Original Article

Respiratory failure and thrombocytopenia in patients with Organophosphorus insecticide poisoning

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Objectives: To investigate the frequency of complications in patients with acute Organo-Phosphorus (OP) poisoning.

Methodology: This cross-sectional study was conducted at the National Poison Control Center (NPCC), Jinnah Postgraduate Medical Center (JPMC), Karachi, Pakistan from May 2012 to August 2012. A total of 100 patients with acute OP-poisoning were included in the study. Hemoglobin (Hb) levels, white blood cell (WBC) count, platelet count, chest-crepts, muscle-fasciculations, score on Glasgow comma scale, serum cholinesterase levels, mortality rates and causes of mortality were recorded.

Results: Of 100 patients, 69 were females and 31 were males with female/male ratio 2:1. The most frequently affected age group was 21-30 years in both genders and the most frequent reason for poisoning was an attempted suicide (98%). 50% patients had serum cholinesterase levels below normal values. 81% patients had Hb levels of 10mg/dl or less. Out of 100 patients, 21(60%) patients died because of sudden respiratory failure, 9 (25%) due to cardiac arrest, 2 (5.7%) due to septic shock and 3 (8.5%) due to CNS depression. 54 patients recovered and discharged on follow up & 11 left against medical advice (LAMA). The mortality rate was 35%.

Conclusion: OP-poisoning, in addition to several other complications, caused respiratory failure, anemia and thrombocytopenia in most of the young patients admitted with suicidal intention using OP compounds. (Rawal Med J 2014;39: 246-250).

Key words: Organophosphorus (OP) poisoning, OP poisoning complications, respiratory failure, thrombocytopenia.

INTRODUCTION

Pesticides comprise a wide range of compounds including insecticides, herbicides and fungicides amongst others. Thus, far more than 1,000 active substances have been incorporated in approximately 35,000 preparations of pesticides used in agriculture.[1] Organophosphate compounds (OPCs), are amongst the most commonly used pesticides and are gradually emerging as an alarmingly increasing cause of accidental and suicidal poisoning. OPCs may be taken via oral, respiratory and/or transdermal routes.[1,2] Organo-phosphorus (OP) pesticide self-poisoning is estimated to kill around 200,000 people each year, largely in the Asia-Pacific region.[3] The principal pharmacological action is the inhibition of acetyl cholinesterase. This inhibition leads to accumulation of acetylcholine at nerve synapses and neuromuscular junctions, resulting in over-stimulation of acetylcholine receptors.[1] The initial over-stimulation is followed by paralysis of cholinergic synaptic transmission in the central nervous system (CNS), in autonomic ganglia, at parasympathetic and some sympathetic nerve endings (e.g., sweat glands), and in somatic nerves.[4,5]

Signs of organophosphate poisoning (OPP) may be classified into effects secondary to muscarinic, nicotinic, and central nervous system receptor over-stimulation. Muscarinic over- stimulation is manifested as hyperactivity of the parasympathetic system, including miosis, bradycardia, lacrimation and bronchial secretion. Nicotinic effects include muscle fasciculation's, cramping, and weakness while respiratory depression, seizures, and unconsciousness are the consequence of central

nervous system effects.[6] The aim of this study was to determine the frequency of complications in patients with acute OPP.

METHODOLOGY

This study was conducted at The National poison control Center (NPCC), Jinnah postgraduate medical center, Karachi, Pakistan from May 2012 to August 2012 and included a total of 100 patients. History was taken either directly from the patient or their attendants. Clinical examination of the patients was conducted to determine muscle fasciculation, salivation, crepts in chest, pupil size, gut motility and level of consciousness (GCS). Serum samples were taken for complete blood picture (CP), serum urea, createnine, electrolyte, coagulation profile and serum cholinesterase. Serum cholinesterase levels were checked on the day of admission, after 24 hours, 3rd day, 5th day and 6th day post admission.

Table 1. WHO atropine protocol.

Stat dose inj	4mg
Every 15 min for first 48hours	2mg
Half hourly for next 24 hours	1mg
1 hour for next 24 hours	1mg
2 hour for next 24hours	1mg

Patients were managed using standard protocol and general measures were taken for all patients: nothing per oral (NPO), gastric lavage, oxygen, nasogastric tube, Foley catheter, antibiotics and diazepam, as per requirement. After gastric lavage, patients were shifted to the intensive care unit (ICU), maintaining two intravenous (IV) lines. Subsequent to nasogasrtic tube, atropine was started as per WHO guidelines for six days (Table 1). Data were analyzed using SPSS version 15.

RESULTS

Out of 100 patients, there were 69 female and 31 male with female/male ratio was 2:1. The most frequently affected age group was 21-30 years in both sexes (Table 2). The most frequent reason for poisoning was an attempted suicide (98%).

Table 2. Ages of patient.

Age	Number	Percent
<20	26	26.0
25-30	44	44.0
30-35	10	10.0
35-40	1	1.0
>45	19	19.0
Total	100	100.0

Blood parameters showed altered hemoglobin (Table 3), WBC count (Table 4), serum electrolytes. Importantly, 16 (16%) of the patients showed decreased platelet counts (Fig. 1 A).

Table 3. Hemoglobin level (gm/dl).

Hb	Number	Percent
7	12	12.0
8	17	17.0
8	1	1.0
9	25	25.0
10	26	26.0
11	1	1.0
12	9	9.0
13	1	1.0
14	4	4.0
15	1	1.0
16	2	2.0
18	1	1.0
Total	100	100.0

Serum cholinesterase level was below the normal value in 50% patients. The mortality rate was 35%. Out of 100 patients, 21(60%) patients died because of sudden respiratory failure, 9 (25%) patients due to cardiac arrest, 2 (5.7%) of them due to septic shock and 3 (8.5%) due to CNS depression (Figure 1B, Appendix VI). 54 patients recovered & discharged on follow up & 11 left against medical advice (LAMA) (Table 5). Clinical features of patient (chest crept, muscle fasciculation's & GCS score and serum cholinesterase level are shown in Fig. 2).

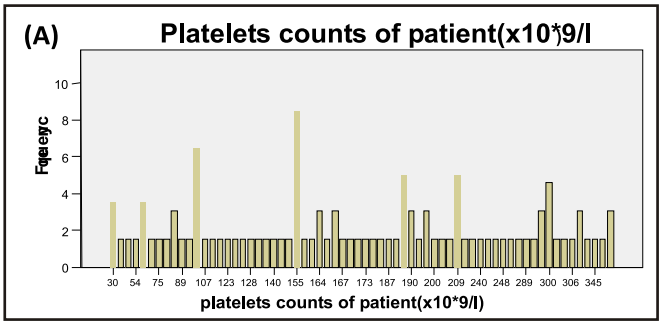
55 patients were treated with mechanical ventilation, 30 cases of endotracheal intubation; tracheostomy tube in 5 patients, 20 patients recovered spontaneous breathing, 35 patients died.

Table 4. White blood cells counts (x10*9/l).

WBC	Number	Percent
4	1	1.0
5	13	13.0
6	10	10.0
7	10	10.0
8	14	14.0
9	11	11.0
10	7	7.0
11	5	5.0
12	13	13.0
13	1	1.0
13	14	14.0
15	1	1.0
Total	100	100.0

Table 5. Mortality in OPP.

Cause of death	Number	Percent
Death due to respiratory failure	21	21.0
Cardiac arrest	9	9.0
Septic shock	2	2.0
CNS depression	3	3.0
Discharge	54	54.0
LAMA	11	11.0
Total	100	100.0



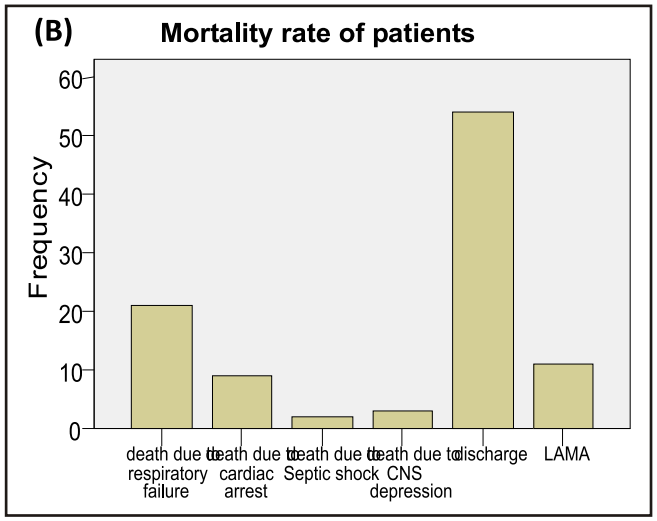


Fig. 1. (A) Platelet counts in patients with acute OP poisoning. (B) Mortality rates in patients with acute OP poisoning.

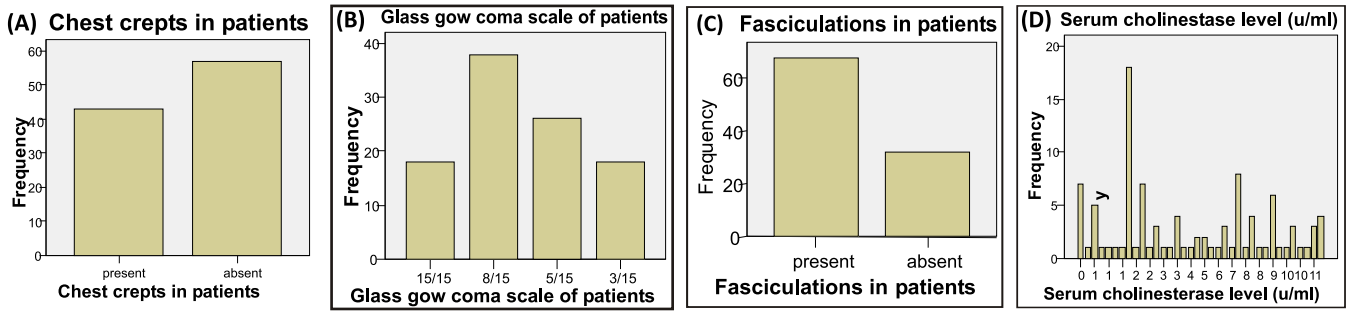


Fig. 2. Chest crepitus (A), Galasgow Comma Scale (B), Fasciculations (C) and serum cholinesterase levels (D) in patients with OP poisoning.

DISCUSSION

Organophosphorus (OP) compounds have been widely used in agriculture for crop protection and pest control. Some of the OPs have also been successfully used for treating various medical conditions. Examples include the use of diisopropyl phosphorofluoridate (DFP), tetraethyl pyrophosphate (TEPP), and octomethyl pyrophosphotetramide (OMPA) for myasthenia gravis and esters to treat glaucoma (Ecothiopate). Some highly potent OP anticholinesterase compounds, including tabun, sarin, soman, and VX have been used as "nerve gases" in chemical warfare.[7] Organophosphorus compounds exert a wide range of toxicological effects. They cause a central failure of breathing leading to rapidly

progressive bradypnea and loss of central inspiratory drive.[8] OP detoxification takes placein liver and they are eliminated primarily through kidneys.[9] The histopathological changes observed in human liver observed in a forensic laboratory were congestion, centrilobular necrosis, fatty changes, alcoholic hepatitis and sinusoidal dilatation.[10] Cardiac manifestations include an increase in creatinine kinase and lactate dehydrogenase levels, sinus tachycardia, sinus bradycardia, hypertension, hypotension, impaired heart rate and force contraction.[11] ECG changes include prolonged QTc interval, ST segment elevation, low amplitude T waves, extrasystole and prolonged PR interval.[12]

OP leads to a delay in stimulus classification, affecting memory system of the brain and this impairment appears to persist even 6 months after poisoning.[13] Several chronic CNS disturbances include parkinsonian and pseudobulbar signs, alterations in effect, libido and memory, psychiatric or more insidious neuropsychological dysfunction and a cerebellar syndrome.[7] Hormonal imbalance especially sex hormones leading to adverse developmental outcomes related to pesticide exposure, including fetal death, intrauterine growth restriction, congenital malformations and male/female fertility have been reported.[14] Living in rural areas where large amounts of pesticides are applied represents a risk factor for fertility.[15]

It has been reported that the chronic exposure to pesticides leads to kidney failure.[16] Studies have shown that OP poisoning is associated with enhanced lipid peroxidation, reduced Glutathione levels and elevated antioxidant status and increased oxidative stress.[17] Acetylcholinesterase present in human red blood cells is the same as that found in the target synapses, and changing concentrations of red blood cell acetylcholinesterase are assumed to mirror the effects of OP agents in the target organs, provided the OP agent has equal access to the blood and synapses.

The usefulness of cholinesterase level estimations is limited by the physiological variations that occur within and between individuals in health, and the influence of disease states, medication and genetic variations in the enzyme.[18] Thus, serial measurements are of greater benefit than a single estimation. Further caution is required as there is no uniformly accepted standard technique each method has its own 'normal' range. In chronic exposure, depression of normal cholinesterase activity in blood by 80% is generally considered to be diagnostic of poisoning.[19]

Fasciculation's and other neuromuscular signs and symptoms may develop with depression of acetylcholinesterase in excess of 80% and there is a risk of death with depression of 90% or more.[20] However, animals can survive depression of 100% and humans have had 90-95% depression and recovered without treatment.[21] A study from Portugal concluded that cholinesterase recovery to above 10% of normal correlates with a good prognosis.

CONCLUSION

We found that OP poisoning caused respiratory failure, anemia and thrombocytopenia in most of the young patients who were admitted with suicidal intention using OPs. This information may be useful in future for preventing the incidence of poisoning by educating the population. Moreover, further studies (including appropriate controls) are required in this regard to confirm/second these findings.

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Conception and design: SIF, TAP
Collection and assembly of data: SIF, RAS, SK
Analysis and interpretation of the data: All
Drafting of the article: All
Critical revision of the article for important intellectual content: All
Statistical expertise: All
Final approval and guarantor of the article: All
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