Research Article

USEFULNESS OF MEASURING PRETREATMENT BUTYRYLCHOLINESTERASE ACTIVITY IN THE MANAGEMENT OF ORGANOPHOSPHORUS COMPOUND POISONING IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To evaluate the benefits of measuring pre treatment Butyrylcholinesterase activity in the management of organophosphorus poisoning.

Methodology: The case records of OP poisoning were studied retrospectively from January 2007 to January 2011. Out of 90 patients, only 62 were included as the BuChE levels were not measured in the remaining patients. Butyrylcholinesterase levels were measured on admission. The information regarding the total dose of Atropine, Pralidoxime, length of hospital stay and need for ventilation was recorded.

Result: Out of 62 case records evaluated, 29% had BuChE activity inhibition of 30-70%. More than 70% inhibition was seen in 38% of patients and rest had normal levels. The correlation between BuChE inhibition levels and the duration of hospital stay was statistically significant (P<0.001). Around 60% of patients with >70% inhibition required higher dose of atropine and ventilator support, though it was not statistically significant.

Discussion: In the present study, measurement of pre treatment levels of BuChE was found to be useful as significant correlation was observed between the BuChE activity and morbidity of patients in terms of prolonged duration of hospital stay. But the total amount of atropine needed, use of pralidoxime and the need for mechanical ventilation did not correlate with the derangement of BuChE levels at the time of admission.

Conclusion: BuChE levels at the time of admission definitely influences the morbidity. More prospective studies are needed together with BuChE level measurement and clinical scores to accurately predict the outcome in OP poisoning patients.

Keywords: Butyrylcholinesterase, Organophosphorus poisoning, Atropine, Pralidoxime, Mechanical ventilation

INTRODUCTION

Organophosphorus (OP) insecticide self-poisoning is a global health problem[1], with deaths ranging from hundreds to thousands each year[2, 3]. According to World Health Organization the incidence of OP poisoning has doubled in developing countries during the past 10 years[4].

There are two types of cholinesterases, acetylcholinesterase and butyrylcholinesterase. OP insecticides inhibit both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) enzymes[5]. Cholinesterases are enzymes involved in the metabolism of organophosphates and also various drugs like acetylcholine, succinylcholine, mivacurium, cocaine.

BuChE is synthesized in the liver and found in high concentrations in blood plasma, liver, heart, vascular endothelium, brain white matter, pancreas, skin, smooth muscle cells and adipocytes.

BuChE activity is more easily measured than AChE activity and also assays for BuChE are widely available.

The mortality rate in OP poisoning is high, fatality is often related to two reasons, a delay in diagnosis or an improper management. Early diagnosis and appropriate treatment, are often life saving, although the clinical course of OP poisonings may sometimes be quite severe and may need intensive care management

There is strong association between exposure to organophosphorus compounds symptoms and BuChE activity is significantly reduced[6,7]. Monitoring of Plasma BuChE has been recommended in the OP poisoning, as this could be a useful biomarker to predict outcome of OP poisoning [8].

The usefulness of this approach has been much debated. Despite studies showing BuChE to be a poor predictor of outcome and response to therapy [9, 10], some clinicians continue to use it in the early assessment of OP pesticide severity [11-13].

The present study aims to correlate BuChE level at initial presentation and the severity of poisoning. The correlation may help in predicting the clinical outcome and in making timely decision regarding transferring the patients for intensive care management.

MATERIAL AND METHODS

This retrospective study examined the comprehensive medical, nursing, and intensive care records of 90 patients of OP poisoning between January 2007 to January 2011. Initial diagnosis was established in all cases based on cholinergic clinical features, the odour of OP in the gastric contents, history, and other circumstantial evidence, such as the poison or a label of an OP containing product found by relatives.

All patients were given the standard of care treatment for OP poisoning. Gastric lavage, whole body surface washing, activated charcoal administration, intravenous atropine and pralidoxime, and supportive measures such as mechanical ventilation (if necessary).

Upon the confirmation of the OP poisoning, patient's venous blood samples were taken for serum cholinesterase level assay. The patients were routinely managed in the units, with pralidoxime and intravenous atropine bolus and drip, maintaining the adequate level of atropinization.

For clinical outcome, the total duration of hospital stay or death were considered. Complete recovery or death was used as the end point. The total amount of atropine used in each patient was calculated. The BuChE level were divided to three groups of inhibition, <30% inhibited, 30-70% inhibited and >70% inhibited.

The degree of inhibition of BuChE was calculated by the following formula

$$\% \text{ inhibition} = \frac{\text{lower normal level of the laboratory - blood level of patient} \times 100}{\text{lower normal level of laboratory}}$$

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 17. Univariate correlation between severity of poisoning and the serum cholinesterase level were evaluated using Pearson correlation coefficient Chi Square test and Fisher's exact test.

Table 1: Characteristics of patients with acute organophosphate poisoning

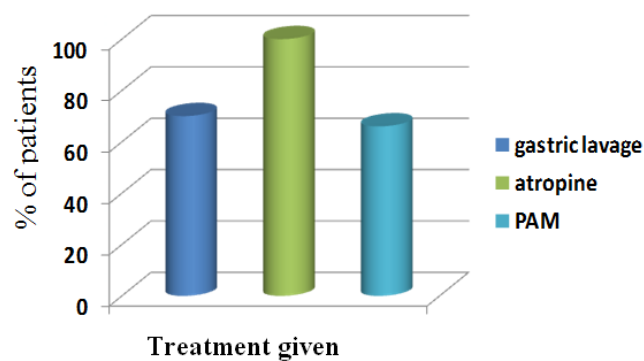| Variables	Value
Number of patients	62
Male : Female	38:24
Age in years	36.02±5.71†
Type of compound	
unknown	48
methyl parathion	4
cyphalothrin	1
baygon(carbamates)	2
cypermethrin	2
mortein	2
endosulfan	1
dyflos	1
diazinon	1
Estimated amount ingested, mL	70 (6-500)*
Serum cholinesterase, IU/L	239 (6-2507)*
Ventilation required	5
Death	2

†Mean±SD.

*Median (range).
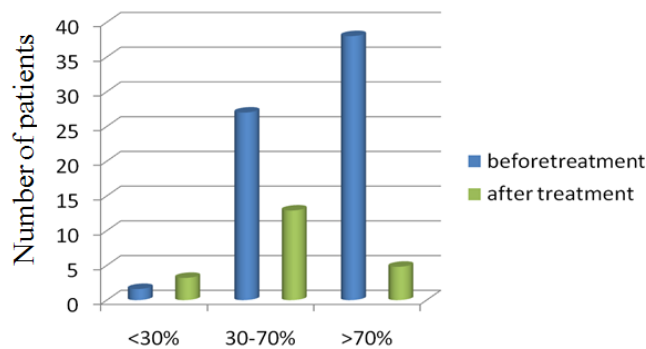

Fig. 1: Treatment given to patients

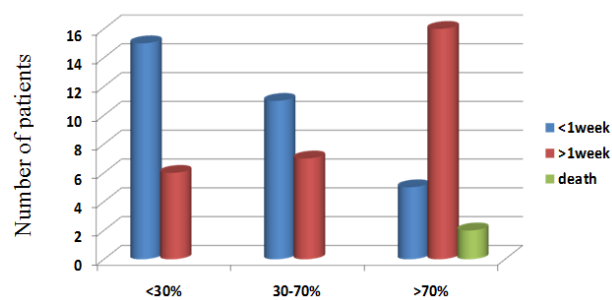**Fig. 2: Percentage of butyrylcholinesterase inhibition**

Fig. 3: Correlation between butyrylcholinesterase inhibition & length of hospital stay/mortality

Table 2: Correlation between different parameters of the patients

Parameters	Pearson Correlation (r)	P value
1) Serum cholinesterase and	0.486† (Moderate degree positive correlation)	<0.001
hospital stay		(<7days)
2) Serum cholinesterase	0.618† (High degree positive correlation)	<0.001
and hospital stay		(>7 days)
3) Serum cholinesterase	0.536† (Moderate degree positive correlation)	<0.001
and death		
4) Serum cholinesterase and	‑0.348* (Low degree negative correlation)	0.029
total atropine		
5) Hospital stay and	0.758† (High degree positive correlation)	<0.001
total atropine		

† Correlation is significant at the 0.01 level (2 tailed). *Correlation is significant at the 0.05 level (2 tailed)

RESULTS

The general characteristics of the 62 patients, who had OP poisoning at presentation, are summarized in Table 1. Out of 62 case records evaluated, 29% had BuChE activity inhibition of 30-70%. More than 70% inhibition was seen in 38% of patients and rest had normal levels. The correlation between BuChE inhibition levels and the duration of hospital stay was significant (P<0.005). Around 60% of patients with >70% inhibition required higher dose of atropine and ventilator support, though it was not statistically significant.

DISCUSSION

Organophosphates are widely used in the household and in agriculture. Poisoning with organophosphates is a worldwide problem and may cause severe morbidity and mortality The insecticide agent was unknown in majority of the patients in our study, and diagnosis was based on clinical findings and low BuChE levels. This may be due to the fact that most of the cases occurred at home, and the Patients or the relatives did not know the exact pesticide for the poisoning.

The present study was carried out to evaluate the benefits of measuring pre treatment BuChE activity in the management of organophosphorus poisoning. BuChE measurement on admission has been used by some clinicians to stratify severity. From a review published by Namba et.al of OP poisoning in 1971[14] and values <10% of normal indicating a severe poisoning.

BuChE levels as well as clinical findings were used as a means of diagnosis of the intoxication. As expected, the degree of inhibition increased as the clinical manifestations worsened. However, since the degree of its inhibition becomes maximal a few hours after the intoxication, it cannot serve as an indicator for the severity of the intoxication immediately after it occurs. Plasma BuChE is inhibited immediately after the intoxication, but there is no relation between its activity or inhibition and that of acetylcholinesterase activity or inhibition.

The reactivation of BuChE in the plasma lasts a few hours, while in the synapse it lasts a few days, and in the red blood cells a few weeks. Therefore, although BuChE may be used in the early diagnosis of OP intoxication, its inhibition should not be used to predict or serve as a measure of the severity of the intoxication, as mentioned in previous studies [15]. It is important to mention that BuChE levels are low in children, and in burns, malignancies, sepsis, and diseases of the liver or kidney [16].

There was significant correlation between the Serum cholinesterase and hospital stay (>7 days)

(P<0.001), and hospital stay and total atropine (P<0.001) as shown in table 2. The longest hospital stay was a male patient who had consumed parathion and was in hospital for 24 days. He developed respiratory arrest on the third day of poisoning and was put on the ventilator for 11 days, with complete recovery as the outcome.

There was no correlation between mortality of the patients and use of pralidoxime. However, it is difficult to comment as the dose was different and was not administered to all the patients BuChE activity must be interpreted carefully. Some patients with mild to moderate OP poisoning had severely inhibited BuChE on admission and BuChE was not severely inhibited in patients with hospital stay of <1week.

In summary, a BuChE level at admission is useful only when the OP pesticide has been identified and its sensitivity and specificity is known for that particular OP. For example, the dimethoate active metabolite (omethoate) inhibits cholinesterases more slowly, and BuChE activity can be near normal in symptomatic patients[17], and the active metabolite of chlorpyrifos (chlorpyrifos-oxon) is >500-times morepotent an inhibitor of BuChE than AChE[18]. Decline in Plasma butyrylcholinesterase in the present study supports earlier findings[19, 20].

Limitations of the study

The limitation of the study is it was a retrospective study, and the sample size was small. More prospective randomized trials with large sample size are needed to accurately determine usefulness of pre treatment butyrylcholinesterase activity measurement in the management of organophosphorus poisoning

CONCLUSION

BuChE levels at the time of admission definitely influences the morbidity. BuChE activity on admission can provide useful information but it must be interpreted critically along with clinical scores when the particular OP is known. BuChE levels at presentation appear useful in assessing the severity of poisoning, particularly in terms of prolonged duration of hospital stay required for the management. The patients with evidence of moderate and severe degree of poisoning need to be monitored closely.

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