Brief Communication

Pseudocholinesterase as a predictor of mortality and morbidity in organophosphorus poisoning

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Abstract

Background: Organophosphorus (OP) pesticide poisoning is a major clinical and public health problem in India. Mortality rate remains high at 15%–30%. **Aims:** This prospective, observational study examines the relationship between pseudocholinesterase (PChE) activity and morbidity and mortality in OP poisoning. **Setting and Design:** OP poisoning cases admitted to a tertiary care center Intensive Care Unit (ICU) over 5 years from 2010 to 2014 were studied. **Methods:** Patients <16 years of age, those on steroids and those with neuromuscular weakness, were excluded from the study. Serum PChE level at admission was estimated and the severity of poisoning assessed accordingly. Primary outcome measures were ICU length of stay and ventilator-free days. Secondary outcome measures included vasopressor-free days, amount of atropine given, hospital length of stay, and ICU mortality. **Results:** There were 37 patients included in the study, aged between 24 and 44 years, of which 65% were male. They were divided into two groups according to PChE levels. Group A with PChE levels more than 1000 IU/L had twenty patients and Group B with levels <1000 IU/L had 17 patients. Group B had longer ICU length of stay ($P < 0.001$) and fewer ventilator-free days ($P < 0.001$). They also had a fewer vasopressor-free days and a longer stay in hospital. **Conclusions:** PChE level at presentation is a reliable indicator of the severity of OP poisoning and a predictor of the need for mechanical ventilation and the duration of stay in the ICU.

Keywords: Atropine, Glasgow coma scale, morbidity, organophosphorus poisoning, pseudocholinesterase

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Introduction

Poisoning with organophosphorus (OP) compounds is a global problem. The World Health Organization estimates that one million serious unintentional poisonings occur every year in addition to two million cases of suicide attempts, with pesticides.[1] India is a predominantly agrarian country where pesticides are routinely used for farming. These are the third most common agents implicated in suicidal poisonings after household agents and drugs, according to the National Poison Information Centre, India.[2] Data from the National Crime Bureau of India show consumption of pesticides account for 19.4% and 19.7% of all cases of suicidal poisonings in the year 2006 and 2007, respectively.[3]

Factors to assess the severity of organophosphate poisoning and predict outcome have been studied extensively. These include pseudocholinesterase (PChE), Glasgow coma scale (GCS) score, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and creatine phosphokinase. Of these, PChE remains the

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main prognosticator. However, while most studies agree that a low PChE level does indicate OP poisoning, they differ in whether it also indicates severity.

This study intends to observe if morbidity, in terms of ventilator-free days and hospital length of stay, could indeed be assessed from PChE level. The impact of other parameters such as APACHE II score and GCS score was also assessed. This could be of help in identifying patients in need of intensive monitoring and treatment.

Methods

Design

This prospective observational study was conducted at a tertiary care, referral Intensive Care Unit (ICU). It included patients admitted following OP poisoning over a 4-year period from May 2010 to October 2014. It was cleared by the institutional ethics committee. All patients admitted with a history of intake of OP compounds, irrespective of the route, were considered for the study. Exclusion criteria were age below 16 years, patients on steroid medications and those with neuromuscular weakness. The normal range for PChE was taken as 2000–5000 IU/L, with levels below 1000 IU/L indicating more severe poisoning than those above 1000 IU/L.

Data collection

Data were retrieved from the electronic medical records and daily case sheets, including demographics, APACHE II score, GCS score, and serum PChE level at the time of admission. The time interval between intake of the poison and presentation was noted. Primary outcome measures were ICU length of stay and need for mechanical ventilation. Secondary outcome measures included vasopressor-free days, hospital length of stay, amount of atropine given, and ICU mortality.

Statistical analysis

A total of 37 patients were included in the study. Data were analyzed using the statistical software IBM SPSS version 20.0, IBM Corporation, USA 2010. Descriptive statistics of intubation, inotropes were summarized in percentage. ICU length of stay, ventilator-free days, hospital length of stays, and need for tracheostomy were summarized in terms of median and IQR. Mann–Whitney U-test was used to compare between the two groups. $P < 0.05$ was considered statistically significant.

Results

The demographics and clinical scores, at time of admission, of the 37 cases included in this study are summarized in Table 1. They were classified into Groups A and B with serum PChE levels >1000 IU/L and <1000 IU/L, respectively. The mean age in both groups was about 35 years, with male constituting 65% of the study population. All cases were of attempted suicide by ingestion of the OP compounds. The majority of patients were brought to hospital within 6 h of exposure. Commonly manifested signs included drowsiness, excess salivation, tremors, fasciculations, and muscle weakness. The GCS scores were significantly higher in Group A.

The salient features during stay in the ICU and hospital are presented in Table 2. The need for invasive ventilation and vasopressor support was significantly more in Group B compared to Group A. Group B also had greater failure rates in weaning off mechanical ventilation and subsequently, higher rates of tracheostomy. Mortality was higher in Group B, but this was not statistically significant. Hospital length of stay and APACHE II scores were significantly higher in Group B. The mean dose of atropine given on the 1st day after admission in both groups was about 24 mg.

Discussion

Organophosphate poisoning is a serious clinical entity that carries considerable morbidity and mortality. Symptoms result from the unopposed action of the

Table 1: Demographic data and clinical scores of organophosphorus poisoning patients in this study

	Group A (PChE >1000), *n*=20	Group B (PChE <1000), *n*=17	*P*
Age	35.9±10.3	34.65±9.0	0.710
Sex (male/female)	10/10	14/3	0.04
GCS at admission	13.0 (13.0, 14.0)	7.0 (6.0, 13.0)	0.001
APACHE II Score	10.0 (10.0, 10.0)	12.0 (10.0, 15.0)	0.048

APACHE: Acute Physiology and Chronic Health Evaluation; GCS: Glasgow coma scale; PChE: Pseudocholinesterase

Table 2: Salient features of the stay in Intensive Care Unit and hospital of patients in this study

	Group A (PChE >1000), *n*=20	Group B (PChE <1000), *n*=17	*P*
Number of endotracheal intubations (%)	4 (23.5)	14 (85)	0.001
Vasopressor free days	5.0 (5.0, 6.0)	1.0 (1.0, 2.0)	<0.001
Vent free days	6.0 (5.3, 6.0)	1.0 (1.0, 2.0)	<0.001
Mean dose of atropine	24.0 (23.4, 24.0)	24.0 (23.4, 24.0)	0.407
Tracheostomy (%)	7 (41.2)	14 (85)	0.005
ICU LOS	3.5 (2.0, 6.0)	15.0 (12.0, 18.0)	<0.001
Hospital LOS	5.5 (3.5, 11.5)	21.0 (14.0, 30.0)	<0.001
28 days mortality (%)	1 (4)	4 (23.5)	0.1
ICU mortality (%)	1 (4)	4 (23.5)	0.1

LOS: Length of stay; ICU: Intensive Care Unit; PChE: Pseudocholinesterase

neurotransmitter acetylcholine at muscarinic and nicotinic receptors, due to inhibition of acetylcholinesterase by the OP compound. Atropine has a muscarinic antagonist action and remains the main antidote in OP poisoning. Pralidoxime (PAM) is another antidote, which helps in recovery of neuromuscular transmission at nicotinic synapses.

The estimated mortality ranges from 10% to 20%.[4-7] Morbidity and mortality indicators have been identified by several studies. In one such study, an APACHE II score more than 26 was reported to be a poor prognostic indicator.[8] An Indian study reported that a low GCS and high APACHE II correlate with a high poisoning severity score, which in turn, indicate severe and life-threatening toxicity.[9] Others have reported that both high APACHE II score and GCS <13 predict poor outcome.[9,10]

Serum PChE is used as an indirect measure of acetylcholinesterase activity. A study by Goswamy *et al*. states that the measurement of PChE is useful in predicting the prognosis in OP poisoning.[10] This finding is supported by Chaudhary *et al*. who observed that PChE levels between 870 and 1200 on admission were associated with prolonged ventilation and high mortality.[11] However, studies by Aygun *et al*. and Rehiman et al report that while low levels of PChE support the diagnosis of acute OP poisoning, they do not indicate clinical severity.[12,13]

The amount of compound ingested is often inaccurate and misleading, with most of the information given in terms of number of sips or amount left in the container.

Eddleston *et al*. reported that different organophosphates have different chemical characteristics and poisoning outcomes. For instance, chlorpyrifos and dimethoate have different sensitivities for acetylcholinesterase. The relationship between enzyme inhibition and mortality in one is not applicable to the other.[14] In our study, a variety of organophosphate agents were involved. However, the specific OP compound ingested could not be obtained in most cases, and hence, analysis of the compound could not be done.

In the present study, GCS score at admission, APACHE II score, and initial serum PChE level were used to evaluate the severity of poisoning. It was clear that the group with a higher serum PChE had a better outcome. They had a lesser need for ventilator and vasopressor support, greater success rates with extubation, and a shorter length of stay in both ICU and hospital. PChE level was estimated only at the time of admission. Daily estimation of PChE levels would have been more informative in prognostication and to monitor the effectiveness of therapy.[15] Nevertheless, we can still conclude that the PChE should be routinely estimated in OP poisoning, at least at time of admission, because of its prognostic significance.

In our study, administration of PAM in addition to atropine was ineffective in reducing hospital LOS, use of mechanical ventilation, and mortality. This corroborates Eddleston *et al*'s findings that PAM does not improve survival or reduce need for mechanical ventilation.[16]

There was no significant difference in the total amount of atropine required in either group. Thus, it supports the findings of Chugh *et al*. that PAM does not alter the dose requirement of atropine.[17] There was no correlation between the dose of atropine with the serum PChE levels. On the contrary, Avasthi and Singh observed an inverse relation between atropine requirement and the serum PChE levels.[18]

Most cases in our study were young males (below 40 years of age) belonging to rural areas with easy access to OP compounds used in the agriculture industry. The major route of poisoning was ingestion, with suicidal intent.

Limitations of the study

This study is limited by the facts that sample size was small. Serum PChE level was estimated only at the time of admission. The study was not randomized, but rather prospective observational study.

Conclusions

PChE levels <1000 IU/l are associated with a more morbid course in organophosphate poisoning, with a need for prolonged mechanical ventilation and vasopressor support and a longer duration of stay in ICU and hospital. Further studies with a larger sample size are required to make definitive conclusions.

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Conflicts of interest

There are no conflicts of interest.

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