Clinical Research

KEYWORDS: Acute organophosphate poisoning, PeradeniyaOrganophosphorus Poisoning score, Serum acetylcholinesterase level.

CORRELATION OF CLINICAL SCORE AND SERUM ACETYLCHOLINESTERASE LEVEL, AS A PREDICTOR OF OUTCOME AMONG PATIENTS WITH ACUTE ORGANOPHOSPHATE POISONING ADMITTED IN EMERGENCY WARD OF TERTIARY HOSPITAL IN EASTERN NEPAL

Volume-2, Issue-9, September - 2017

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Article History
Received: 12.07.2017
Accepted: 20.08.2017
Published: 10.09.2017

ABSTRAC

Introduction:
Organophosphorus (OP) insecticide self-poisoningis a major clinical and public health problem across much of rural Asia with hundreds of thousands of deaths each year.Owing to the limited availability of facilities and resource constrained settings, it is necessary to rely on clinical scores to assess the poisoning severity. Monitoring a patient's serum acetyl cholinesterase status after organophosphate poisoning enables the verification of substantial exposure to anticholinesterase agents. The present study was done to correlate serum acetylcholinesterase level with POP (Peradeniya Organophosphorus Poisoning) score with outcome among patients with acute organophosphate poisoning.

Methods: A cross-sectional study was conducted amongst the patients fulfilling the inclusion criteria were included and patients were categorized according to POP scale. The study was conducted at B.P Koirala Institute of Health Sciences in the period of Jan 2016 to Dec 2016. POP score was applied and serum acetylcholinesterase level was estimated. Spearman's Rho Coefficient and Kruskal- Wallis statistical methods were applied for correlation and variables and P value of <0.05 was considered as significant.

Results:
The correlation between severity of poisoning as assessed by POP scale and serum acetylcholinesterase was significant (P= 0.01). Spearman's Rho Coefficient showed 0.471 is a better negative correlation between POP score and serum acetylcholinesterase level.

Serum acetylcholinesterase level also correlated better with POP score for the need of Atropine vs. Pralidoxime (PAM) (Coefficient=0.449 vs. 0.427; P= 0.01) and (Coefficient= 0.589 vs. 0.33; P= 0.01). Serum acetylcholinesterase correlated well with the length of hospital stay (Coefficient= 0.374;P= 0.01) as compared to POP score (Coefficient= 0.244; P= 0.05).

Kruskal-Wallis test correlated well with POP score, Serum acetylcholinesterase level and duration of hospital stay (P= 0.004, P= 0.021 and P= 0.010 respectively).

Conclusions:
POP scale and Serum acetylcholinesterase level had shown well negative correlation and enhances these tools to be used in predicting outcome among patients with acute organophosphate poisoning.

BACKGROUND

Organophosphorus (OP) insecticide self-poisoning is a major clinical and public-health problem across much of rural Asia with hundreds of thousands of deaths each year. [1-2]

Due to its wide use and easy availability Organophosphate (OP) compounds are important insecticides used in agriculture and are possibly the most common acute poisonings in developing nations like Nepal and India are likely resulting to high morbidity and mortality.[3-4]

Owing to the limited availability of facilities and resource constrained settings, it is necessary to rely on clinical scores to access the poisoning severity.

RBC cholinesterase level is sensitive indicator but its estimation is difficult and is usually not available in all laboratories, so serum acetylcholinesterase level can be good option which can be estimated with simple kit in most of the laboratories.[7]

Organophosphorus compound inhibits Acetylcholinesterase (AChE) enzymes resulting in overstimulation of muscarinic and nicotinic receptors [5, 12, 13]

The Acetylcholinesterase test is a blood test used to measure the effect of exposure to cholinesterase-affected insecticides needed by the physician for a complete understanding of the individual's cholinesterase situation.[14-17]

Monitoring a patient's AChE status after organophosphate poisoning enable the verification of substantial exposure to anticholinesterase agents.It can facilitate the decision about when to stop oximes treatment and allow cautious weaning of a patient from a ventilator.

POP scoring system done by Senanayake N et al, 1993 in OP poison which included respiratory rate, pulse rate, pupil size, level of consciousness, seizure activity and fasciculation had shown significant correlation between the deranged serum acetylcholinesterase level and the morbidity of the patients in terms

of prolonged duration of hospital stay.[6, 18]

Many studies have shown significant correlation between severity of OP poisoning categorized by POP scale and serum acetylcholinesterase level following the acute prognosis of OP poisoning with incidence of mortality was significantly associated with lower cholinesterase level.[8-11]

The study was aimed to find correlation of POP score with serum acetylcholinesterase level as a predictor of outcome among all patients with acute organophosphate poisoning in emergency ward of BPKIHS.

METHODS

This was aprospective observational study of patients attended with history of acute organophosphate poisoning from Jan 2016 to Dec 2016in the Emergency Ward of B.P Koirala Institute of Health Sciences (BPKIHS), Dharan Nepal.

All the acute organophosphate poisoning cases presented within 24 hours confirmed by history, physical evidence and characteristic clinical manifestations were included. Upon the confirmation a 2ml of venous sample was withdrawn and sent for the analysis of plasma acetylcholinesterase activity by kinetic method based on hydrolysis of butyrylthiocholine by cholinesterase.19Clinical scores were assessed on the basis of POP score systemassessed on a three - points scale varying from 0 to 2 as shown in Table 1.The score is obtained at index presentation and before any medical intervention. A score of 0 to 3 was considered as mild poisoning, 4 to 7 wasmoderate poisoning and 8 to 11 was considered as severe poisoning.

Table-1.Peradeniya Organophosphorus Poisoning (POP) Scale

Parameter	Clinical criteria	Score
Pupil Size	>2 mm	0
	<2 mm	1
	Pin-point	2
Respiratory rate	<20/min	0
	>20/min	1
	>20/min with central cyanosis	2
Heart rate	>60/min	0
	41–60/min	1
	<40/min	2
Fasciculation	None	0
	Present, generalized or continuous	1
	Both, generalized and continuous	2
Level of consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No response to verbal commands	2
Seizures	Absent	0
	Present	1
	Total Observed Score	

The clinical score wasthen correlated with serum acetylcholinesterase level. The patients were routinely managed with intravenous fluids, pralidoxime and with adequate level of atropinization. The patients werecontinuously followed in medical wards or Intensive Care Unit (ICU) and till discharge from the hospital.The outcome of the study was measured as number of death, transferred in ICU ward, inpatient medical wards and duration of stay in hospital. The study was approved by Institutional Review Committee.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSSS) version 11.5. Univariate correlation between these with POP scale severity of poisoning and serum acetylcholinesterase level were evaluated using Spearman's rho correlation coefficient, Chi Square test and Kruskal Wallis test were applied to find out the significant difference between dependent and independent variables at 95% CI where P value of less than 0.05 was considered to be significant.

RESULTS

One Hundred (n=100) patients were enrolled in the study where 55% were females and 45%were males. The age of the patients ranged from 14 to 80 years with mean age of 30.28 years.About 42% of patients range from 21 to 30 years. Patient presented in Emergency ward within mean interval of 4.15 hours after intake of OP poison.

Thirty nine percent 39% subjects were homemaker, 33% farmers, 19% students and the remainder 14% had diverse industrial occupations including drivers, laborers, shopkeepers and Industrial worker or businessmen. 73% of the cases of OP poisoning were found in people attaining primary and secondary level of education. The incidence of OP poison was found higher in married population 70% than in unmarried groups 30%. 38%patients were from Sunsari district, 19% were resident of Saptari, 9% from Morang and 9% from Siraha and remainder 25% were from various regions of Eastern Nepal.

The most common organophosphates consumed were Chlorpyriphos 53%, Phorate 14%, Dimethoate8%, Methyl parathion 8% and Dichlorovos 6% respectively.

The most common cause of OP poisoning was family dispute 82%, 9% was of unknown cause while 5% was found to be with psychiatric illness and 4% of OP poison was accidental. The majority of OP poison consumed were during January17%, February 15%, in March 16% and April 12% and increased till the month of August 16% and Dec 8%.

Majority of patients (74%) were recovered completely, (12%) Left Against Medical Advice (LAMA), (7%) were referred to other hospital due unavailability of Intensive Care Unit beds. 4% of cases died in Emergency during treatment course. 3% reported Discharged on Personal request (DOPR).

Around 84% of patients presented with miosis, 88% of patients with tachypnea, 38% presented bradycardia, 25% presented with fasciculation, 43% of patients with altered sensorium and 3% of cases developed seizures shown in Table 2.

Table- 2. Clinical features of OP poisoning at presentation

Clinical features	Percentage %
Miosis	84
Tachypnoea	88
Bradycardia	38
Fasciculation	25
Altered Sensorium	43
Seizures	3

When compared with POP Score 47% had been recovered in inpatient ward that developed mild score. 25% showed improvement in moderate group of poisoning. A total of 3% of death was observed in moderate and 1% in severe POP score group during the study period.

Most of the patients (74%) survived after medical management while 4% mortality was observed during the course of treatment i.e. 2 cases reported death in Quinalphos, 1 in methyl parathion and 1 in Dimethoate.

A total of 57% of patients of mild poisoning presented with mean serum acetylcholinesterase level of 3744.56 U/L, 38% of moderate

poisoning cases were 1729.57U/L and 5% of severe poisoning was 376.80U/L as shown in Table 3.

Table-3Distribution of mean acetylcholinesterase level in relation to POP score

POP Scale Score	Grades of poisoning	Serum Acetylcholinesterase Mean (SD)	Percentage %
0-3	Mild	3744.56(2604.809)	57
4-7	Moderate	1729.57(1796.530)	38
8-11	Severe	376.80(324.456)	5

There was significant correlation between the severity of organophosphate poisoning and the serum acetylcholinesterase level at the index visit of the patients.

Table-3.Correlation between different parameters of the patient

Parameters	Spearman's rho correlation coefficient	P-Value
POP score and Serum Acetylcholinesterase	-0.471Ŧ	0.001
Acetylcholinesterase and Hospital stay	-0.374Ŧ	0.001
Acetylcholinesterase and Atropine	-0.449Ŧ	0.001
Acetylcholinesterase and PAM	-0.427Ŧ	0.001
POP score and Hospital stay	0.244 *	0.005
POP score and Atropine	0.589Ŧ	0.001
POP score and PAM	0.333Ŧ	0.001

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

DISCUSSION

In this present study, more than two thirds of the cases were 10-30 years of age the majority of the populations were female with female male ratio of 1:1.2which are quite consistent with various studies except in the study done by (CH. SrinivasRao et al. 2005) where male outnumbered female (57% vs. 43%) with all kind of pesticides.The study also showed that female population consumed more organophosphate poisoning till 40 yearsand then vice-versa till 60 years of age which is comparable to other study. 20 Homemakers and famers are most common 39% and 33% respectively followed by students 19% and 9% shopkeeper and industrial worker/ businessman.Patients who were married outnumbered the unmarried 70/ 100% versus 30/100% which are also quite consistent with other study done by (Bhattarai et al. 2006).[21]

Incidence of poisoning was also seen higher among the people who pursued secondary education 37%.38% of OP poisoning cases were from Sunsari, 19% from Saptari, 9% from Siraha and 9% from Morang. Remaining 25% were from various part of eastern Nepal.

The major causes of OP poisoning were family dispute 82%, unknown 9%, psychiatric illness 5% and accidental 4%.

As per availability and use till date of OP compound Chlorpyriphos showed highest consumption 53%, Phorate 14%, Dimethoate 8% Dichlorovos 6% and Methylparathion 8%. This is quite different from the other study done by (Kar SM et al. 2010) which showed Methyl Parathion consumption rate was highest 64.62%.[22]

The monthly breakdown of all 100 cases the incidence was found higher during January till April 60% and July till September 23% especially in age groups of 21-30 years. Surprisingly, no cases were recorded in the month of May, one case seen in June and increased till the month of August 16% and Dec 8% which consistent with Mishra A et al. where Jan till March was 116.96% and Kar S.M et al Jan to April was 16.92%. The cause of poisoning during this month might be due to post exam results or marital disparity like extramarital relationships and others.

On POP score system 54% pupils were less than 2mm, 30% had pin-point pupil. 88% were tachypnoeic, 8% were associated with central cyanosis while 4% were bradynoeic. 35% developed bradycardia. Fasciculation was observed in 47%. 31% had impaired response to verbal commands, 12% had no response to verbal commands. Seizures were observed in 3% cases comparable to other study (Batra AK et al. 2003).[23]

57% of the POP score fell into mild symptoms, 38% were moderate and 5% were with severe symptoms with mean score of 3.48 and 1.94SD.

With mild POP score Acetylcholinesterase level was normal in 31% subject, in 26% level was below normal. In moderate POP score Acetylcholinesterase (AchE) level drops to 34% and in severe form AchE decreases to 5%.

The study done by (Paudyal BP et al 2005) states that psuedocholinesterase value below 10% is been associated with increase mortality and length of hospital stay.[24]

The current study observed significant correlation between the level of serum Acetylcholinesterase and level of POP score at the initial presentation.

The higher the POP score a significant negative correlation of serum acetylcholinesterase level was observed and the mortality and duration of hospital stay which was comparable with the study done by (Reihman et al. 2008)

The requirement of atropine was also significantly correlated with POP score similar to the study done by (Jha et al. 1989) on the first day of admission.[25]

Significant correlation was observed when compared with Serum Acetylcholinesterase level with duration of hospital stay atropine use at index visit and concurrent use Pralidoxime (PAM).

It's also been observed in the present study that of 100 patients there were 3 mortalities out of them 2 patients had moderate grade of poisoning(score 4) and 1 had moderate grade of poisoning (score 9) which are quite comparable with other study done by (Dubey et.al.2016).[26]

Even though patient with moderate score the mortality is been observed. These categories of patient might require ICU admission and ventilatory support without being noticed during the phase of treatment or at the night shifts in the Emergency Ward. So it's a challenging for the treating emergency physician that at least all the patients of moderate as well as severe forms of poisoning should have ICU backup and need to be frequently monitored during maintenance or stoppage of antidotes particularly atropine.

CONCLUSIONS

POP score and serum acetylcholinesterase was negatively correlated to each other and was found to be useful at the index visit in terms of predictor of outcome i.e., higher the degree of POP score the higher the degree of derangement of acetylcholinesterase, prolonged duration of hospital stay, higher the requirement of atropine and increase the chance of ICU admission, ventilator support and mortality.

LIST OF ABBREVIATIONS

AChE: Acetyl cholinesterase;
BPKIHS: B.P. Koirala Institute of Health Sciences;
ICU:Intensive care unit;
LAMA:Left against medical advice;

OP: Organophosphate;
POP: Peradeniya Organophosphorus Poisoning Scale;
PAM: Pralidoxime.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

RC made substantial contribution to article concept, designing, data collection, analysis, write up and literature review and gave approval to final version. RB, GM and ML made substantial contribution to analysis and write up. MP made substantial contribution on data collection and analysis and gave approval to final version.

ACKNOWLEDGEMENTS

The authors wish to thank the faculty and staff at BP Koirala Institute ofHealth Sciences, Dharan, Nepal for invaluable support. In particular, thanks to Mr. Sunil Parajuliand Mr. Dharanidhar Baral for help with data gathering andanalysis.

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