ORIGINAL ARTICLE

Cardiovascular Effects of Acute Organophosphate Poisoning

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Abstract

Background: Cardiovascular effects of acute organophosphate (OP) poisoning are common. This study was aimed to assess the cardiovascular effects of OP poisoned patients in Nepal.
Methods: This was a prospective hospital-based cross-sectional study of 115 acute OP poisoned patients presenting in emergency department of a tertiary care teaching hospital of central Nepal during November 2008 to October 2011. Cardiovascular manifestations were assessed by physical examination and electrocardiogram (ECG). All data including demographic features, clinical findings and outcomes were entered into a pre-structured proforma.
Results: A total of 115 OP poisoned patients were studied. Mean age of the patients was 29.8±13.9 years. Fifty-seven patients (49.6%) developed cardiac effects that all had sinus tachycardia. Sinus bradycardia was observed in 3 patients (2.61%). Hypertension was detected in 23 patients (20%) and pulmonary edema developed in 24 patients (20.9%). The most common ECG abnormalities recorded were prolonged QTc in 21 patients (18.26%) and ventricular extrasystole in 14 patients (12.2%). Five patients developed polymorphic ventricular tachycardia (VT) and 3 patients developed ventricular fibrillation (VF) which could not be reverted back despite adequate treatments and led to death (mortality rate: 6.9%).
Conclusion: Cardiac effects of OP poisoning can be life-threatening. Prompt diagnosis, early supportive and definitive therapies with atropine and oximes along with vigilant monitoring of the patients for prominent cardiac effects such as QT prolongation, VT or VF during hospital stay can definitely save lives of the victims.

Keywords: Cardiovascular Abnormalities; Electrocardiography; Long QT Syndrome; Organophosphate Poisoning

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INTRODUCTION

Organophosphorus (OP) pesticide poisoning is a major clinical and public health problem across the world including much of rural Asia (1). It accounts for as much as 80% of pesticide-related hospital admissions (2). Many studies estimate that OP pesticides are responsible for nearly two-third of self-harm deaths, a total of 200,000 a year (3). Hospitals in rural areas should handle the impact of this problem with a case fatality of 15–30% (4).

The possible mechanisms of cardiac toxicity are related to sympathetic and parasympathetic over-activity, hypoxemia, acidosis, electrolyte derangements and a direct toxic effect of the compounds on myocardium (8). On the other hand, the use of atropine as the antidote for OP poisoning itself may induce lethal arrhythmias (9).

The OP induced cardiac effects and their consequences have not been adequately studied in Nepal. The lack of timely identification of the poisoning or its clinical toxidrome and failure to proper cardiac monitoring for potential life threatening complications may endanger the lives of the patients. This study was designed to analyze the frequency of cardiovascular effects of acute OP poisoning.

METHODS

In this prospective cross sectional study, patients with alleged ingestion or exposure to OP compounds presenting to emergency department of College of Medical Sciences-Teaching Hospital (COMS-TH) in Bharatpur, Nepal were enrolled during November 2008 to October 2011. Patients with documented history of cardiac diseases were excluded from the study. At emergency unit, the patients were assessed with blood pressure (BP) monitoring, pulse rate, electrocardiogram (ECG), serum electrolytes, renal function tests, chest X-ray, arterial blood gas (ABG) analysis and other relevant investigations if required. The patients were subsequently admitted to the intensive care unit (ICU) or medical departments depending upon the severity of the poisoning. They were monitored vigilantly every day for ECG changes, BP and pulse variations throughout their hospital stay. The severity of poisoning was assessed as per Peradeniya Organophosphorus Poisoning (POP) scale which includes assessment of pupil size, fasciculation, level of consciousness, respiratory rate, pulse rate and seizure in OP poisoned patients (10).

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Immediately after admission to emergency care unit, the patients were atropinized according to a well-known protocol (11), by administration of 1.8-3 mg bolus atropine intravenously (IV) followed by doubling of the dose every 5 minutes until achievement of full atropinization. The atropinization was evaluated based on dry secretions, dilated pupils and tachycardia (pulse rate ~ 110-120/minute). Once the patient was atropinized, 20-30% of the total atropinization dose was calculated and maintained as IV infusion per hour and was continued for 2 to 3 days until the patient's need to atropine reduced and the patient was stabilized. Subsequently, the infusion dose was tapered at a rate of 1/3 to 1/4 of the daily dose. High dose pralidoxime (PAM) infusion was used as per World Health Organization guidelines (12). Initial loading dose was 30 mg/kg body weight IV bolus followed by maintenance dose at 8mg/kg/h IV infusion.

Patients' characteristics including age, gender, occupation, intention of poisoning and its severity, elapsed time from poisoning to admission to emergency room, systemic complications, treatment and outcome of the patients were studied. Cardiac parameters including hypertension (considered as over 140/90 mmHg), hypotension (< 90/60 mmHg), tachycardia (> 100 bpm), bradycardia (< 60 bpm) and ECG changes including QTc prolongation, ST/T changes, supraventricular (tachy/bradyarrhythmias) and ventricular arrhythmias were noted. QTc was calculated with Bazett's formula, and QTc of over 460 msec in men and over 470 msec in women were considered as prolonged.

Data were entered into the pre-structured proforma and analyzed using Statistical Package for the Social Sciences version 15 (SPSS Inc., Chicago, IL, USA). Chi square test was used to analyze the correlation of categorical variables. P values of less than 0.05 were considered as significant.

Informed consent was taken from the patients or their relatives and ethical clearance was taken from the ethics board committee of COMS-TH, Bharatpur, Chitwan, Nepal before conduction of the study.

RESULTS

Demographic features

A total of 115 OP poisoned patients were studied. Mean age of the patients was 29.8 ± 13.9 (range: 1-75) years. Most of the patients belonged to the population of active productive age group (86.9% were between 15 and 45 years of age). Women constituted 59.1% of the cases. The distribution of age and gender are illustrated in figure 1. Majority of the patients (47.8%) were farmers followed by students (28.7%).

Circumstances of poisoning

The intention of poisoning was suicidal in most of the cases (93.9%). The majority of patients (66.1%) presented to the hospital within 2-6 hours post-ingestion. The most common OP compound consumed was chlorpyrifos plus cypermethrin. The severity of poisoning was moderate (according to POP scale) in most cases (Table 1).

Clinical findings

The poisoned patients presented with muscarinic effects in 110 patients (95.6%), nicotinic effects in 27 patients (23.48%) and central effects in 105 patients (91.3%). Cardiovascular manifestations of the patients are shown in table 2. A total of fifty-seven patients (49.6%) developed cardiac effects. The most common cardiac sign was sinus tachycardia (49.6%) followed by pulmonary edema (20.9%). The most common ECG abnormality was QTc prolongation (18.3%) followed by ventricular extrasystole (12.2%). ST elevation/depression and isolated T inversion mostly in anteroseptal leads were noticed in 8.7% of patients. Majority of these patients were elderly with documented hypokalemia (40.9%), mixed acidosis (6.1%)

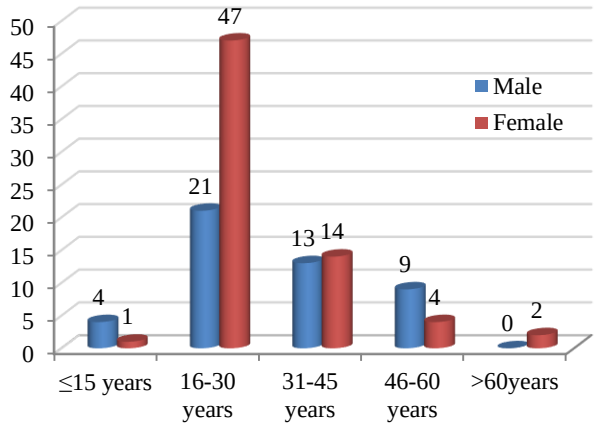

Figure 1. Distribution of age and gender in OP poisoned patients

Table 1. Circumstances of poisoning (n = 115)

Variable	No. (%)
Intention of poisoning	
Suicidal	108 (93.9)
Accidental	6 (5.2)
Homicidal	1 (0.9)
Elapsed time between poisoning and admission (hour)	
< 2	26 (22.6)
2-6	76 (66.1)
> 6	13 (11.3)
Type of organophosphate compound consumed	
Chlorpyrifos + Cypermethrin	70 (60.9)
Dichlorvos	21 (18.3)
Methylparathion	10 (8.7)
Unknown	5 (4.3)
Dimethoate	4 (3.5)
Profenfos + Cypermethrin	2 (1.7)
Chlorpyrifos	2 (1.7)
Triazos	1 (0.9)
Poisoning severity	
Mild	31 (27.0)
Moderate	78 (67.8)
Severe	6 (5.2)

Table 2. Cardiovascular effects of acute OP poisoning (n = 115)

Feature	No. (%)
Clinical	
Tachycardia (with sinus rhythm in ECG)	57 (49.6)
Pulmonary edema	24 (20.9)
Hypertension	23 (20.0)
Hypotension	6 (5.2)
Bradycardia (with sinus rhythm in ECG)	3 (2.6)
ECG changes	
Prolonged QT interval/QTc	21 (18.3)
Ventricular extrasystole	14 (12.2)
Atrial extrasystole	2 (1.7)
T inversion	5 (4.3)
ST elevation	3 (2.6)
ST depression	2 (1.7)
1st degree heart block	4 (3.5)
2nd degree heart block	1 (0.9)
Polymorphic ventricular tachycardia	5 (4.3)
Ventricular fibrillation	3 (2.6)

Table 3. Complications developed in OP poisoned patients (n = 115)

Complications	No. (%)
Atropine toxicity	74 (64.3)
Hypokalemia	47 (40.9)
Respiratory failure	27 (23.5)
Hyponatremia	27 (23.5)
Non-cardiogenic pulmonary edema	21 (18.26)
Acute kidney injury	13 (11.3)
Hypernatremia	11 (9.6)
Mixed acidosis	7 (6.1)
Metabolic acidosis	6 (5.2)
Hyperkalemia	5 (4.3)
Respiratory acidosis	3 (2.6)
Intermediate syndrome	3 (2.6)

and non-cardiogenic pulmonary edema (18.3%).

Complications of OP poisoned patients are tabulated in table 3. Atropine toxicity was the most common complication observed in the patients (64.3%). Out of 27 patients with respiratory failure based on ABG analysis, 16 patients (13.9%) required intubation and mechanical ventilation whereas the rest 11 patients improved with oxygen therapy with face masks. In addition, 3 patients (2.6%) developed intermediate syndrome (IMS) and required ventilatory support.

Patients' outcome

The duration of hospital stay ranged between 1-18 days with mean of 7.2 days. One hundred patients (86.9%) were discharged after full recovery while 8 patients (6.9%) died and the rest 7 (6.1%) left the hospital against medical advice after few days of admission.

The causes of mortalities were attributed to respiratory failure in 3 patients (2.6%), ventricular fibrillation (VF) in 3 (2.6%), aspiration pneumonia in 1 (0.9%) and status epilepticus in 1 (0.9%). Deaths mostly occurred among patients who ingested a combination of OP compounds belonging to WHO class I and II categories such as dichlorvos, methylparathion and chlorpyrifos (5 out of 8, 62.5%).

DISCUSSION

Cardiovascular effects of acute OP poisoning are common. Early detection of the cardiac effects may help to well plan the management of these complications. Ludomirsky et al. described three phases of cardiac toxicity after OP poisoning (13): phase 1) a brief period of increased sympathetic tone; phase 2) a prolonged period of parasympathetic activity and phase 3) QT prolongation leading to torsade de pointes (TdP) and VF.

In this study, prolonged QTc was one of the frequent findings and was the most common ECG abnormality observed in 18.3% of patients. This complication may induce VT and even cause death if timely identification and intervention is not instituted. This cardiac effect was also the most common finding in studies done in Nepal, Turkey and Inida (14-16); though, its frequency was higher (37.8%, 55.5%, 62.5%, respectively). In overall, the frequency of QTc prolongation in several series of severe OP poisoning was shown to be 20 to 80% depending on the severity of the poisoning and the type of the toxic agent (14-18). This complication usually starts during the second to third day and may last up to two weeks post-intoxication (18). Predisposing factors for QT prolongation and development of TdP that requires meticulous care even in mild OP-poisoned patients include: older ages, female gender, low left ventricular ejection fraction, left ventricular hypertrophy, ischemia and electrolyte abnormalities including hypokalemia and hypomagnesemia (19). In this respect, high frequency of hypokalemia (12/21, 57.14%) and acidosis (5/21, 23.81%) in our patients with prolonged QTc could be the major contributing risk factors for this dangerous ECG abnormality.

In our study, nearly half of the patients had sinus tachycardia while bradycardia was recorded in only 3 patients. Similar observation was made in the study by Karki et al. (14). Sinus tachycardia could be related to nicotinic effects of OP compounds while sinus bradycardia can be attributed to muscarinic effects (20). Although bradycardia is thought to dominate in the early cholinergic phase of the OP poisoning, sinus tachycardia was a more frequent finding in our study probably due to the fact that most of the patients were visited in antimuscarinic phase of OP toxicity (20).

Extrasystole in the form of premature ventricular contractions was also a frequent finding in our study. Administration of atropine in high doses has been implicated in the development of ventricular arrhythmias (17). In the present study two-third of patients developed atropine toxicity that can be the cause of this kind of arrhythmias. However, Ludomirsky et al. and Lyzhnikov et al. found no correlation between atropine therapy and ventricular arrhythmias in OP poisoning (13,18). The high rate of atropine toxicity in the present study can be due to the

relatively high dose regimen of atropine given to the patients.

Karki et al. reported non-cardiogenic pulmonary edema in 21.6% of OP poisoned patients (14), which was similar to our findings (24%). However, in the study done by Saadeh et al. in Jordan, the rate of non-cardiogenic pulmonary edema was higher (43%) (19). The reason for this discrepancy might be the higher severity of cases they studied.

In the present study, atrioventricular (AV) block developed in less than 5% of patients. This resembles to a Russian series that intraventricular conduction defects and AV block were described in 5.4% of OP poisoned patients (18). Correspondingly, Paul et al. reported AV block following OP poisoning in 8.4% of patients (16). In our study, 5 patients developed polymorphic VT and 3 patients developed VF which could not be reverted back despite defibrillation, advanced cardiopulmonary resuscitation and correction of hypokalemia/ hypomagnesemia, and consequently led to death. In the study by Karki et al. two patients died from non-cardiogenic pulmonary edema and one from VF, giving a hospital mortality rate of 8.1% (14), similar to our study (6.9%).

LIMITATIONS

Many of the patients in this study were referred cases from local health care centers and hospitals that anticholinergic drugs were administered prior to admission to our center. Thus sinus tachycardia was a common finding. The identification of OP compounds was based on the sample brought by the patient relatives though in few cases this could not be done and so the poisoning was diagnosed according to clinical toxidrome. Measurement of the red blood cell cholinesterase or plasma cholinesterase was not done because of the non-availability of the tests during the study period.

CONCLUSION

Cardiovascular effects are quite common following acute OP poisoning. These effects pertain to different muscarinic and nicotinic effects on the heart, electrolyte disturbances, ABG disorders, respiratory failure and over-atropinization. Prompt diagnosis, early supportive and definitive therapies with atropine and oximes along with vigilant monitoring of the patients for life-threatening cardiac effects such as QT prolongation, VT or VF during hospital stay can definitely save the lives of the victims.

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