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Original Research Article

Efficacy in treatment of moderate to severe degree organophosphorus poisoning with fresh frozen plasma, atropine and 2-pyridine aldoxime methyl chloride as compared to treatment with atropine and 2-pyridine aldoxime methyl chloride in Western Odisha

Purna C. Karua*, Surya K. Parida

Department of Medicine, Veer Surendra Sai Institute of Medical Science and Research, Burla, Odisha, India

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***Correspondence:**
Dr. Purna C Karua,
E-mail: karuapcvss@gmail.com

ABSTRACT

Background: Organophosphorus (OP) compounds are one of the most common agents used for suicidal poisoning. People in the middle socioeconomic status are mainly affected. The most important determinant of death in OP poisoning is the severity. The ideal treatment of OP poisoning, this study was undertaken to compare the efficacy of fresh frozen plasma (FFP) along with the standard regimen of atropine and oximes.
Methods: 80 patients were taken in this study (40 cases and 40 controls) with history and biochemical pictures suggestive of acute OP poisoning. Normality assumption and equality of variance were satisfied for most of quantitative variables. As a comparison of the baseline data of the study groups did not reveal any significant difference ($p>0.05$), the result at a given point of time between two groups were also compared with the same methods of assess the comparative changes.
Results: Total 80 patients >15 years of age were taken for the study. Out of the total 63.7% are female and 36.3% are males. OP compounds are commonly used as suicidal agent. Salivation is the most common presenting symptoms in both cases and controls. The mean value of serum cholinesterase on day -1 in cases and controls are nearly same but the subsequent mean values as the days progresses are higher in cases than that controls.
Conclusions: FFP showed its positive effect in reducing the development of intermediate syndrome/ fatality/ ventilatory support.

Keywords: Fresh frozen plasma, Organophosphorus poisoning, Reduction in fatality/ventilatory support

INTRODUCTION

According to World health organization (WHO) poisoning with organophosphorus (OP) compounds is a global health problem and more than 3 million cases of pesticide mainly OP poisoning occurs every year across the world.[1] Organophosphorus (OP) compounds constitutes a heterogeneous category of chemicals specifically designed for the control of pest's, weeds and plant disease. There implication is still the most effective for the protection of plants from pests and has contributed significantly to enhance agricultural productivity and crop yields. It is estimated that 90% of fatal pesticide poisoning occurs in developing countries. As agriculture is the main occupation in developing countries so pesticides are easily available in lethal and concentrated forms. As estimated by National Crime Bureau of India, suicides by consumption of pesticides account for 19.4

and 19.7% of all cases of suicidal poisoning in the year 2006 and 2007.[2] Psychological stress may force, a person to consume poisons such as OP compounds due to its low price, high toxicity and availability. Clinical manifestation of OP poisoning are caused by Excessive synaptic accumulation of acetylcholine (ACH)-OP compounds irreversibly inhibits the enzyme acetyl cholinesterase (ACE) resulting in excessive accumulation of acetylcholine which act in the central nervous system, autonomic ganglia, parasympathetic IV ending and Nn Junctions. The leading cause of death in op poisoning is respiratory failure which results from a combination of respiratory depression, increased bronchial secretion, bronchospasm and pulmonary odema. In treatment of OP poisoning atropine remains the mainstay of therapy worldwide. Atropine is a competitive antagonist of acetylcholine at the muscarinic post synaptic membrane and in the CNS. It will block the muscarinic manifestations of OP poisoning. Oximes which help to regenerate ACE at muscarinic, nicotinic and CNS sites are widely used. The beneficial effects of oximes have been much debated due to absence of adequate studies and results. A Cochrane review and two other meta-analysis of oxime have been published.[3] The Cochrane review reported no clear benefits of oxime therapy. Plasma cholinesterase (Butyryl cholinestrase-BuChE) in plasma can bind to OP and inactivate it, thereby protecting the AchE. A significant improvement in OP/enzyme stoichiometry may be achieved in vitro as well as vivo by enzyme replacement therapy. A well timed administration of BuChE can prevent initial physiological crisis, development of intermediate syndrome and delayed toxicity following exposure to OP compounds. Though atropine and oximes are classically used in treatment of OP poisoning, the outcome is far from success with a case fatality of 15-30%.

METHODS

80 patients (40 cases and 40 controls) of acute OP poisoning admitted to Department of Medicine, Veer Surendra Sai Institute of Medical Science And Research (VIMSAR), Burla, Sambalpur, Odisha were taken into study. Patients between age group of >15 years and having plasma CHE level <1000 and/or having clinical features suggestive of moderate to severe grade of OP poisoning were included in this study. Patients divided in two groups i.e. group A cases and group B controls. Group B received atropine infusion to maintain a state of atropinisation. Injection Oxime was given 3gm in NS twice daily as slow continuous infusion for 1 week. Group A received treatment like group B along with FFP 2 units, each containing 150 ml, consecutively for 3 days. Amount of cholinesterase levels were measured on day 1, day 3 and on day of discharge (DOD) in both the groups. At the end of study group A & group B were compared in relation to rise in serum cholinesterase levels, hospital stay, development of intermediate syndrome, use of ventilator in patients & mortality by using standard statistical methods. Descriptive statistical parameters (mean and standard deviation) were calculated for each quantitative variable. Between different groups, comparisons of qualitative data were done using tests (with Yates correction). As normality assumption and equality of variance were satisfied for most of quantitative variables. As a comparison of the baseline data of the study groups did not reveal any significant difference ($p>0.05$), the result at a given point of time between two groups were also compared with the same methods to assess the comparative changes. In the case of significant results, Turkey's multiple range tests were used to identify the pairs of observations with significant results. The results were considered significant at the 5% level ($p<0.05$).

RESULTS

A total 80 patients (40 cases and 40 controls) were taken for the study. Diazinon is the commonest OP compound 25% in case and 20% in controls used for poisoning followed by chloropyriphos 15% in case and 17.5% in control (Table 1). Majority of age group is between 15-30 yrs of age i.e. (75% in cases and 80% in controls) and a total of 77.5% out of all cases. There is no significant difference in age distribution between cases and controls. In study group distribution females are the major group i.e. 65% in cases and 62.5% in controls followed by males i.e. (35% in cases and 37.5% in controls). So there is no difference in gender distribution between cases and controls. OP compounds are commonly used as suicidal agent. In cases suicidal is 95% and control it is 90%. No homicidal use of OP compounds has been observed. In accidental exposure the no. is 2 in cases and 4 in controls while spraying without proper protection.

Table 1: Common OP compounds are used for poisoning.

Poison	Case	Control	Total
	N (%)	N (%)	N (%)
Diazinon	10 (25)	8(20)	18 (22.5)
Diclorovos	4 (10)	6 (15)	10 (12.5)
CP	6 (15)	7 (17.5)	13 (16.25)
CP+CM	6 (15)	2 (5)	8 (10)
Dimethoate	3 (7.5)	6 (15)	9 (11.25)
Malathione	6 (15)	3 (7.5)	9 (11.25)
Other	5 (12.5)	8(20)	13 (16.25)
Diazinon	10 (25)	8(20)	18 (22.5)

Salivation is the most common presenting symptoms in both cases and controls followed by altered sensorium, tachyponea, vomiting. The presenting symptoms are almost identical in both case and control groups (Table 2). Constricted pupil (80% vs 70%) followed by tachycardia (90% vs 90%) and crepitations (80% vs 80%). The presenting signs are almost identical in both cases and controls.

Table 2: Distribution of study subjects by symptoms during presentation.

Symptoms	Case		Control		Total	
	N	%	N	%	N	%
Salivation	20	50.0	16	40.0	36	45.0
Tachypnoea	16	40.0	24	60.0	40	50.0
Vomiting	18	45.0	16	40.0	34	42.5
Diarrhoea	03	07.5	03	07.5	06	07.5
Altered sensorium	18	45.0	20	50.0	38	47.5
Pain abdomen	02	05.0	04	10.0	06	07.5

The mean value of serum cholinesterase (CHE) on day 1 in both cases and controls are nearly same but the subsequent mean values as the days progresses are higher in cases than that of controls (Table 3). The difference in rise of mean CHE values as the days progresses are higher in cases than that of controls.

Table 3: Mean rise in serum cholinesterase from day 1 to DOD.

Subjects	Mean CHE Day 1	Mean CHE Day 3	Mean CHE Day 5	Mean CHE DOD
Case	539.4± 215.5	929± 760.5	1724± 1476.8	2898.3± 1987
Control	485± 185.4	590.2± 256.7	1027.15± 435.6	2023.2± 608.5

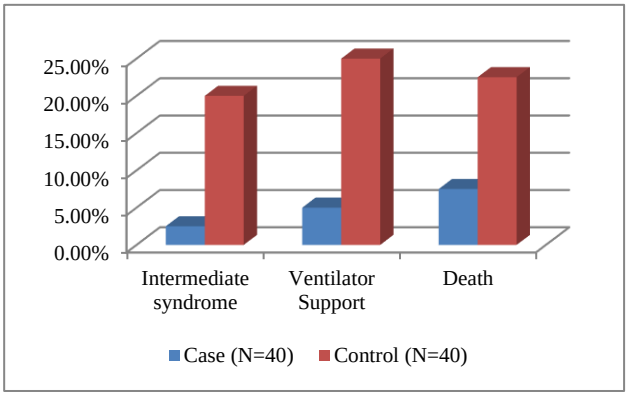

Figure 1: Complications of OP poisoning.

Out of the all subject's development of intermediate syndrome is higher in controls than cases. Need for ventilator support is also higher in controls than cases. Percentage of mortality is higher in control group (22.5%) than in case group (7.5%). Inter mediate syndrome development more common in controls than cases (Figure 1). The p value is significant i.e. $p<0.05$. Ventilator needed is more in controls than cases. p value is <0.05. Number of deaths is more in control group as compared to cases. p value is nearly equals to 0.01. Controls have got a higher period of hospital stay than cases.

DISCUSSION

During the study group A (cases) and group B (controls) each having 40 nos. of patients with features of moderate to severe grade of OP poisoning were taken. Group A was given FFP along with 2-pyridine aldoxime methyl chloride (PAM) & atropine while Group B was given only PAM & atropine. Diazinon was the commonest OP compound responsible for poisoning in both cases (25%) and control (20%). Following chloropyriphos the other OP compounds responsible are diclorvos, chloro pyriphos and cypermethrine (CP+CM), dimethoate (DM), malathione. Diazinon is known in local terms as basudin. It is widely used in agricultural field in odisha, it is cheap and easily available in the household. In various parts of the world the type of OP compound poisoning depends upon the availability of the compound in the locality. In a study from Sri Lanka Eddleston et al, reported no diazinon compound, whereas there were 439 cases of chloropyriphos, 264 cases of dimethoate and 94 cases of fenthione.[4] Jhonson S in 1995, has reported methyl parathion and monocrotophos as the commonest OP poisoning and not a single case of diazinon poisoning.[5]

Rao S in 2005 reported from warangal district of A.P. as methyl parathion and monocrotophos to be the commonest. They have reported 21 cases of diazinon with overall case fatality rate of 19%. Accordingly, methyl parathion, mono crotophos have a case fatality rate is 60% and 35% respectively. In the present study both cases (group A) and controls (group B) have got 40 no. of patients each. Out of 40 cases 75% were within age group 15-30 yrs followed by 15% in between 30-45 age groups and 10% are >45 yrs of age. Similarly, in control subjects 80% were in 15-30 age group followed by 12.5% in 30-45 yrs age group and 7.5% were >45yrs age. So younger age groups were more prone for OP poisoning. In this study mean age group presentation in cases was 27.8 yrs and controls it was 27.6 yrs which were almost similar. Females were more in number in both cases and controls having 65% and 62.5% respectively.[6]

Males were more in number in both cases and controls having 65% and 62.5% respectively. Female to male ratio in this study was 1:7:1. Similar study results was also been observed in odisha by Das et al study in 2004.[7] Students included a major portion in OP poisoning having 45% in cases and 50% in controls followed by housewives and farmer. Hence to reduce OP poisoning, depression in students and housewives in age group of 15-30 yrs. has to be addressed. So, there is no difference in distribution of age, sex, socioeconomic status and occupation in both case and control subjects. Based on symptoms both case and control subjects have got similar presentations. Salivation was the most prominent among symptoms in both case and control followed by

tachypnoea and vomiting. Such observations were more or less universal in most series of Sungur et al.[8]

Among the signs tachycardia is the major finding followed by crepitation, pupil constricted and dries mouth. All the signs are predominantly of cholinergic crisis. Though bradycardia was expected due to cholinergic effect, it was not found rather tachycardia was seen due to previous atropinisation at peripheral hospital. Wadia et al found in their study miosis in 95% of cases which is not similar to this study. Both symptoms and signs are almost identical in both cases and controls. Features of cholinergic crisis like salivation, altered sensorium, vomiting, crepitations, moist mouth, diarrhea are significantly higher in subjects who have died than who survived.[9]

As the days progresses the CHE values is also gradually increased but the rate of rise in CHE values was much more faster cases those receiving fresh frozen plasma than in controls. In comparison between day 1 and day 3 CHE values, in cases it was 539.4 on day 1 which increased up to 929 on day-3 but in controls it increased from 485.2 to 590.2 from day -1 to day 3. The p value for CHE rise from day 1 to day 3 was 0.0045 which signifies that subjects receiving fresh plasma (cases) have got faster rate of rise of CHE than those who did not receive FPP (controls). Similarly comparing between day 1 and day 5 CHE values it increased from 539.4 to 1724 in cases receiving FFP and 485.2 to 1027.15 in control not receiving FFP which has got a significant p value of 0.0034. On the date of discharge (DOD) the subjects receiving fresh frozen plasma (cases) have got a substantial rise in CHE value than those who did not (controls). CHE values increased from 539.4 to 2898.3 in cases receiving plasma and 485.2 to 2023.2 in controls not receiving fresh frozen plasma. It has got a significant p value of 0.0024.

In this study it denoted that a subject receiving FFP which is rich in BUCHE helps to increase in plasma CHE at a rate which is significantly higher than subjects not receiving FFP because BuChE administration by giving FFP neutralizes OP compounds before they inhibit ACHE at target sites and it also helps to dilute plasma volume. The mean period of hospital stay also increased in cases receiving FFP as they had to stay more time in hospital for receiving FFP than controls. It was 7.15 days in cases and 10.3 days in controls. Mortality rate was 7.5% in subjects receiving FFP (cases) in comparison to control not receiving FFP (control) that was 22.5% which was significantly higher and got a p value of 0.01. So subjects getting FFP (cases) have got a faster rise in plasma CHE (BuChE) values and death rate was significantly lower compared to subjects not receiving FFP (controls). Survival in cases was higher (982.5%) in comparison to controls (77.5%). Therefore, FFP is a source of BuChE and can be used in the management of patients of OP poisoning. [10,11,12,13]

CONCLUSION

This study is unique which has been designed to evaluate the effect of FFP in the treatment of OP poisoning along with PAM and atropine. It has been proved that use of FFP in OP poisoning not only raises the plasma CHE value rapidly but it also helps reducing the development of intermediate syndrome and the subsequent use of ventilator in these patients. Mortality rate was reduced in those cases who received FFP than control who didn't receive it. FFP is useful in OP poisoning because of its role in preventing the destruction of CHE enzyme at synapses and FFP helps in increasing the amount of plasma CHE which are destroyed by OP compounds. Hospital stay also decreased in case as they received FFP during that period. So the study revealed that use of FFP showed its positive effect in reducing the development of intermediate syndrome, the use of ventilator in these patients and mortality which is quite beneficial to the patients.

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