

Apache II Scoring as an Index of Severity in Organophosphorus Poisoning

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Abstract

Objectives: The purpose of the study was to determine the mortality rate in organophosphate poisoning patients and relationship between the clinical severity of OPP with APACHE II score and serum cholinesterase levels.

Methodology: This is a cross sectional study conducted in medical intensive care unit. Baseline variables and clinical characteristics were summarized with frequencies (percentages) for categorical variables and mean (standard deviation) for continuous variables. Receiver operating characteristic (ROC) curves were generated with a 95% CI to assess the relationship between individual APACHE II scores and mortality rates.

Results: The patient's average age was 25.16 ± 9.95 years. 56.6% were female and 78.8% patients were suicidal. Patient who had stayed in the hospital >15 days had 33.3% mortality ($p=0.13$). Total 12 (10.6%) patients required mechanical ventilation out of which only one (8.3%) patient expired ($p=0.86$). The average APACHE II score was 3.73 ± 3.95 . The APACHE II score for predicting death risk had fair discrimination as indicated by ROC curve of 0.67 (CI: 0.512-0.833). There was no significant association ($p=0.29$) between serum cholinesterase level and APACHE II score regarding the severity of poisoning. However, significant association ($p<0.001$) was found between outcome and serum cholinesterase levels.

Conclusion: The mortality rate reported was 9.7%. There was no significant association between serum cholinesterase level and APACHE II score regarding the severity of poisoning. However, significant association was found between outcome and serum cholinesterase levels.

Keywords: Organophosphorus; Poisoning; APACHE II; Serum cholinesterase; Mortality; Complications

Introduction

Acute poisoning is a major public health issue in many countries around the world [1]. Pesticide self-poisoning is killing an estimated 350,000 people every year [2]. The World Health Organization (WHO) has identified pesticide poisoning as the single most common method of suicide worldwide [3]. Worldwide, an estimated 3,000,000 people are exposed to organophosphate (OP) or carbamate agents each year, with up to 300,000 fatalities [4,5]. In the United States, there were more than 8000 reported exposures to these agents in 2008, resulting in fewer than 15 deaths [5,6]. According to WHO two million people attempt suicide and one million accidental poisoning cases occur each year worldwide. However it is the deliberate self-poisoning that causes the great majority of the deaths and the immense strain the pesticides put on hospital services particularly Asia [7]. In India, rate of suicidal poisoning with OP compounds ranges from 10.3 to 43.8% [8]. OP poisoning is the most common cause (27.64%) and has the highest death rate (13.88%) of poisoning in Bangladesh [9]. The incidence in Sri Lanka is 10,000–20,000 hospital admissions annually [10]. It is estimated that there are 34,000 suicides annually in the Middle East region and 20% of suicides in the Middle East region are the result of pesticide ingestion [11,12]. OP is the commonest suicidal agent in Pakistan. The exact prevalence of OP poisoning is unknown in

Pakistan as many cases are un-notified due to religious, social or cultural reasons. However reported incidence of deliberate self-poisoning (DSP) in Pakistan is about 8 per 100,000 in men and women [7,12,13].

OP insecticides are the most important pesticides and act through phosphorylating the active site of cholinesterase's, resulting in acetylcholine build-up. This produces excessive cholinergic stimulation, causing clinical features in both the peripheral and central nervous systems [2]. Toxicity generally results from accidental or intentional ingestion of, or exposure to, agricultural pesticides [4,7].

The Acute Physiology and Chronic Health Evaluation (APACHE II) is a severity score and mortality estimation tool developed from a large sample of ICU patients in the United States by Knaus et al. in 1985 [14]. Twelve physiological variables have been included in the APACHE II model in which the effects of chronic health status and age included in the model, weighted on the basis of their relative effect, to provide a single score along with a maximum of 71 are incorporated. Later admission in the ICU, in the first 24 h worst value was recorded used for each physiological variable [15]. The APACHE-II scoring system was found useful for classifying patients according to their disease severity. There was an inverse relationship between the high score and the length of stay as well higher chances of mortality [14]. The purpose of this study was to assess correlation of APACHE II score with the mortality of patients of organophosphorus poisoning and to

determine the association of cholinesterase level and APACHE II score regarding the severity of poisoning.

Materials and Methods

This is a cross sectional study conducted in medical intensive care unit in Abassi Shaheed Hospital from December 2013 to March 2014. All patients were admitted through the emergency room and diagnosed on the basis of history/exposure to the OP compound. History/exposure to OP compound in any form that is liquid, tablet, powder, and gaseous or direct contact with skin were included. Patients or attendants of patients giving history of ingestion were asked to bring bottle/container of the compound. Some of them were already carrying container with them. While diagnosing these cases clinical signs suggestive of muscarinic involvement like excessive salivation, sweating, miosis, lacrimation, diarrhea was taken in account. The diagnosis of acute OPP in patients was based on the following criteria: (A) ingestion of insecticide, pesticide oral or injectable (B) characteristic clinical sign and symptoms of OPP (C) decreased serum cholinesterase activity.

All patients admitted in intensive care unit aged >15 years (as this study was done in a adult medical intensive care unit) with organophosphorus poisoning within 48 h of taken OP were included in the study. Other argochemical, carbamate, paraquet or drug poisoning were excluded from the study.

Outcome Measures

Mortality rate of OPP.

Clinical grading of severity by bardin classification.

APACHE 2 scoring.

Serum cholinesterase levels

Patients were evaluated with regard to demographic information, mode of exposure, frequency of clinical signs and symptoms, duration of hospitalization, complications and outcome of each patient was recorded. All the patients were graded regarding clinical findings in relation to Bardin classification [16,17]. As indicated in the Table 1, patients were graded (grade 0,1,2,3) according to the clinical findings on admission in acute organophosphate intoxication.

Grade 0:	No Clinical Manifestations
Grade 1:	Hypersecretion, Fasciculation, Consciousness
Grade 2:	Grade 1+Hypotension, Unconsciousness
Grade 3:	Grade 2+Stupor, Abnormal Chest X-Ray, PO ₂ <10 mmHg

Table 1: The degree of organophosphate poisoning.

Laboratory parameters

The following labs were done in all patients as per requirement of patient and for APACHE II scoring: complete blood count, urea, creatinine, electrolytes, arterial blood gases, and serum cholinesterase level. APACHE II score was calculated for every patient. Normal cholinesterase levels in our laboratory were 5400-13200 U/l. Severity of OPP was classified into 3 groups [18,19]. According to serum cholinesterase activity severe was <500, moderately severe was

500-1000 and mild was >1000 U/l. All patients were treated under a single treatment protocol.

Treatment protocol for all patients

Gastric lavage in emergency room: Atropine infusion in pediatric chamber @8 micro drops per minute till patient is fully atropinized (that is resolution of bronchorrhea, heart rate of >80 bpm). If these targets were achieved than 150 mg of atropine is diluted in normal saline and given at 8 micro drops per minute. It takes 24-48 h to completely atropinized and thereafter it is slowly tapered off.

Oximes: Inj pralidoxime methylsulphate was given to patients with a loading dose of 2 gm. I/V infusion in 0.9% saline and then 1 gm 8 hourly.

Benzodiazepines: are used for patients in agitation and/or psychosis (diazepam 0.05-0.3 mg/kg/dose, lorazepam 0.05-0.1 mg/kg/dose or midazolam 0.15-0.2 mg/kg/dose). Decontamination dermal spills- wash the head and body with soap and water and removal of contaminated clothes, shoes and any other material with spills. Complications like aspiration pneumonia, sepsis, and hospital acquired infections were dealt accordingly.

Statistical analysis

Baseline variables and clinical characteristics were summarized with frequencies (percentages) for categorical variables and mean (standard deviation [SD]) for continuous variables. The chi-squared test was used for comparing the proportions of categorized measurements. Receiver operating characteristic (ROC) curves were generated and the area under the curve (AUC) calculated together with a 95% CI to assess the relationship between individual APACHE II scores and mortality rates [20].

Results

The patients ranged from 14 to 65 years of age, with an average age of 25.16 ± 9.95 years. More than half of patients were female. About 40% were married and less than one third of the study participants were from poor families and non-educated (Table 2). One hundred and three patients (91.2%) were attempted first time and 10 (8.8%) had history of previous poisoning. With regard to the nature of incidence, 89 patients (78.8%) were suicidal and 24 (21.2%) were accidental. Almost all patients (99%) have taken liquid form of OP. Among the all patients 96 (85%) had no history of psychiatric illness and 17 (15%) were with psychiatric illness in which 3 (2.7%) had family history.

According to Bardin grading of clinical severity 63 (55.8%) were in Grade 0, 33 (29.2%) were in Grade 1, 15 (13.3%) were in Grade 2 and only 2 (1.8%) patients were in Grade 3. Percentage of patients presented with a GCS of 10-15 was 89.4% and 10.6% patients had a GCS ranged 3 to 9. Patients with a low GCS had a mortality of 25% while those with a better GCS had a mortality of 7.9% (P=.06). Only one patient suffered from seizures. The mean duration of stay in the hospital was 7.33±8.6 days. Patient who had stayed in the hospital for <15 days had 8% mortality rate and those stayed >15 days had 33.3% mortality (P=.13). Total 12 (10.6%) patients required mechanical ventilation out of which only one (8.3%) patient died (P=.86). A total 16 (14.1%) patients suffered from complications. Two patients (1.7%) suffered from acute respiratory distress syndrome (ARDS) and both expired, aspiration pneumonia was reported in four (3.5%) patients out of which two passed away, sepsis was seen in five (4.4%) patients in

which four deceased, urosepsis was found in two (1.7%) patients both treated successfully, Ventilator acquired pneumonia (VAP) was seen in four (3.5%) patients wherein three failed to survive.

Variables	Subcategory	n (%)
Gender	Male	49 (43.4)
	Female	64 (56.6)
Marital Status	Unmarried	46 (40.7)
	Engaged	15 (13.3)
	Married	47 (41.3)
	Divorced	3 (2.7)
	Widow	1 (0.9)
	Multiple Marriages	1 (0.9)
Education	Uneducated	31 (27.4)
	Under Matric	45 (39.8)
	Matric	24 (21.2)
	Inter	10 (8.8)
	Graduate	3 (2.7)
Socioeconomic Status	Poor	34 (30.1)
	Average	66 (58.4)
	Satisfactory	13 (11.5)

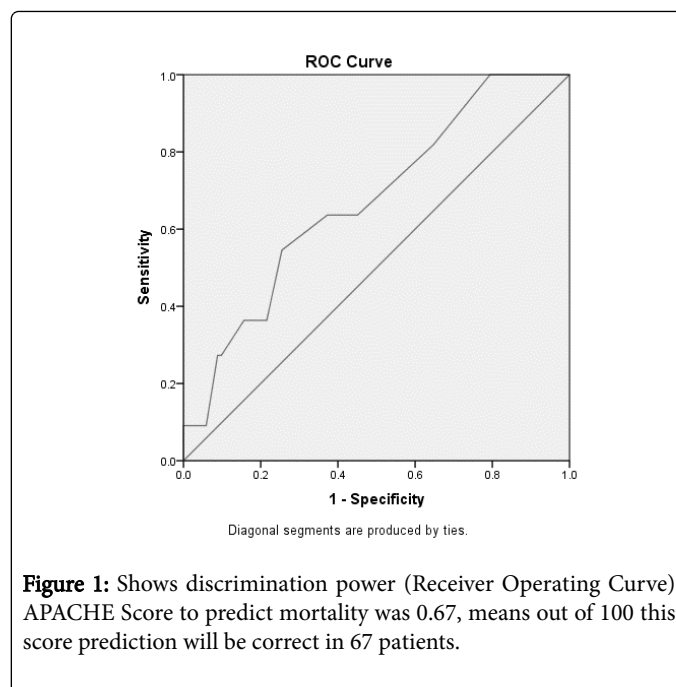
Table 2: Patients demographics.

The patients' average APACHE II score was 3.73 ± 3.95 . Table 3 shows the distribution according to APACHE II score intervals and that 94% of the patients were in the interval between 0 and 10. The receiver operating characteristic curve, based on the sensitivity and complemented specificity of predicted death risk, shows an area under the curve of 0.67 CI: 0.512-0.833 (Figure 1).

APACHE II Score	Survived	Deceased	Total
0-5	80 (70.8)	7 (6.2)	87 (77)
43014	16 (14.2)	3 (2.7)	19 (16.8)
42309	4 (3.5)	0	4 (3.5)
>15	2 (1.8)	1 (0.9)	3 (2.7)
Total	102 (90.3)	11 (9.7)	113 (100)

Table 3: Apache II score ranges and outcomes of treatment.

The mean serum cholinesterase levels were 4390.57 ± 4259 . There was no significant association ($P=0.11$) observed between serum cholinesterase level and APACHE II score regarding the severity of poisoning (Table 4). However, significant association ($P<0.001$) was found between patient's outcomes and serum cholinesterase levels. Patients with cholinesterase level >1000 were 77 (68.2%), 500-1000 were 32 (28.3%) and <1000 were 4 (3.5%).



	APACHE				Total	P Value
	0-5	6-10	11-15	>15		
Cholinesterase Level						0.011
<500	2 (1.8)	1 (0.9)	0	1 (0.9)	4 (3.5)	
500-1000	22 (19.5)	5 (4.4)	3 (2.7)	2 (1.8)	32 (28.3)	
>1000	63 (55.8)	13 (11.5)	1 (0.9)	0	77 (68.1)	
Total	87 (77)	19 (16.8)	4 (3.5)	3 (2.7)	113 (100)	

Table 4: Apache score and cholinesterase level: Mild to severe poisoning

There was no significant relationship between Apache 2 score and the clinical grading of severity by Bardin criteria ($P=0.9$). There was also no significant association ($P=0.64$) of clinical grading of severity and serum cholinesterase levels (Table 5).

	Bardin Criteria				Total	P Value
	Grade 1	Grade 2	Grade 3	Grade 4		
APACHE Score						0.9
0-5	48 (42.5)	24 (21.2)	13 (11.5)	2 (1.8)	87 (77)	
43014	11 (9.7)	6 (5.3)	2 (1.8)	0	19 (16.8)	
42309	3 (2.7)	1 (0.9)	0	0	4 (3.5)	
>15	1 (0.9)	2 (1.8)	0	0	3 (2.7)	

Total	63 (55.8)	33 (29.2)	15 (13.3)	2 (1.8)	113 (100)	
Cholinesterase						0.64
<500	3 (2.7)	1 (0.9)	0	0	4 (3.5)	
500-1000	19 (16.8)	11 (9.7)	2 (1.8)	0	32 (28.3)	
>1000	41 (36.3)	21 (18.6)	13 (11.5)	2 (1.8)	77 (68.1)	
Total	63 (55.8)	33 (29.2)	15 (13.3)	2 (1.8)	113 (100)	

Table 5: Apache Score and Cholinesterase level with clinical grading of severity.

Discussion

Our study found that the mean age of patients was 25.16 ± 9.95 years, with more than half females. Our mortality rate in OPP patients was 9.7%. 89.4% had a GCS of 10-15. Patients with a low (3-9) GCS had 25% mortality while those with a better GCS (10-15) had 7.9% mortality. Only one patient had suffered from seizures. 12 (10.6%) patients required mechanical ventilation and only one died. A total 16 (14.1%) patients suffered from complications. Two patients (1.7%) suffered from acute respiratory distress syndrome (ARDS) and deceased, aspiration pneumonia was reported in four (3.5%) patients out of which two expired, sepsis was seen in five (4.4%) patients in which four passed away, urosepsis was found in two (1.7%) patients both treated successfully, Ventilator acquired pneumonia was seen in four (3.5%) patients three died. There was no significant association observed between severe cholinesterase level and APACHE-II score in context to the severity of poisoning. Significant association was found between patient's outcome and severe cholinesterase level.

A study conducted in Singapore on 23 OPP cases observed an ICU mortality of 13% [18], while we had a mortality rate of 9.7% they also found that an APACHE-II score of 26 or higher accurately predicted death with 95% sensitivity and 100% specificity. In contrast to our study, they have concluded that APACHE-II score differentiated patients in to 3 severity groups ($P=0.004$) and co-related well with severity of OPP and cholinesterase levels [18]. Mechanical ventilation was required in 74% while in our study only 10.6% required mechanical ventilation another study found that APACHE-II score to be correlated with the severity of OPP, cholinesterase level and mortality ($P<0.05$) [21]. Previous studies have reported mortality in OPP cases between 10% and 89%, [22]. However, with intensive care management, mechanical ventilation for respiratory failure and use of atropine remains at 10-20%, [23,24] whereas our patients mortality rate was 9.7%.

A study conducted retrospectively in 48 patients showed a mean age of 32.5 ± 16.4 years with 34 females [25]. Study results found that 87.5% had attempted suicide while in our study 78.8% were attempted suicide and 21.1% were accidental. Their mean cholinesterase level on admission was 1281.4 ± 4259 (our mean serum cholinesterase levels were 4390.57 ± 4259). Mechanical ventilation was required by 58% of patients, while in this study 10.6% of patient's required mechanical ventilation. The average duration of length of ICU stay was 10.3 ± 9.22 days, [23] whereas the mean duration of stay of our patients was 7.33 ± 8.7 days. The most common complication reported by them in 48 patients was aspiration pneumonia in 12 patients, ARDS in seven patient's sepsis in nine patient's septic shock in five patients and

renal failure in five patients. While our complication rate was much lower which was two patients had ARDS, aspiration pneumonia in four patients, sepsis in five patients, urosepsis in two patients and four suffered from VAP. They showed that APACHE-II score was inversely correlated with serum cholinesterase level at admission. They significantly correlated mortality with GCS and APACHE-II score. They reported a mortality rate of 22% which was much higher than this study [25].

There are no validated scoring systems for categorizing severity of predicating outcome, although many have been proposed. The highly variable history and the fact to determine the ingested dose make it difficult to predict the outcome for an individual. Thus, early discovery, quick access to medical care careful maintenance of patency of airway, meticulous attention towards presenting aspiration pneumonia and aggressive oxime and atropine therapy may reduce morbidity and mortality.

Conclusion

The mortality rate reported was 9.7%. There was no significant relationship between the clinical grading of organophosphate poisoning, Apache II score and serum cholinesterase levels. However, significant association was found between patient's outcomes and serum cholinesterase levels.

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