Correlation of Serum Cholinesterase Level, Clinical Score at Presentation and Severity of Organophosphorous Poisoning

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ABSTRACT

The aim of the study was to correlate between the clinical score described by Peradenya Organophosphorus Poisoning (POP) scale, serum cholinesterase level at presentation and severity of poisoning. Consecutive patients of organophosphorous poisoning attending Bir Hospital from August 2004 to September 2005 were studied. Patients were grouped into mild, moderate and severe poisoning groups according to the POP scale. Fifty patients fulfilled the inclusion criteria. The severity of poisoning directly correlated with serum cholinesterase level ($P<0.001$). The differences in the mean requirements of atropine on the first day of admission, in the total amount of atropine needed to treat and in the average duration of hospital stay were significant ($P<0.05$). There were 26% patients in moderate poisoning and only 4% patients in severe poisoning, but a total of 14% of the patients died, indicating that patients with even moderate degree of poisoning had also died. Both the POP scale severity and derangement in serum cholinesterase levels at initial presentation did not correlate with mortality, which could be due to various other co-morbidities and inadvertent stoppage of atropine infusion particularly at night in the wards. The POP scale and serum cholinesterase at presentation appeared useful to assess the severity of poisoning, particularly in terms of higher amount of atropine and prolonged duration of hospital stay. The patients with evidence of moderate and severe degrees of poisoning need close monitoring. Further studies to evaluate the factors likely to cause deaths, particularly by closely monitoring of moderate and severe organophosphorous poisoning in intensive care units, are required to clarify the correlation with mortality.

Key words: *organophosphorous poisoning, peradeniya organsophosphorous poisoning scale, serum cholinesterase*

INTRODUCTION

Poisoning is one of the commonest causes of admission of young adults in the medical wards in Nepal, and organophosphate (OP) is one of the commonest poisons consumed.[1-12] Owing to the limited availability of facilities and resources, all OP poisoning patients are not managed in intensive care units in Nepal. It is therefore important that the clinical features and other factors which indicate the severity of poisoning and the criteria to predict the need of ventilatory support be identified at the initial examination. Red blood cells (RBC) cholinesterase level is a sensitive indicator, but its estimation is difficult and is usually not available. Serum cholinesterase level, which can be routinely estimated locally, is depressed after OP poisoning, as

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also reported by a previous study done (unpublished work).[13] The Peradenya Organophosphorus Poisoning (POP) scale assesses the severity of the poisoning based on the symptoms at presentation and is simple to use. In a study by Senayeke et al, patients with a high score on the POP scale had a high rate of morbidity and mortality.[14] The present study aims to correlate serum cholinesterase level and the clinical criteria score described by the POP scale at initial presentation and the severity of poisoning. The correlation may help in predicting the clinical outcome and in making timely decisions regarding transferring the patients for intensive care management.

MATERIAL AND METHODS

This is a prospective, observational, descriptive, intention-to-treat study of the patients of OP poisoning attending the emergency department of Bir Hospital, Kathmandu, from August 2004 to September 2005. Consecutive patients of OP poisoning who attended the emergency within 24 hours after poisoning, and who had not received any kind of treatment before assessing the clinical severity and collection of blood sample was done and who were followed-up in the medical ward till the final outcome were enrolled in the study. Immediately after the arrival of the patients at the emergency department, history was taken to confirm the type of OP compound taken and the interval between the consumption of poison and arrival at the emergency. Consent of the patient and or guardian was taken. Apart from the routine and detailed clinical examination, assessment was also done based on the POP scaling system, which included pupil size, respiratory rate, pulse rate, level of consciousness of the patient and the presence or absence of convulsion and fasciculation. Based on this assessment, a score was given to the patients. Upon the confirmation of the OP poisoning, patients' venous blood samples were taken for serum cholinesterase level assay. The patients were routinely managed in the units, with pralidoxime and intravenous (IV) 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 who survived was calculated. The study was approved by the Ethical Review Board for Research of the National Academy of Medical Sciences.

PERADENIYA ORGANOPHOSPHOROUS POISONING (POP) SCALE

The Peradeniya Organophosphorous Poisoning (POP) Scale is a scoring system introduced by N Senanayake, H J de Silva and L Karalliedde in 1993.[14] Common clinical manifestations of OP poisoning are selected as parameters and each is assessed on a three-points scale varying from 0 to 2 (Table 1).

The score is obtained at initial presentation before any medical intervention and it represents the muscarinic, nicotinic and central effects of the acute cholinergic manifestations of OP poisoning. A score of 0 to 3 is considered as mild poisoning, 4 to 7 as moderate poisoning and 8 to 11 as severe poisoning. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.5. Univariate correlation between these with the POP scale severity of poisoning and the serum cholinesterase level were evaluated using Pearson correlation coefficient Chi Square test and Fisher's exact test. A P value of less than 0.05 was considered to be significant.

RESULTS

A total of fifty consecutive patients of OP poisoning who attended the emergency above in the material and Methods and who fulfilled the inclusion-criteria mentioned were enrolled in the study. Among them, 62% were female. The age of the patients ranged from 15 to 70 years with 70% of them between 15 to 25 years. Among the 15 to 25 year-old patients, the number of females was twice that of males. Above the age of 25 years, the number of males was relatively more than that of females (Figure 1). House wives and students were the most common group of patients in our study (28% and 22% respectively), followed by laborers (16%), farmers (14%) and the unemployed (14%). The remaining patients were businessmen (4%) and shopkeepers (2%).

A total of 68% of the patients had consumed parathion methyl and 26% dichlorovos. Four percent had taken poison mixed with alcohol and kerosene. All the patients who expired had consumed parathion methyl. The symptoms and signs at presentation are shown in Figure 2. None of the patients developed seizures. The values of different parameters in the three grades of poisoning as per the POP scale are shown in Table 2.

There was significant correlation between the severity of poisoning categorized by the POP scale and the serum cholinesterase at the time of initial presentation of the patients ($P<0.001$), requirements of atropine on the first day of admission, the total amount of atropine needed ($P<0.001$) and the average duration of hospital stay ($P<0.05$) (Table 3). The longest hospital stay was of a female patient who had consumed parathion and was in hospital for 26 days (POP scale 8). She developed respiratory arrest on the third day of poisoning and was put on the ventilator for 13 days, with complete recovery as the outcome.

Table 1. **Peradeniya Organophosphorous Poisoning (POP) Scale**[14]

	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

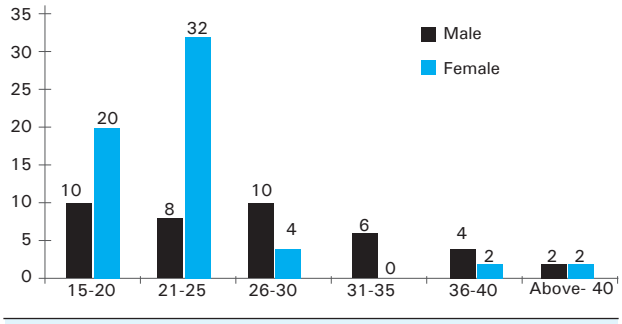

Figure 1. **Age and sex distribution of patients**

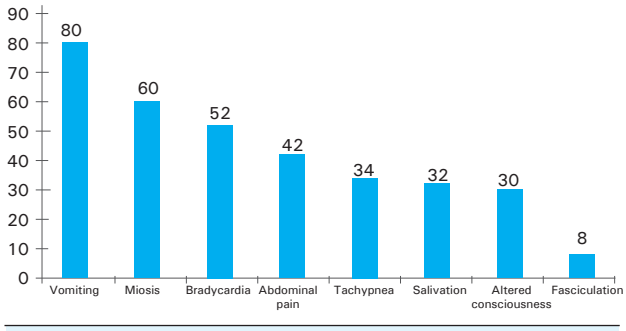

Figure 2. **Signs and symptoms at presentation**

There was no correlation of the morbidity of the patients with the age-groups of the patients or the types of organophosphate and organocarbomate compound consumed (P=0.343 and P=0.463 respectively). Ninety-two percent of the study subjects received various doses of pralidoxime ranging from 1.5 gm to 6 gm (6 gm received by 2 patients, 4 gm by 5, 3 gm by 19, 2 gm by 3, 1.5 gm by 17) and 8% of the patients did not receive any. These dose variations are attributed to the decision of the treating physicians and financial affordability of the patient. A total of 14% of the study population died during the study period. Although the POP scale severity and derangement in serum cholinesterase levels at initial presentation correlated well with the mean requirements of atropine on the first day of admission, the total amount of atropine needed to treat and the average duration of hospital stay, both of these variables did not correlate with the mortality of the patients. 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 not all patients received it.

DISCUSSION

In this study, more than two thirds of the patients were 15 to 30 years old, which is comparable to other studies.[3] This may be due to the increase in stress

Table 2. Values of different parameters in the three grades of poisoning as per the POP scale

POP Scale	N (%)	S. cholinesterase Mean (±SD)	Atropine ampoule (mg)		Hospital stay
			First day	Total	mean ±SD (days)
0–3 (mild)	35 (70)	2647.7 (±391)	94 (56.4)	367.8 (220.7)	7.83±0.5
4–7(moderate)	13 (26)	200.2 (±39)	146 (87.6)	631.9 (379.1)	10.46±1.3
8–11 (severe)	2 (4)	124.5 (±39.5)	170 (102)	2134 (1280.4)	14±12

Table 3. Correlations between different parameters of the patients

Parameters	Pearson Correlation (r)	P value
POP and serum cholinesterase	−0.669† (Moderate degree negative correlation)	<0.001
POP and hospital stay	0.414† (Low degree positive correlation)	0.003
POP and starting-dose atropine	0.474† (Low degree positive correlation)	0.001
POP and total atropine	0.537† (Moderate degree positive correlation)	<0.001
Serum cholinesterase and hospital stay	−0.351* (Low degree negative correlation)	0.012
Serum cholinesterase and starting-dose atropine	−0.341* (Low degree negative correlation)	0.015
Serum cholinesterase and total atropine	−0.318* (Low degree negative correlation)	0.025
Hospital stay and starting-dose atropine	0.506† (Moderate degree positive correlation)	<0.001
Hospital stay and total atropine	0.788† (High degree positive correlation)	<0.001
Starting-dose atropine and total atropine	0.751† (High degree positive correlation)	<0.001

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

because of unemployment, poverty and conflicting relationships in young couples. Females were found to be more vulnerable to self-poisoning, as reported in other studies.[2,5] But with advancing age, this pattern of female to male ratio is reversed as also seen in other reports.[3] As reported in various other studies, housewives and students were the common groups involved in self-poisoning.[15,16] In this study, 68% of the patients consumed parathion methyl and 26% took dichlorovos. This was consistent with other studies done within the country.[11,17] These agents are widely used and easily available in the agricultural market of Nepal. A study regarding pesticides poisoning in the developing world also revealed this problem.[18] There was no accidental poisoning reported in this study. In comparison with deliberate self-harming by poisons, accidental poisonings are far less frequent in other studies as well.[11,19] This may be due to the fact that most of the patients enrolled in the study had some level of educational background. On the contrary, a retrospective analysis of poison cases done at TU Teaching Hospital revealed 6% of accidental poisoning among 178 study subjects.[4]

Abdominal pain, bradycardia, vomiting along with miosis were the most common and consistent clinical findings of OP poisoning, but fasciculation was infrequent. These are comparable with the results of similar types of studies published in the past.[15] In 1987, workers from Sri Lanka described intermediate syndrome, which included signs of paralysis appearing in 10 to 40% of patients 24 to 96 hours after exposure, i.e.

after admission and before the delayed neurotoxicity.[21] Clinically, this syndrome is supposed to be the same as the type II signs (nicotinic signs) described from India more than a decade ago, like the inability to lift the neck, inability to sit up, ophthalmoparesis, slow eye movements, facial weakness, swallowing difficulty, limb weakness (proximal >distal), areflexia, respiratory failure and death.[22] The intermediate syndrome and delayed neurotoxicity were not specifically defined for observaton in the study. The patients requiring a ventilator or those that died dying could have had the intermediate syndrome.

The current study observed significant correlation between the degree of derangement in serum cholinesterase level and severity of poisoning at the initial presentation. The higher the score on the POP scale, the higher was the degree of derangement in the serum cholinesterase level. A significant correlation was also observed between the deranged serum cholinesterase level and the morbidity of the patients in terms of prolonged duration of hospital stay. The total requirement of atropine was also higher along with the doses for the initial-day atropinization. Similar findings have been reported in other studies.[22] Good correlation was found between the POP scores and the need for mechanical ventilation and the total dose of atropine. A study from India also concluded with the need of a higher amount of atropine and mechanical respiratory supports in the management of severely poisoned patients.[23] The mortality rate of 14% in this study is comparable with 6% to 13% of mortality in other studies from the country.[7,11] A report from outside the country is also similar.[25] Many studies revealed the promising role of pralidoxime in the management OP poisoning, but some others did not.[25-30] the role of pralidoxime on mortalilty and morbidity was beyond the scope of this study.

Although the 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, 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. Although 26% of patients were in the moderate poisoning group and only 4% of patients in the severe poisoning group as categorized by the POP scale, 14% of patients died in the study. This indicates that even moderate degree poisoning as categorized by the POP scale can lead to mortality due to various other factors. The co-morbid conditions like pneumonia, septicemia, cardiac arrhythmias, and inadvertent stoppage of atropine infusion particularly at night in the wards etc, also have a role in the mortality after OP poisoning.[17] So, the interplay of these factors in this study could have affected the correlation. Fatalities from acute OP poisoning generally result from respiratory failure due to a combination of depression of the CNS respiratory center, neuromuscular weakness, excessive respiratory secretions, bronchoconstriction, and occasionally due to cardiovascular collapse.[31,32] Such a situation is likely to occur quietly without the patients' deteriorating condition being noticed if there is an inadvertent stoppage of atropine infusion particularly at night in the general wards.[17] Larger studies controlling most of the factors likely to cause deaths, particularly by closely monitoring of at least all the patients of moderate and severe OP poisoning in intensive care units, might clarify the relation with mortality.

CONCLUSION

In summary, the POP scale and where available, serum cholinesterase at presentation appear useful in assessing the severity of poisoning, particularly in terms of a higher amount of atropine needed and a 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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