the management of OPC poisoning patients.*

Key words: *Organophosphorus compound, Poisoning, Atropine, Pralidoxime.*

Introduction

Acute OPC poisoning is widespread in agricultural developing countries. Overall its frequency has increased over the years. The toxicity of the agent and paucity of appropriate medical services has resulted in high mortality rates.[1] Majority of death occurs following self poisoning.[2] OPC poisoning is more commonly seen in rural areas. Its incidents is 20% to 30% of total poisoning cases as reported in Japan, Taiwan and Thailand.3 OPC exerts an acute toxic effect on central and peripheral nervous system by blocking acetylcholinesterase (AchE) leading to accumulation of acetylcholine (Ach) at muscarinic and nicotinic receptors.[4]

The OPCs are of two groups: Phosphates and Carbamates, which bind to the active amino acid site serine on the acety1cholinesterase enzyme and phosphorylate or carbamylate it respectively. The phosphorylated enzyme is very stable, degrades slowly after days to weeks, making acety1cholinesterase essentially inactive. Carbamylated enzyme degrades within minutes to hours so that the enzyme at the site is eventually regenerated.[5]

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OPC poisoning effects can be summarized as: a) Muscarinic effects- salivation, bronchorrhoea, bronchospasm, lacrimation, diarrhoea, urination, emesis, miosis, excessive sweating. b) Nicotinic effects- muscle fasciculation, cramping, weakness, diaphragmatic paralysis, respiratory failure, tachycardia, hypertension. c) CNS effects- confusion, seizure and coma.[6]

The treatment options are anticholinergic drug intravenous atropine, intravenous pralidoxime to reactivate acetylcholinesterase, supportive measures and assisted ventilation. Mortality is high in hospitals without facilities for assisted ventilation.7 Pralidoxime was discovered by Wilson and Colleagues in 1950 and successfully used for patients with parathione poisoning. Its effectiveness has been much debated with many Asian clinicians for the treatment of OPC poisoning, although WHO recommended its use.8 The results of the earlier oxime trials did not demonstrate a favourable outcome. Recent trial suggested benefit of pralidoxime in very early presentation i.e. within six hours of intoxication of moderately severe OPC poisoning patients. Oximes can produce respiratory depression, cardiac arrhythmia and neurological weakness.[9] There has been extensive debate about the effectiveness of oximes for the treatment of organophosphorus insecticide poisoning. Asian doctors have reported no benefit from pralidoxime.10 Intravenous pralidoxime is being used along with intravenous atropine for the treatment of OPC poisoning for at least one decade in many hospitals of Bangladesh. We found no study in Bangladesh comparing the effectiveness of atropine and pralidoxime, in the management of OPC poisoning patients.

This experimental study was conducted to see the usefulness of pralidoxime in the treatment of OPC poisoning patients. This study also reveals the clinical profile of OPC poisoning patients.

Materials and methods

Selection of patients: This study was a randomised clinical trial. All patients with organophosphorus compound poisoning admitted in medicine ward of Khulna medical college hospital, Khulna, Bangladesh from 15 January 2013 to 14 January 2014, were enrolled for this study. During this one year period 109 OPC poisoning patients were admitted. Informed consent was taken from the guardian of each patient. The detail history was taken and clinical examination was performed. The medical data of each patient was recorded in writing.

Ethical approval: Ethical clearance from ethical review committee of Khulna medical college was taken for this randomised clinical trial.

Treatment plan: The total number of patients were 109 and they were divided into two groups according to the alternate day of admission. All the OPC poisoning patients of one admission day was put in group (A) and all the admitted OPC poisoning patients of next day was put in group (B). The patients of group (A) was treated with atropine only and all the patients of group (B) was treated with atropine plus pralidoxime. All patients received other supportive therapy with stomach wash, i.v. fluid, antibiotics, and O2 inhalation as required. Every patient was followed up by careful clinical examination. Patients developing respiratory failure was identified by clinical examination and by using pulse oximetry. Sa02 was <80%. in 8 patients, 4 from each group developed respiratory failure during treatment. These patients were treated in ICU of Khulna medical college hospital and assisted ventilation support was given. Both groups were further analysed from the start of poisoning to arrival at hospital and upto recovery.

Laboratory studies done were: Complete blood count, Blood sugar, serum amylase, urine analysis, serum creatinine, and ECG were done according to the need of patient.

Drug: Inj atropine and Inj pralidoxime was supplied from hospital store and purchased by the patient from market when required. Each ampoule of inj atropine contained 0.6 mg atropine sulphate and each vial of inj. pralidoxime contained pralidoxime 1gm. Both drugs were used in iv route. Inj. pralidoxime was given as intravenous infusion over 4 minutes to avoid hypotension. Both antidotes were administered as per recommended dosage schedule.

Study parameters: All data regarding particulars of patient, clinical features including serious manifestations such as fasciculation, respiratory failure, adverse effects of drugs, complications and outcome of treatment in each patient were collected in predesigned proforma.

Statistical analysis: All data collected in writing were entered, saved and analyzed in SPSS programme version 22. Frequency and percentage were calculated for age distribution, gender distribution, cause of poisoning, treatment outcome as recovery and mortality. p. value was calculated by chi square test and the $p < 0.05$ was considered as statisticaly significant.

Result

In this experimental study a total of 109 OPC poisoning patients were included. Age of these patients was from 13 to 90 years. The age distribution of the patients are shown in table 1. The incidence of poisoning was highest 33 (30.27%) in 13-18 years age group.

Table I

Age distribution of OPC poisoning patients

Age of the patient in years	No. of patients	% of patients
13-18	33	30.27
19-24	30	27.53
25-30	26	23.88
31-36	6	5.5
37-42	3	2.75
43-48	4	3.66
49-54	6	5.5
55-60	0	0
61-66	0	0
67-72	0	0
73-78	0	0
79-84	0	0
85-90	1	0.91
Total	109	100

Sex distribution revealed that 56 (51.38%) patients were male and 53 (48.62%) patients were female. In our study there is slightly higher mortality rate among female (18.87% Vs 12.50%) but this fails to attain statistical significance (p=0.360) (Table II).

Table II

Sex distribution and outcome of treatment

Sex	Total No. & % patients	Recovery No. & %	Death No. & %	p value
Male	56(51.38)	49(87.50)	7(12.50)	
Female	53(48.62)	43(81.13)	10(18.87)	0.360
Total	109	92	17(15.60)	

The causes of OPC poisoning were identified as far as possible. The highest incidence of 48 (44.03%) patients was due to various familial problems. In a significant number of cases (25-22.93%) the cause was non-specific, unknown and 16 (14.67%) were due to psychosocial problems. Baseline data of the patients was also shown in Table III

This study included 109 patients of OPC poisoning. The patients were divided into two groups according to the alternate day of admission. Group A of 49 patients was treated with the antidote Inj atropine iv and another group B of 60 patients was treated with inj atropine iv plus inj pralidoxime iv. All these patients received other supportive measures as needed. Total 8 patients, 4 from each group developed respiratory failure and was given ICU management with assisted ventilatory support in Khulna medical college hospital ICU. All these 8 patients recovered. Out of 109 patients 17 died and the mortality rate is 15.60%. Death rate is higher among female (18.87% vs 12.50%), but it fails to attain statistical significance (p=0.360).

Table III

The causes and baseline data of patients

Causes of poisoning	Male		Female		Total
	Married	Unmarried	Married	Unmarried	
Familial dis-harmony	15(13.76)	8(7.33)	18(16.5)	7(6.42)	48(44.03)
Non-specific	3(2.25)	6(5.50)	11(10.09)	5(4.58)	25(22.93)
Social problems	2(1.83)	8(7.33)	5(4.58)	1(0.91)	16(14.67)
Love rejection	-	8(7.33)	-	3(2.75)	11(10.09)
Failure in examination	-	2(1.83)	-	3(2.75)	5(4.58)
Psychiatric disease	2(1.83)	1(0.91)	-	-	3(2.75)
Accidential ingestion	-	1(0.91)	-	-	1(0.91)
Total	22(20.18)	34(31.19)	34(31.19)	19(17.44)	109(100)

It reveals that survival rate is higher (42-85.72%) and death rate is lower (7-14.28%) in group A patients treated with atropine alone. Survival rate is lower (50-83.34%) and death is higher (10-16.66%) in group B patients treated with atropine plus pralidoxime. Atropine with pralidoxime intervention group shows high mortality rate in comparison with atropine alone (16.66% Vs 14.28%) but this difference is not statistically significant (p=0.733) and we can conclude that pralidoxime intervention reveals no better outcome.

Although higher rate of ventilation is observed in atropine treated group (8.16% Vs 6.67%) this difference is not statisticaly significant (p=0.766). The outcome of the management is shown in the table IV below.

Table IV

Outcome of management of OPC poisoning patients

Treatment options	No. of patients	Reco-very (%)	Death No. (%)	p value	Respi- failure & ventil	p value
Atropine	49	42(85.72)	7(14.28)	0.733	4(8.16)	0.766
Atropine+ Pralidxime	60	50(83.34)	10(16.66)		4(6.67)	
Total	109	92	17(15.60)		8	

Discussion

OPC is a pesticide and used in agricultural country like Bangladesh for saving crops from the attack of insect. So this pesticide is kept in rural and also in urban houses. Some people ingest this highly poisonous compound to do self harm, even suicide. Death occasionally occurs due to respiratory failure. Intravenous atropine and intravenous pralidoxime is used as anti dote along with gastric lavage and other supportive measures. Assisted ventilation for respiratory paralysis is given in few centers where facility is available. But there is controversy regarding the effectiveness of pralidoxime. Experimental study reveals that pralidoxime is effective only in mild cases of OPC poisoning and pralidoxime is generally less potent.[11,12] Reactivation of acetylcholinesterase (AchE) is shown to be complete when oximes are given within one hour of poisoning.[13] One study in India described the development of myopathy after the use of pralidoxime.[14] In the Bangladeshi scenario the admission of OPC poisoning patient is late. So it is rarely possible for us to use pralidoxime within one hour of poisoning. In our study a total of 109 patient was included. Among them one group of 49 patient was treated with atropine alone. Out of these patients 42 (85.72%) recovered and 7 (14.28%) died. Another group of 60 patient was treated with atropine plus pralidoxime Out of these patients 50 (83.34%) recovered and 10 (16.66%) died. Atropine plus pralidoxime intervention group shows high mortality rate in comparison with atropine alone (16.66% Vs 14.28%) but we can not conclude clearly that combination therapy is inferior to atropine (p=0.733). However we can conclude that pralidoxime intervention gives no better outcome. Clinical trial in India with atropine alone and atropine plus pralidoxime reveals that difference in the rate of mortally is not significant (p value >0.05). So the study concluded that pralidoxime in treatment of moderate to severe OPC poisoning does not add any advantage over atropine.15 Our study also reveals similar result. During this study pralidoxime was administered in patients with mild, moderate and severe toxicity of OPC poisoning irrespective of their duration of poisoning, that means in case of early and also in late admitted patients.

In this study 4(8.16%) patients of atropine treated group and 4(6.67%) patients of pralidoxime intervention group developed respiratory failure and was treated in ICU with assisted ventilation. All 8 patients recovered completely. Although higher rate of respiratory failure is observed in atropine treated group (8.16% Vs 6.67%), this difference is not statistically significant (p=0.766)

So it is observed that 8(100%) patients survived when ventilatory support in ICU was provided. This experimental study suggests that better outcome regarding death of OPC poisoning can be achieved if ICU management with ventilatory support can be made available in the hospitals of Bangladesh.

We can also analyse the profile of OPC poisoning patients shown in this study. The causes of OPC poisoning are multifactorial. Most common cause is familial disharmony (44.03%), other causes are social problems, failure in examination, psychiatric disorder, love rejection and accidental ingestion of OPC. In a significant number 25 (22.93%) of cases the cause of poisoning could not be identified.

This study revealed that OPC poisoning is a bit higher in male 51.38% (56) than in female about 48.62% (53). Mortality rate is 15.60%. Death rate is higher among female (18.87% vs 12.50%), but it fails to attain statistical significance (p=0.360).

In this study we observed that addition of pralidoxime did not increase the survival rate in comparison to the patients group treated with atropine alone. So this experimental study suggests that this costly drug pralidoxime is not necessary in the treatment of OPC poisoning patients. Further large scale study can be done using pralidoxime in patients with mild toxicity of OPC and in patients admitted in hospital within one hour of ingestion of OPC.

There is limitation of this study as we did not observed the effectiveness of pralidoxime by administering it within few hours of ingestion of OPC.

Conclusion

The benefit of pralidoxime is insignificant in the treatment of OPC poisoning patients. This experimental study reveals that addition of pralidoxime did not decrease the death rate of OPC poisoning patient. Death rate can be markedly decreased if adequate ICU management with ventilatory support can be given in all the medical college hospitals.

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