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STUDY OF ORGANOPHOSPHORUS POISONING IN CONTEXT TO CHANGES IN ELECTROCARDIOGRAPHY, ECHOCARDIOGRAPHY, AND CARDIAC MARKERS

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Abstract

Background: Organophosphorus compounds are varied form of chemicals, produced by esterification of phosphoric acid and alcohol. Although such compounds are commonly encountered in everyday practices, these are toxic to human. The aim of the current investigation was to identify alterations in electrocardiography, echocardiography, and cardiac biomarker concentrations in cases of organophosphorus poisoning. **Materials and Methods:** A clinical prospective study was conducted on 50 individuals with organophosphorus poisoning. Clinical features, elctro- and echo- cardiographic changes were monitored. Cardiac enzymes were analyzed qualitatively using laboratory examinations. The statistical validation was done using Microsoft Excel and GraphPad Prism. **Results:** The results revealed that maximum patients examined were between 21-30 years (30%) with female:male ratio of 3.14:1. The mean age of patients was 27.54 ± 9.04 years. Majority of patients were of low-income groups. Most of the patients were admitted within 3.14 ± 1.6 hours. Vomiting (92%) and abdominal pain (66%) was common complaints of patients. Electrocardiographic changes included arrhythmia in 6% cases with 4% ventricular tachycardia and 2% ventricular fibrillations. 42% patients had bradycardia and 20% had tachycardia. No cardiac pathology was diagnosed in the echocardiograph. Specific cardiac enzymes creatine phosphokinase-MB and troponin-I were normal. Lactate dehydrogenase was elevated in three patients; however normal liver function and urine test ruled out probability of myocardiac and hepatic injury. **Conclusion:** The present findings concluded that patients with organophosphorus poisoning are detected with electrocardiographic change; however, most of the cardiac damages can be healed with time except ventricular fibrillation and associated pulmonary edema. Mortality rate of 6% could have been prevented with advanced diagnostic and prompt therapeutic interventions.

INTRODUCTION

Organophosphorus compounds are varied form of chemicals that are produced by esterification of phosphoric acid and alcohol.[1] Such compounds are commonly used in agricultural, domestic and industrial practices.[2] These are common constituents of pest control agents such as parathion and malathion as well as nerve gas such as sarin, tabun, soman, VE and VX. These are also extensively used in the production of plastics, lubricants and solvents.[1] In agriculture-based countries like India, the organophosphates are widely used to protect crops in the form of pesticides, herbicides or insecticides.[2] Because of their easily availability in nearly every general store at a cheap rate, these agents are also misused for suicidal purposes globally.[3-6] Their acute or chronic exposure is highly toxic for all living beings. Organophosphorus poisoning in human can occur due to either direct skin contact or inhalation and ingestion of organophospahtes.[1] Storekeepers often store these components inappropriately due to unawareness about their hazards which increases the chance of poisoning with these compounds among the personnel handling them.[6]

According to an estimation by World Health Organisation (WHO), the overall incidence of organophosphorus poisoning is 3 million per year with approximately 3,00,000 deaths.[6] Out of 3

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million cases, approximately 1 million cases are due to accidental exposure, and 2 million cases are of suicidal poisonings.[7] The rate of fatal cases in developing countries due to organophosphorus poisoning have been estimated to be 20% higher than developed countries.[8] Suicidal poisoning with organophosphorus has been estimated as 40-60% in African countries, 10-36.2% in developed countries, and 65- 79.2% in developing countries.[8] According to a survey report, the suicidal cases due to organophosphorus chemical consumption are 10.3%- 43.8% in India and 56.4% in Nepal.[9] However, due to enforcement of law regarding controlled and wise use of organophosphorus chemicals and advancements medical facilities, the fatality rate related to such poisoning has declined. According to a systematic review in the 1990s, there were 3,72,000 deaths/year due to organophosphorus pesticides usage which decreased to 1,68,000 deaths/year in 2010–2014 in India.[10]

Organophosphorus compounds are toxic chemicals and act as acetylcholine esterase inhibitor. Acetylcholine esterase regulates neurotransmitter acetylcholine by breaking it down to choline and acetate.[6,11] Irreversible binding of organophosphorus compounds to acetylcholine esterase leads to accumulation of acetylcholine, resulting in over-stimulation of nicotinic and muscarinic receptors present in central and peripheral nervous system.[12] Organophosphorus exposure exhibits mild to severe clinical pathological manifestations on the basis of nature of compounds, amount consumed, and the duration gap between the contact and presentation time in the hospital. It affects cardiovascular, central nervous, gastrointestinal, renal and respiratory system. Organophosphorus poisoning causes restlessness, anxiety, excessive sweating, nausea, vomiting, diarrhoea, abdominal cramp, loose stools, frequent urination, weakness and increased salivation/lacrimation.[13] Cardiac toxicity due to organophosphorus compounds is characterized by hypo-/hyper- tension, sinus bradycardia, sinus tachycardia and cardiac arrest.[14] The cardiac complications are often fatal; however it can be prevented if diagnosed early and treated properly.[6] Electrocardiography and echocardiography are promising diagnostic procedure to detect cardiac damages. Electrocardiographic changes such as QTc prolongation, ST-T changes, and other arrhythmias are dangerous for patients.[2] Moreover, in recent times, measurement of biochemical cardiac markers such as creatine phosphokinase-MB (CPK-MB), troponin I (cTn-I) and lactate dehydrogenase (LDH), along with clinical history and interpretation of electrocardiogram and echocardiogram, plays crucial role in rapid confirmation of myocardial injury.[6,14,15] The present study was aimed to detect the electrocardiographic and echocardiographic changes as well as the concentrations of cardiac biomarkers in case of acute organophosphorus poisoning.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective clinical study which was conducted from March 2021 to September 2022 (18 months) at the Department of Medicine, Darbhanga Medical College and Hospital (DMCH), Laheriasarai, Bihar, India.

Study Population

The study was conducted on patients who consumed organophosphorus insecticides and were admitted in medicine wards of DMCH within 24 hours of consumption of the poison. Prior approval for the study was obtained from the hospital ethical committee. Patients with multiple poisonings with other drugs such as opioids, diazepam, barbiturates; concomitant cardiovascular diseases or who were already treated outside were excluded from the study.

After explaining the possible prognosis procedure for organophosphorus poisoning, an informed consent was obtained each patient or their guardian before ~~the~~ initiating the study. Detailed history, clinical examinations and laboratory investigations were noted down in a pre-set proforma. The privacy of every patient was maintained.

Data Collection Techniques and Tools

A 12 leads electrocardiography was performed by the standard method as recommended by American Heart Association with speed of 25 mm/second and 1 mv = 10mm standardization. The data were recorded in the graphical peak form called electrocardiogram. Trans-thoracic 2-D, M-mode and Doppler echocardiography was employed ~~done~~ once the patient's condition was stabilized. Patient's blood was drawn for analyzing hemoglobin level, total and differential count, erythrocyte sedimentation rate, blood sugar, blood urea, serum creatinine, serum electrolytes, serum CPK-MB, serum LDH & cTn-I using commercially available rapid test kit according to the manufacturer's instructions. If serum LDH level was found to be elevated in patients then amylase, lipase and serum creatine phosphokinase (CPK) level were also measured to determine alternate sources of elevated serum LDH.

Statistical Analysis

The statistical analysis was performed to validate the results using GraphPad Prism and Microsoft Excel. The results were described as percentages, mean ± standard deviation and frequencies wherever applicable. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 50 patients fulfilling inclusion-exclusion parameters and were poisoned with organophosphorus insecticides were included in the study. All the selected cases were studied after receiving a written approval from their side. The

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diagnosis was initiated with routine investigations regarding type of organophosphorus compound ingested and time taken for hospital presentation after ingestion of the toxic compound.

Demographic details of patients

The patients selected for the study were between 12 and 51 years old. The mean age of the patients was 27.54 ± 9.04 years. The data revealed that maximum patients admitted of organophosphorus poisoning belonged to age group 21-30 years (44%) followed by 11-20 years (28%; Table 1). Cases of poisoning in individual above 50 years were least. The ratio of female and male in the present study was 3.16:1. Total 38 female ~~patients~~ (76%) and 12 male patients (24%) were involved in study (Figure 1A).

Out of 50 patients, 25 (50%) were married, 17 (34%) were unmarried and 8 (16%) were widow (Figure 1B). Total 15 (30%) patients had graduation or higher qualification and 14 (28%) patients had cleared higher secondary education, 14 (28%) were illiterate and 7 (14%) patients were literate (Figure 1C).

Based on occupation-wise distribution, 23 (46%) patients were house wives, 12 (24%) were students, 7 (14%) worked at service sector, 5 (10%) were unemployed and 3 (6%) were farmers (Figure 1D). Patient's monthly family income has been listed in Table 2.

Mode and type of organophosphorus poisoning

All the poisoning occurred via oral intake of organophosphorus poisoning and the number of accidental cases were much higher (78%) as compared to intentional intake (22%; Figure 2a). 21 (42%) cases was due to intake of temephos, a diphenyl sulphide group of organophosphorus compounds, 13 (26%) consumed malathion, 8 (16%) each ingested carbo phenothion and ethyl parathion (Figure 2b).

Time of manifestation before hospital presentation

Average time interval of patient's admission to hospital was 3.14 ± 1.6 hours. Maximum patients were presented to hospital within an hour of the incidence (Table 3).

Common clinical manifestations of organophosphorus poisoning

The study found that lacrimation, shedding of tears was the most common symptoms of organophosphorus poisoning which was experienced in 96% of patients. This was followed by vomiting (92%), conjunctival redness of eye (92%), vision blurring (90%) and excessive saliva formation (90%). Other important muscarinic symptoms such as urinary incontinence, diarrhoea, excessive sweating, tightening of chest and tachypnoea were also observed (Table 4). The patients were also observed for nicotinic and central nervous system symptoms. Fasciculation and muscular twitching were experienced by 42% and 40% patients. Convulsion and unconsciousness were also seen in 6% and 11% cases respectively (Table 4).

Cardiac effect of organophosphate poisoning

Total 12 electrographic leads were taken at the time of admission to hospital. The electrocardiographic readings were taken every day or when required. Analyzing the changes in ST segment and type of T-wave, it was found that 42 (84%) has no change in their ST segment and 38 (76%) patients had normal upright T-wave. However, non-specific ST changes and ST depression was present in 7 (14%) and 1 (2%) case respectively. Also, T-wave flattening and inversion was analyzed in 7 (14%) and 5 (10%) cases. The diagnosis revealed that 7 (14%) and 2 (4%) patients had right bundle branch block and left bundle branch block respectively. In 4 (8%) cases prolonged QTc interval was present. Right and left axis deviation was present in 9 (18%) and 5 (10%) patients respectively. However, 36 (72%) patients had no changes in their axis deviation (Table 5).

Transthoracic echocardiography using 2-dimensional, M mode and Doppler was performed for all patients once their stable health condition was attained. Three patients died due to complications of poisoning. Left Ventricular End systolic and diastolic diameter, Interventricular Septal Thickness, Left Ventricular Fractional Shortening, Ejection Fraction, Right Ventricular Internal Dimension, Regional Wall Motion Abnormality and Diastolic Dysfunction was monitored. All 47 patients presented normal echocardiogram. No structural and functional abnormalities were diagnosed.

Effect of organophosphorus poisoning on cardiac enzymes

The cardiac enzymes such as lactate dehydrogenase (LDH), creatine phosphokinase (CPK), and troponin-I (cTn-I) play important role in regular maintaining of vital functions of body. Therefore, the cardiac enzymes concentrations were analyzed at different time intervals using available laboratory kits. CPK-MB fraction was found to be within normal limits. cTn-I was also tested negative for the patients (Table 6). Serum LDH concentration was found to be elevated in three patients; however normal level was attained till day 7.

Since, specific cardiac enzymes CPK-MB and cTn-I was within normal limits, there was high probability that elevation in LDH was not due to myocardiac effect. There are several reasons for the raise in LDH level in an individual. Acute organophosphorus poisoning is often found to be associated with myocardial damage, liver damage or pancreatitis. In order to predict the actual reason for the rise in the concentration of serum LDH and rule out the chance of increase in LDH due to myocardium, various other clinical investigations were carried out in those patients. Concentration of serum creatine phosphokinase, amylase, lipase and liver function test was analyzed. Clinical and microscopical examination of urine was also performed. In all the patients' ultrasonic examination was used to determine pancreatitis if any. Concentration of lipase and amylase were

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elevated at initial days of admission; however, it came within normal limit till the day of discharge. Urine and liver function test gave normal report. Ultrasound showed features of pancreatitis. These all consequences pointed that the raised LDH level was due to pancreatitis instead of myocardium or liver damage.

Complications of organophosphorus poisoning and Mortality rate determination

On summarizing all the diagnostic analysis, it was found that out of 50 patients, complications due to organophosphorus poisoning were developed in total 10 (20%) cases. These included ventricular fibrillation (2%), ventricular tachycardia (4%), pulmonary edema (6%), aspiration pneumonia (4%), and Mycobacterium infection (4%); however, among them 7 patients recovered (Figure 2c). Total 3 patients died of complicated medical conditions. 1 patient died of ventricular fibrillation and rest 2 died of pulmonary edema.

The outcome of the study was that among the investigated population, majority of patients 47 (94%) survived, whereas 3 patients (6%) died of organophosphorus poisoning (Table 7).

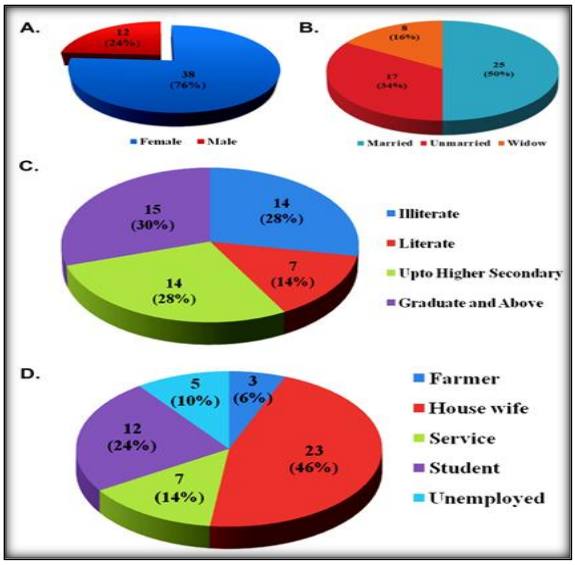

Figure 1: Demographic details of patients according to their (a) Sex; (b) Marital status; (c) Education; and (d) Occupation

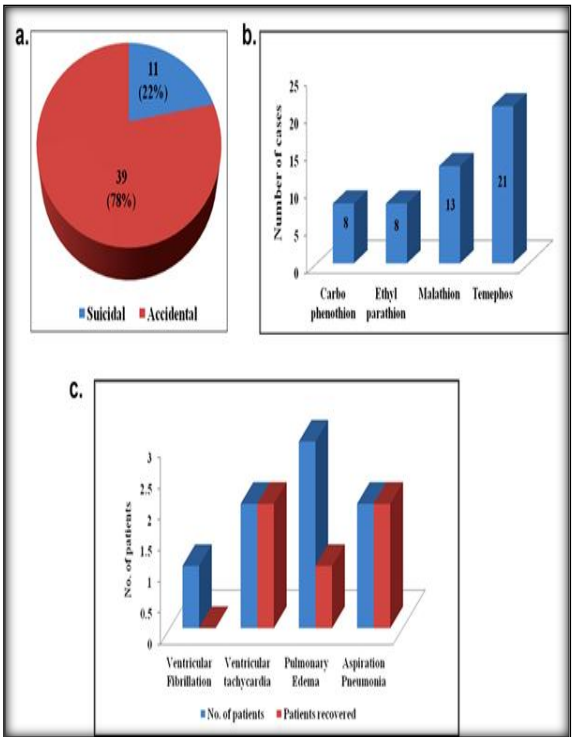

Figure 2: Description of (a) Mode of poisoning; (b) Type of poisoning; and (c) Complications of organophosphate poisoning

Table 1: Age-wise distribution of patients

Age Group (in years)	No. of patients	Percentage (%)	p-value*
11 – 20	14	28	0.08
21 – 30	22	44	
31 – 40	8	16	
41 – 50	5	10	
>50	1	2	
Total	50	100	

*The statistical evaluation was done using ANOVA, p-value ≤0.05 was considered significant.

Table 2: Economic status of the patients

Economic Status (Monthly Income in Rs.)	No. of patients	Percentage (%)	p-value*
100-499	14	28	0.01
500-999	16	32	
1000-1999	9	18	
2000-4999	4	8	
5000-9999	2	4	

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>10000	5	10	
Total	50	100	

*The statistical evaluation was done using ANOVA, p-value ≤0.05 was considered significant.

Table 3: Time taken to admit in hospital after ingestion of chemical

Time Interval (Hours)	No. of patients	Percentage (%)	p-value*
0-1	15	30	
>1-2	**8**	**16**	
>2-3	5	10	
>3-4	**9**	**18**	**0.04**
>4-5	9	18	
>5-6	**4**	**8**	

*The statistical evaluation was done using ANOVA, p-value ≤0.05 was considered significant.

Table 4: Common symptoms observed in patients

Variables	No. of patients	Percentage (%)
MUSCARINIC SYMPTOMS		
Ocular		
Diminution and blurring of vision	45	90
constricted pupil	35	70
Lacrimation	48	96
Eye ache	44	88
Conjunctival redness	46	92
Genitourinary		
Urinary incontinence	14	28
Gastrointestinal		
Vomiting	46	92
Diarrhoea	21	42
Abdominal cramp	33	66
Salivation	45	90
Sweating	32	64
Respiratory		
Tachypnea	10	20
Depression	2	4
Tightness in chest	40	80
Dyspnea	12	24
Basal crepitations in the lung	7	14
Cardiovascular		
Brachycardia	21	42
Hypotension	14	28
NICOTINIC SYMPTOMS		
Fasciculation	21	42
Muscular twitching	20	40
Tachycardia	10	20
Hypertension	7	14
CENTRAL NERVOUS SYSTEM SYMPTOMS		
Convulsion	6	12
Unconscious	11	22

Table 5: Findings of electrocardiography at the time of admission

Electrocardiographic findings	No. of patients	Percentage (%)	p-value*
1. Heart beat rate			
Normal	19	38	
Bradycardia	21	42	0.09
Tachycardia	10	20	
2. ST Segment and T wave Changes			
ST elevation	0	0	
ST depression	1	2	0.006
Non-specific ST changes	7	14	
T wave flattening	7	14	0.0009
T wave inversion	5	10	
3. Rhythm			
Normal	47	94	
Ventricular tachycardia	2	4	0.0001
Ventricular fibrillation	1	2	
4. Conduction			
Normal	37	74	0.0002

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QTc interval prolongation	4	8	
Left bundle branch block	2	4	
Right bundle branch block	7	14	
5. Axis			
Normal Axis	36	72	
Right Axis Deviation	9	18	0.004
Left Axis Deviation	5	10	

*The statistical evaluation was done using ANOVA, p-value ≤0.05 was considered significant.

Table 6: Cardiac enzyme concentration analysis in patients

Cardiac enzyme concentration	No. of patients on Admission	No. of patients on day 1	No. of patients on day 2	No. of patients on day 5	No. of patients on day 7
CPK-MB Level Normal	50	49*	-	-	-
CPK-MB Level Elevated	0	0	-	-	-
Troponin-I –ve test	50	49*	-	-	-
Troponin-I +ve test	0	0	-	-	-
Normal Serum LDH (100-190 U/L)	49	46*	46	44**	47
Elevated Serum LDH (>190 U/L)	1	3	3	3	0

*1 patient with acute organophosphate poisoning died between admission and 24 hours.
**2 more patients with acute organophosphate poisoning died between day 1 and 5.

Table 7: Number of mortality cases during the study

Outcome	No. of Cases		Total (%), n=50	p-value*
	Female (%), n=38	Male (%), n=12		
Recovered	36 (94.73%)	11 (91.67%)	47 (94%)	0.02
Expired	2 (5.26%)	1 (8.33%)	3 (6%)	

*The statistical evaluation was done using ANOVA, p-value ≤0.05 was considered significant.

DISCUSSION

Organophosphorus compounds or anti-cholinesterase compounds are one of the major compounds utilized in preparation of artificial insecticide/herbicide all across the world. In developing countries like India, it is widely used in agricultural practices and at home for pest control. It is one of the most common poisonings that occur either accidently or purposely. The poisoning may be due to oral intake, skin absorption or inhalation of organophosphorus compounds.

It has been found to cause serious cardiac complication, liver misfunctioning or pancreatitis which may be fatal; however early recognition and proper on-time treatment are the factors that could potentially prevent the disastrous outcome of the poisoning. The irony is that in light of limited studies related to frequency and pathogenesis of multifactorial toxicity, many medical practitioners are not completely aware of complications of organophosphorus poisoning. There are paucity of data and accurate evidence in support of prevalence and prognosis of cardiac toxicity associated with organophosphorus poisoning.[16] In the present study the extent of cardiac toxicity and organophosphorus poisoning was elucidated using electrocardiography changes, echocardiography and cardiac markers in patients.

Baseline investigations associated with organophosphorus poisoning

The study population included 50 patients with organophosphorus poisoning. The patients or their guardians were enquired about type and mode of organophosphorus compound consumed, delay in hospital admission, and symptoms experienced by them after ingestion. The age of the patients ranged from 12 to 51 years with their mean age was 27.54 ± 9.04 years. Soomro et al. and Amir et al. also studied organophosphorus poisoning and reported mean age of the patients was 29.61 ± 8.65 and 24.10 ± 9.44 years.[17,18]

Female dominance was observed in present study with female:male ratio of 3.16:1. Similar observation was reported by Baseer et al., Rehiman et al., and Banday et al. with female:male ratio 1.5:1, 1.47:1, and 3.2:1 respectively.[13,19,20] In contrast, few studies had also reported male dominance as in articles by Soomro et al. reported 1.2:1 and other mentioned 1.5:1 male:female ratio.[17,21] This difference may be attributed to the small sample size or regional differences.

Majority of patients belonged to 21-30 years (44%) followed by 11-20 years (28%) however least patients were above 50 years (2%). Similar pattern was observed by Gannur et al., where 44.62% were aged 21-30 years, 11-20 years were 30.99% and only 1.08% were above 50 years.[22] Amir et al. also reported that maximum organophosphorus poisoning was among individuals in their teens or below 30 years old.[18] It was reported that 44.67% patients of age 20-30 years and 17.33% are below 20 years. Selvaraj and Sudharson, and others also reported maximum (39%) patients of 20-30% and least patients (3.5%) above 50 years.[21,23]

In the present study 50% were married than single (34%). Similar observations had been reported by

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Ali et al. (69.23%), Jawarkar et al. (60.23%) and Hoq et al., (78%).[24-26] In present study, 28% were illiterate and only 14% were literate. 30% patients had educational qualification graduate or above and 28% only completed their higher studies. Pradhan et al. also mentioned that 76.42% were illiterate and 23.58% were literates.[8]

On occupation-wise analysis of patients, it was found that 46% of them were housewives, 24% were students, 14% were employed, 10% were unemployed and 6% worked on farms. Study by Kamath and Gautam also reported that 46% of studied population were housewives and 24% were farmers.[9] Banerjee et al. also reported 42% of cases of organophosphorus poisoning were among housewives followed by farmers, workers and students.[27] The present study envisaged that the organophosphorus poisoning was significantly dependent on economic status of the individuals. Maximum patients (78%) had their monthly family income below Rs. 2000, 12% had monthly income between 2000 and 10000 Rs. and 10% had monthly income of more than Rs. 10000. Jawarkar et al. and Woyessa and Palanichamy also reported that maximum patients of poisoning belonged to lower class groups, followed by middle and least by upper class.[25,28]

All patients were poisoned due to oral ingestion of organophosphorus compound either accidently (78%) or intentionally (22%). The result corroborated with Baseer et al. publication which stated that 87% cases of organophosphorus poisoning were due to accidental exposure.[19] This indicates that careful handling of, and raising awareness regarding organophosphorus compounds may reduce the cases of poisoning among individuals. On the contrary few publications reported intentional consumption of compound was higher rather than accidental ingestion.[21,27,29] These contradictions may be attributed to differences in socio-economic values, inadequate personal precautions, unawareness and problem handling capacity of individuals.

In present study maximum cases (42%) were due to ingestion of temephos, followed by malathion (26%). Ethyl parathion and carbo phenothion consumption was found 16% in each case. Auib et al. stated that although temephos is good insecticide at low concentration but possesses detrimental effect at higher concentration.[30] Satriawan et al. also reported it to be genotoxic, harmful for fetal growth and causes neuro-developmental defect.[31] In another study by Banerjee et al. parathion was found to be most common type of organophosphorus compounds consumed.[27]

The current study showed that the incidence of acute poisoning significantly depended on time taken to present the patient in hospital after ingestion of the compound. 30% of patients were admitted within an hour of consumption of various organophosphorus compounds. Only 8% patients were presented after 6 hours of ingestion. The study showed that the patients were admitted to hospital within an average of 3.16 hours of poisoning. Similar observations were made by Usha et al. the author stated that maximum patients (28.66%) were admitted within an hour of exposure of organophosphorus compounds and least patients (13%) beyond 6 hours.[32] Hoq et al. reported 18% patients were admitted within 30 minutes of exposure, 27% within 60minutes, 33% within 2-3 hours and 22% after 3 hours.[26] Sungur M, Guven reported that maximum patients were admitted within 9.4 hours of organophosphorus compound ingestion.[33]

Chief Complaints and Common Clinical Manifestations

Since, organophosphorus compounds act as acetylcholine esterase inhibitor, major clinical manifestations of organophosphorus poisoning occur due to increase in acetylcholine concentration leading to muscarinic, nicotinic and central nervous system over-stimulations. The commonest symptoms were related to ocular and gastrointestinal disorder. This included lacrimation (96%), conjuctival redness of eye (92%), vomiting (92%), vision blurring (90%), hypersalivation (90%), abdominal cramp (66%) and diarrhoea (42%). 80% patients have shown tightness in their chest. Other common symptoms included constricted pupil (75%), bradycardia (42%), fasciculation (42%), muscular twitching (40%), tachycardia (20%), tachypnea (20%), hypotension (28%), hypertension (14%), unconsciousness (11%) and convulsion (12%). Peter et al., reviewed clinical features of organophosphate poisoning and similar muscarinic and nicotinic stimulations were observed.[12] Goel et al. also reported vomiting as the most common complaint (97.08%) of patient's admitted.[34] Singh et al. reported blurred vision in all the cases and vomiting in 90% patients of organophosphorus poisoning.[35] Chintakale et al. reported increased salivation in 72.5% cases and stated it to be the most common symptom.[36] Priyadarsini et al., also studied clinical profile of patients with organophosphate poisoning and reported vomiting (50%), excessive saliva formation (36%), fasciculations (24%), tachycardia (20%,), diarrhoea (12%), hypertension (8%), unconsciousness (6%), hypotension (4%), bradycardia (2%) and convulsions (2%). Respiratory symptom as cough and breathlessness was noted in 36% cases.[37]

Cardiac effect of organophosphate poisoning

Cardiac responses are monitored by checking heart beat rate, rhythm disturbances, electrocardiography and echocardiography. In the present study bradycardia was more (42%) than tachycardia (20%) in patients. Similar pattern was reported by Arora et al., where bradycardia was in 46.67% and tachycardia in 21.66% patients.[6] In contrast Pannu et al. also mentioned tachycardia to be more frequent than bradycardia. The author reported 51.3% patients with tachycardia but only 1 case of bradycardia.[16] This difference may be due to different mode, route, type and severity of

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organophosphorus compounds consumed. Agarwal et al. informed bradycardia as early diagnostic parameter whereas tachycardia as indicator of severe poisoning.[38]

Electrocardiographic investigations revealed that majority of patients (84%) had no changes in ST wave segment whereas, 14% patients had non-specific ST changes and 2% has ST depression. None of the case showed ST elevation. Normal upright T-wave was detected in 76% patients. T-wave flattening and inversion was also detected in 14% and 10% patients. Prolonged QTc interval was observed in 8% cases. Left and right bundle branch block was detected in 4% and 14% patients. Axis deviation was also found in 18% (right axis deviation) and 10% (left axis deviation) cases. The electrography findings by Suguna and Aakash reported ST depression in 12% cases, none of the patients had ST elevation, 4% had T-wave flattening and 6% showed T-inversion. QTc interval prolongation was detected in 28% cases.[2] Ludomirsky et al., reported prolonged QTc to be related with severity of organophosphorus poisoning.[39] Pannu et al. also reported 4.1% patients with QTc interval prolonagation and 1.4% with ventricular tachycardia.[16] In 94% cases, patients possessed normal rhythm; however, ventricular tachycardia and fibrillation was present in 4% and 2% patients respectively. This may be attributed to compensatory response against hypoxemic condition after organophosphorus poisoning.[14] The case report by Munta et al. mentioned the presence of ventricular tachycardia due to series of changes in body post organophosphorus consumption which includes activation of sympathetic nerves, hypothermia, electrolye abnormalities leading to myocardial defects in patients.[40]

Two-dimensional colour Doppler echocardiography of 47 patients was performed in the present cases. Total 3 patients died before their condition could be stabilized and taken for further investigation. No abnormalities were detected using echocardiography. Jorens et al. also studied electro and echocardiography and reported normal echocardiography although there were changes in patient's electrocardiography report.[41] Maheshwari and Chaudhary also reported normal echocardiogram in spite of acute atrial fibrillation diagnosed in electrocardiography.[42] Talwar et al., also reported absence of any abnormal features in echocardiography in patients showing platypnea and orthodeoxia.[43] Ustundag et al. also reported 2 cases of paroxysmal atrial fibrillation without any cardiac pathology.[44] This implied that there was no myocardial defect in patients after stabilization and no further examinations were required. The cases would have shown different report if done earlier at bed side instrument was present.

Cardiac enzymes evaluation

The patients were serially studied for serum CPK-MB, cTn-I and LDH. Cardiac markers CPK-MB and cTn-I are ~~they are~~ specific cardiac biomarkers that are used for early detection of myocardial lesions.[15] The present analysis revealed that the CPK-MB level was normal in all the patients evaluated. The rapid kit test also estimated negative result for cardiac troponin-I. High serum LDH concentration was found in three patients, however it came to normal level till the day of discharge. All the patients with raised LDH level were tested for amylase, lipase, liver function test and urine test. Initially, serum lipase and amylase level were above normal range in those patients but gradually lowered to normal concentration till day.[7] Liver function test and urinal investigation showed normal report. The ultrasonic investigation of abdomen and x-ray of chest, normal CPK-MB, cTn-I and other normal reports implied that the reason of elevated LDH concentration was due to pancreatitis, not because of any myocardiac or hepatic defects. Jorens et al. also reported that patients with non-specific ST changes and abnormal T-wave were evaluated with normal cardiac enzymes concentration and ruled out myocardiac defects.[41] Huang et al., and Rompianesi et al. also reported elevated LDH, amylase and lipase concentration in patient with acute pancreatitis rather than myocardium.[45,46] Davies et al. explained that abnormal cardiac enzymes or disturbed electrocardiograph report points out the mechanisms in body induced due to organophosphorus poisoning. The body generates low systemic vascular resistance against organophosphorus compounds ingestion. The present study corroborates with the findings of previous publications. The present investigational study revealed absence of myocardium or hepatic injury by organophosphorus consumption.[47]

Mortality

The present study showed that 20% patients with organophosphorus poisoning had complications like, ventricular fibrillations (4%), ventricular tachycardia (2%), pulmonary edema (6%), Aspiration pneumonia (4%) and Mycobacterium infection (4%) but 14% patients recovered and 6% died of acute poisoning. Among total mortality case, 2% died because of ventricular fibrillation and 4% died due to non-cardiogenic pulmonary edema. Out of 50 patients, 3 patients died in which 2 were female and 1 was male. Total mortality rate ranges between 4% and 30% all over the globe, Kamath and Gautam reported 22% mortality.[9] Debnath et al., also reported 6% mortality due to respiratory failure and multi organ failure in patients with organophosphorus poisoning.[48] Saadeh et al. reported 4.35% mortality due to ventricular fibrillation.[49] Karki et al. reported 8.1% patients died out of 37 patients. Out of these died patients, 2 had non-cardiogenic edema and 1 had ventricular arrhythmia.[5]

The present study in accordance with previous reports suggested that the effective and quick treatment without delay would further reduce the

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mortality rate among patients with organophosphorus poisoning.

Limitations

This was a small single centric study which had a smaller number of patients as a result of which actual differences in clinical findings could not attain statistical significance in all the parameters studied. The present study may not be true reflection of the manifestation of the organophosphorus poisoning in patients likely because of referral bias and pre-treatment of cases by general practitioners. Actual behaviour, signs and symptoms of acute poisoning may be different if referral population is drawn from different communities and geographical areas and cultural backgrounds. Study of other cardiac enzymes such as LDH isoenzymes, natriuretic peptides and histopathological tests would reveal a clearer outcome of complications due to organophosphorus poisoning.

CONCLUSION

Analysis of electrocardiographic changes in ST segment, arrhythmia, and study of cardiac markers are important parameters to diagnose cardiac damage in case of organophosphorus poisoning. Cardiac damage was found in organophosphorus poisoning however it healed with therapy except ventricular fibrillations and pulmonary edema which led to 6% mortality rate. Early diagnosis and social awareness can reduce the mortality rate.

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Declaration of Conflicting Interests

The Authors declare that there is no conflict of any interest.

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