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Clinical Correlation of the Severity and Outcomes of the Organophosphorus Compound Poisoning Cases Admitted to Kathmandu University Hospital based on POP Score and Serum Pseudocholinesterase Level - A Prospective Observational Study in Nepal

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Abstract

Introduction: Poisoning is the most common mode of unnatural death in South East Asia causing hundreds of thousand deaths per year. Among them Organophosphorus (OP) compound, a pesticide poisoning is the major clinical problem in Nepal.

Methods: A prospective observational study was conducted from July 2013 to September 2014 in Kathmandu University Hospital, Dhulikhel Hospital. A total of 110 patients of organophosphorus compound poisoning were evaluated using the clinical score of Peradeniya Organophosphorus Poisoning (POP) scale and level of Serum Pseudocholinesterase (SChE) to determine the correlation between POP scale and the serum SChE activity and their prognostic value in terms of severity and clinical outcomes.

Results: Of the total 110 cases of organophosphorus compound poisoning, the mean age was 32.69 ± 10.96. Majority of them were female (60%) and the most provoking factor was household conflict (85.40%). The most common compound consume was dimethyl (70.9%) over diethyl compound (29.1%). The mean amount of poison was 26.4 ± 31.61 ml and the mean atropinization dose was 14.77 ± 15.21 mg. Similarly, the mean cholinesterase level was 1792.90 ± 2305.9 IU/L and the duration of hospital stay was 3.99 ± 2.63 days. The level of serum SChE and POP score scale differed significantly in male and female (P=0.000 and P=0.010 respectively). There was a significant correlation between low serum cholinesterase and duration of hospital stay P=0.023. However, there was no statistical significance between POP scale score and gender, lag time, atropine dose, ventilator support and clinical outcomes.

Conclusion: The organophosphorus compound is the most common self-poisoning in Nepal. The simple POP score scale is the useful clinical severity assessment tool. Serum cholinesterase level and its activity can be a guide to the physician for predictive and prognostic value.

Keywords: Cholinesterase; Organ phosphorus, Poisoning; Severity

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Introduction

Organ phosphorus pesticide poisoning is a main clinical and public health problem across much of rural Asia [1]. Of the estimated 500,000 deaths from self-harm in the region each year, about 60% are due to pesticide poisoning. Many studies conclude that organophosphorus pesticides are responsible for around two-thirds of these deaths, a total of 200,000 a year [2]. The suicidal intent is the most common mode of poisoning whereas others are an impulsive act, homicidal, accidental and various other triggering factors [3-5]. It is widely used pesticide in Kavre District of Nepal and the commonest mode of poisoning in the patients attending to Kathmandu University Hospital, Dhulikhel Hospital [6,7].

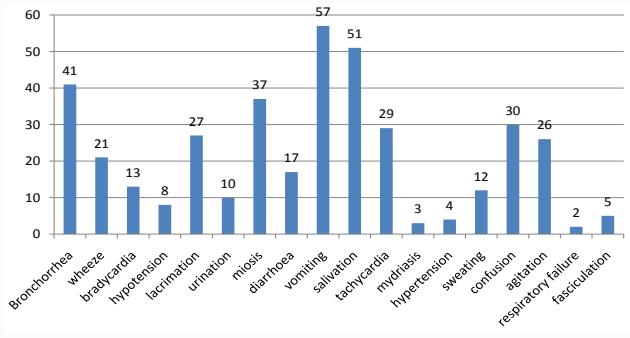

Figure 1: Clinical features of patients consuming OP compounding poisoning.

Organophosphorus pesticides inhibit esterase enzymes, especially Acetylcholinesterase (AChE) in synapses and on red-cell membranes, and butyrylcholinesterase in plasma [8]. The subsequent autonomic, CNS, and neuromuscular features of organophosphorus poisoning are well known as overstimulation of muscarinic and/or nicotinic receptors. The rate and degree of AChE inhibition differ according to the structure of the organophosphorus compounds and the nature of the metabolite namely, AChE-dimethyl complex and AChE-diethyl complex [9-11].

Diagnosis is made on the basis of clinical suspicion, a smell of pesticides or solvents, the characteristic clinical signs and reduced butyrylcholinesterase or acetylcholinesterase activity in the blood. Patients with severe organophosphorus poisoning typically present with pinpoint pupils, excessive sweating, reduced consciousness and poor respiration [12-14]. Acute complications such as bradycardia, convulsions, hypoglycemia, and intermediate syndrome are more common than late complications like organophosphorus induced delayed polyneuropathy, monoplegia and sensory neuropathy.

Treatment includes resuscitation of patients with basic life support, intravenous fluids, oxygen, a muscarinic antagonist (atropine), and an acetylcholinesterase reactivator (an oxime that reactivates acetylcholinesterase by removal of the phosphate group). Gastric decontamination is considered only after the patient has been fully resuscitated and stabilized. Patients should be carefully observed after stabilization for changes in atropine needs, worsening respiratory function because of intermediate syndrome, and recurrent cholinergic features occurring with fat-soluble organophosphorus compound [15].

Since few randomized trials have been done so far, comparison of effectiveness of therapies given in different hospitals is tempting. Unfortunately, such comparisons are confounded by many factors [16]. The case fatality for self-poisoning in developing world ranges from 10% to 20% but for particular pesticides it may be as high as 50% to 70% [3]. However, it is still associated with high morbidity and mortality rates, both in resource-poor settings and in well-developed countries and death attributed to complications other than poison specific is also notably significant [17]. In the present study, we made an effort to evaluate the correlation between the POP score and the serum SChE activity in terms of clinical severity and prognostic outcomes.

Material and Methods

This is an observational prospective study conducted in Kathmandu University Hospital, Dhulikhel, Nepal from July 2013 to September 2014. Prior approval for the study was obtained from the Institutional Review Committee of the Kathmandu University Hospital. Informed consent was taken from the patients/responsible family members after explaining the possible prognosis of the patient. Consecutive patients of OP poisoning who attended the emergency department and had not received any kind of treatment before were included. Patient of age <16 years, pregnant lady, and having multiple debilitating chronic illnesses were excluded.

Immediately after the arrival of the patient in the emergency department, the confirmation of the poisoning and the lag time noted. Based on the POP scale system, detail clinical examination and assessment done. The POP scale is a scoring system introduced by N Senanayake et al., [18] and each clinical parameters is assessed on a three-point scale ranging from 0-2 (Table 2). At the same time, 5 ml of the venous blood samples were collected for serum SChE along with other routine investigations. Serum SChE level was estimated by spectrophotometry method with the reference range of 7000 IU/L to 19000 IU/L.

Based on the serum SChE levels, the severity of poisoning was defined as per Kumar et al., [19]

- Latent: SChE level >50% of normal or >3,500 IU/L.
- Mild poisoning: SChE level 20% to 50% of normal or 1,401 IU/L to 3,500 IU/L.
- Moderate poisoning: SChE level 10% to 20% of normal or 701 IU/L to 1,400 IU/L.
- Severe poisoning: SChE level is <10% of normal or <700 IU/L.

All the patients were routinely managed with bolus dose of atropine till the signs of complete atropinization noted in emergency unit and continuous maintenance infusion in intensive care unit. Pralidoxime was added to those who presented to the hospital within 6 hours of lag time due to rapid aging process in AChE-dimethyl complex and discontinued after 72 hours or after extubation whichever was prolonged [20,21]. After discontinuation of atropine all patients were transferred to general ward for 24 hours to 48 hours for observation. Psychiatry consultation followed by psychosocial counseling was done. The total amount of atropine used and duration of hospital stay were monitored in those who survived. Complete recovery or death was considered as end point of the study. The data are shown in frequencies and percentages [22,23]. Mean, standard deviation and P value are calculated using the Statistical Package for the Social Science (SPSS), version 20. The outcome was considered statistically significant if its P value was <0.05.

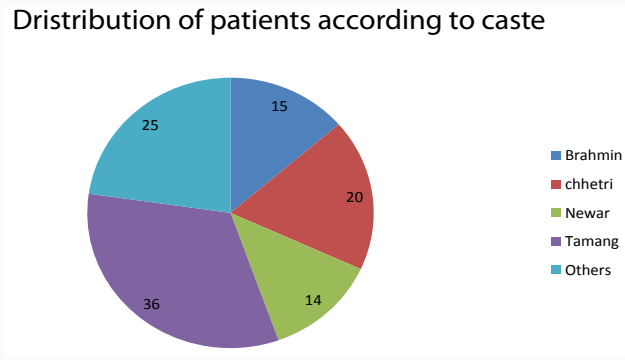

Figure 2: Distribution of patients according to the ethnic group.

Table 1: Baseline characteristics of the patients with organophosphorus compounds poisoning.

Characteristics	Male	Female	P value
Total	44/110 (40%)	66/110 (60%)	
Age group in years			
15 years to 30 years	13/44 (29.5%)	34/66 (51.5%)	0.018
31 years to 45 years	29/44 (65.9%)	24/66 (36.3%)	
46 years to 60 years	1/44 (2.2%)	6/66 (9%)	
61 years to 75 years	1/44 (2.2%)	0/66 (0%)	
Marital status			
single	12/44 (27.2%)	15/66 (22.7%)	0.654
married	32/44 (72.7%)	51/66 (77.2%)	
Organophosphorus compound			
Diethyl	12/44 (27.2%)	20/66 (33.3%)	0.451
Dimethyl	32/44 (72.7%)	46/66 (69.6%)	
Alcohol Influence			
Present	28/44 (66.6%)	43/66 (65.1%)	0.008
Absent	16/44 (36.3%)	23/66 (34.8%)	
Intension			
Accidental	7/44 (15.9%)	2/66 (3%)	0.047
Suicidal	29/44 (65.9%)	53/66 (80.3%)	
Impulsive act	8/44 (18.1%)	11/66 (16.66%)	
Compounding factors			
Depression	3/44 (6.8%)	1/66 (1.5%)	0.221
Failure in study	1/44 (2.2%)	3/66 (4.5%)	
Household conflict	35/44 (79.5%)	59/66 (89.3%)	
None	5/44 (11.3%)	3/66 (4.5%)	
Atropinization dose	11.11 ± 6.97 mg	17.20 ± 5.42 mg	
Pralidoxime used	22/44 (50%)	32/66 (48.48%)	0.876
Pseudocholinsterase level	894.74 ± 1337.57 IU/L	2391.69 ± 2614.4 IU/L	0.492
Hospital stay	6.77 ± 2.70 days	5.42 ± 3.16 days	0.492
complications	9/44 (20.45%)	13/66 (19.69%)	0.341
Ventilator support	3/44 (6.8%)	12/66 (18.18)	0.089
Outcomes			
Improved	43/44 (97.72%)	62/66 (93.93%)	0.49
Death	1/44 (2.20%)	2/66 (3.03%)	
LAMA	0/44 (0%)	2/66 (3.03%)	
POP score scale			
Mild	18/44 (40.90%)	43/66 (65.1%)	0.834
Moderate	11/44 (25%)	12/66 (18.18%)	
Severe	15/44 (34.09%)	11/66 (16.66%)	

Results

Of 110 cases of organophosphorus compound poisoning, the youngest was 16 years old and the oldest was 65 years. The mean age determined was 32.69 ± 10.97 years old. Majority of them were female (60%) as compared to male (40%) and both genders preferably consumed dimethyl compound (70.9%) over diethyl (29.1%) which is statistically insignificant (P=0.831). Concomitant consumption of alcohol is observed in both the gender which is statistically significant, P=0.008. Clinical features and the distribution of patients according to the ethnic groups are projected in Figure 1 and 2 respectively. In the present study, the suicidal attempt is the most common cause of OP poisoning (74.5%) followed by an impulsive act (17.2%) and accidental ingestion (8.1%). Several provoking factors responsible for poisoning are household conflict (85.4%), depressive illness (3.6%) and failure in the study (3.6%). The mean amount of poison consumed was 26.4 ± 31.6 ml with the highest amount of 200 ml and the lowest of 5 ml. However, (8.1%) patient did not know the amount of poison they consumed at the time of hospitalization. The mean lag time between poisoning and arrival to the emergency department

Table 2: Correlation of severity measured by serum pseudocholinesterase level and POP score scale with different variables in patients with organophosphate compound poisoning.

	Serum Pseudocholinesterase Level		POP Score Scale	
	r	p	r	p
Gender	-0.33	0	-0.246	0.01
Lag time	-0.081	0.398	0.056	0.502
Atropinization	0.073	0.446	0.065	0.502
Hospital stay	-0.217	0.023	-0.08	0.406
Ventilator support	-0.179	0.07	0.079	0.414
Complications	0.298	0.002	0.157	0.101
Outcomes	0.155	0.105	0.111	0.248

was 5.36 ± 4.45 hours and the mean amount of atropinization dose was 14.77 ± 15.21 mg of atropine (range, 1.8 mg to 81.60 mg) with the mean maintenance duration of 3.99 ± 2.63days (range, 1 day to 16 days). Similarly, the mean amount of serum cholinesterase level and the duration of hospital stay were 1792.90 ± 2305.59 IU/L and 5.96 ± 3.06 days respectively (Table 1). Over half of the patients, 56 (50.99%), (male=22, female=34) did not receive pralidoxime due to late presentation. The level of serum cholinesterase and POP score scale differed significantly in male and female (P=0.000 and P=0.010 respectively). Also, there is a significant correlation between low serum cholinesterase level and duration of hospital stay (P=0.023). In addition, the number of complications were correlated significantly with decreased serum cholinesterase level (P=0.002) but not with the need for ventilator support (P=0.070). However, the correlations of POP score scale with gender, lag time, atropinization dose, ventilator support, complications and clinical outcomes showed no statistical significance. Similarly, there is no statistical significance between age group and the severity measured by either serum cholinesterase level (P=0.718) or POP score scale (P=0.553) (Table 2). A total of 15 patients needed ventilator support, 3 of them were male and 12 were female (P=0.56) of which 3 patients died and 2 left against medical treatment which we assumed death (P=0.000). Of the 3 mortality, all consumed dimethyl compound, one male of 35 years died due to multi-organ dysfunction syndrome, another female age 40 died due to an intermediate syndrome and the other female age 38 died of acute cholinergic crisis with aspiration pneumonia.

Discussion

Organophosphorus compound poisoning is the global health burden with particularly higher prevalence rate in developing countries. In clinical practice, it is very difficult to evaluate the severity and predict outcomes without early biomarker. The highly variable history of patients and difficulty determining the actual dose and types of the poisoned compound make further challenging to predict the clinical outcome because people admitted in fairly good condition can rapidly deteriorate and may need mechanical ventilation. In this study, we measured serum SChE and established clinical severity scale to determine the several clinical correlations and outcomes after treatment. The current study showed the mean age of patients was 32.69 ± 10.97 years with the female to male ratio of 3:2 and around 3/4 of them consumed with the intention of suicidal attempt. A Similar study performed in Dhaka Medical College, Bangladesh in 2004 also showed OP poisoning was predominant in female gender (60%) and the most common reason was suicide (93.3%). However, another study at Dhamrai Thana Health Complex performed from January 1993 to December 1997 showed that males (61.30%) were predominant than females (38.70%) in poisoning cases which were observed more in the married group (68.64%). In the current study, the household conflict was found as the most provoking factor for self-poisoning (85.4%) which was consistent with other studies. This study showed 70.9% ingested dimethyl compound over diethyl compound which is widely available in the pesticides market of Nepal that can be purchased over the counter. A study by Bhattarai et al., [24] also revealed a similar result and also several other studies in Nepal [9,10]. The commonest clinical features in the current study were vomiting, lacrimation, salivation, miosis and bronchorrhoea but bradycardia and muscle fasciculation were relatively lower which was similar in other studies [24,25]. The current study showed mean lag time, atropinization dose and duration of hospital stay who survived were 5.36 ± 4.45, 14.77 ± 15.21 mg, 5.96 ± 3.06 days respectively. Over half of the patients (50.99%) did not receive pralidoxime due to delayed arrival in the emergency department. Those who received pralidoxime did not show a significant reduction in hospital stay and need for ventilator support statistically, P=0.496 and 0.69 respectively.

In the current study, we observed a significant correlation between lower serum cholinesterase level and duration of hospital stay and complications (P=0.23 and 0.002). This observation was also noted in studies by Bhattarai et al., [24] and kavya et al., [26]. However, other studies reported that low plasma cholinesterase levels support the diagnosis of OP poisoning but are not significantly related to the severity of poisoning [27,28]. In contrast, Rehiman et al., [29] used the POP scale in the grading of severity of OP poisoning and reported that the severity was correlated with the SChE level. In a retrospective study that used the grading system developed by Bardin et al., [30] it was demonstrated that SChE activity was depressed significantly in all grades and that it was related to the severity of OP poisoning. Similarly, the current study showed no correlation between serum cholinesterase level and the dose of atropine and or pralidoxime [31]. This was observed in studies done by Yardan et al., [32] and Nouira et al., [33]. However study done by Bhattarai et al., [24] reported POP scale severity and derangement in serum cholinesterase levels at the initial presentation correlated well with the mean requirements of atropine on the first day of admission, but the total amount of atropine needed to treat the patients and the average duration of hospital stay did not correlate with the mortality of the patients. It is asserted that atropine is only a muscarinic receptor antagonist, whereas cholinergic symptoms are associated with overstimulation, to varying degree, of both muscarinic and nicotinic receptors. In our study, there was no significant difference in serum cholinesterase activity between mechanically ventilated patients and those who did not require mechanical ventilation and thus revealed that cholinesterase level on admission may not be a reliable indicator for the selection of treatment modality. Also, there was no significant difference in cholinesterase level between survivors and non-survivors. These results were consistent with others studies done by Yardan et al., [32] and Nouira et al., [33]. In our study, we measured serum cholinesterase only at the time of admission which has no prognostic value. Its activity may better predict morbidity and mortality if serial monitoring was done at the time of treatment.

Limitations

This was a single hospital-based study with the relatively smaller sample size. Thus, a prospective and controlled study including a larger sample is needed. The study also did not include serial monitoring of

the serum cholinesterase level during hospital treatment which may provide a guide for the physicians in the evaluation and management of patients with OP poisoning. Although all patients who survived were evaluated by the psychiatrist before discharge home, we could not do follow up evaluation.

Conclusion

Organophosphorus is the most commonly used self-poisoning compound. We conclude that simple POP score scale is useful for determining the severity of the poisoning. Also measuring serum cholinesterase level at the time of admission and serial monitoring during treatment would be considered as prognostic and predictive value for future reference.

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