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Evaluation of Serum Potassium Levels as Prognostic Marker in Acute Organophosphorus Poisoning in a Tertiary Care Centre

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Abstract
Background: *It is apparent that although inhibition of cholinesterase plays an important role in organophosphate (OP) toxicity, other factors are also important. One of the contributing factors for its severity is electrolyte imbalances esp. hypokalemia. This study was aimed at evaluating the levels of hypokalemia along with plasma cholinesterase (PChE) levels in predicting morbidity and mortality of acute OP poisoning in patients presenting in our hospital.*
Methods: *In this cross sectional study, patients with definitive diagnosis of OPC poisoning were enrolled. Pre-interventional history and clinical features were noted with severity assessment done according to Proudfoot classification, along with measurement of serum potassium ([K+]) and PChE levels.*
Results: *Thirty OP poisoned patients (22 men, 8 women) were enrolled. A total of 30 cases who presented with clinical features of opc poisoning were classified according to Proud foot classification. Among them, 68.4% of cases (13 out of 17) developed hypokalemia. Muscle weakness and fasciculations developed with mean serum [K+] levels of 2.90 ± 0.11. Ventilatory support was required at the mean serum [K+] levels of ± 0.10 mmol/L. Mortality was noted when the mean serum [K+] reduced to 2.7 ± 0.06 mmol/L. Correlation of the ventilator support and mortality with serum [K+] was significant (P < 0.001). Death was mostly observed among patients who had respiratory distress associated with hypokalemia and severly reduced PChE.*
Conclusion: *With severe clinical features of OP poisoning, there was severe reduction in serum [K+] and PChE levels. Hence, these biochemical findings can be encouraged as predictive markers of severity of op poisoning. Clinicians and medical toxicologists should consider hypokalemia as an alarming sign of poor prognosis in OPC poisoned patients.*
Keywords: *Hypokalemia ; Organophosphate Poisoning; Prognosis.*

Introduction

Organophosphate (OP) compounds are the most commonly consumed poison in India owing to their easy availability. Deliberate self-poisoning with pesticides, especially OP compounds, is an important public health problem worldwide which kills 200,000 people annually and its incidence keeps rising.

Table 1: Types of Organophosphorus Compounds

Dimethyl OP	Diethyl OP
PARATHION	METHYL PARATHION
DIAZINON	DICHLOROVOS
CHLOROPYRIFOS	DIMETHOATE
DICHLOROFENTHION	MALATHION
COUMAPHOS	FENTHION

OP compounds act by inhibiting the acetyl cholinesterase enzymes at muscarinic and nicotinic receptors, present in post synaptic membrane. As a result, erythrocyte cholinesterase and plasma cholinesterase (PChE) levels reduce in OP poisoning. It is apparent that although inhibition of cholinesterase plays a key role in the toxicity of OP compounds, individual susceptibility, inhibition of other enzymes and the direct effects of OPs on tissues are also important. One of the contributing factors for severity of OP poisoning is electrolyte imbalances. Hypokalemia is a frequent finding in Organophosphorus poisoning. In acute OP poisoning, the most common cause of mortality is respiratory arrest and acidosis as the result of respiratory muscle paralysis. Associated hypokalemia increases the muscle weakness. Hence, hypokalemia can be considered as an important cause for intensifying the poisoning.

Signs and symptoms of organophosphate poisoning

Muscranic manifestations :	
Bronchial tree	Bronchoconstriction, increased bronchial secretions, dyspnoea, cyanosis, pulmonary edema
Gastrointestinal	Anorexia, nausea, vomiting, cramps, diarrohea, fecal incontinence, tenesmus
Sweat glands	Increased sweating
Salivary glands	Increased salivation
Lacrimal glands	Increased lacrimation
Cardiovascular	Bradycardia, hypotension
Pupils	Miosis, occasionally unequal
Ciliary body	Blurred vision
Bladder	Urinary incontinence
Nicotinic manifestations :	
Striated muscle	Muscular fasciculations, cramps, weakness, Areflexia, muscle paralysis
Sympathetic ganglia	Hypertension, tachycardia, pallor, mydriasis
CNS manifestations :	
Early	Restlessness, emotional lability, headache, tremor, drowsiness, confusion, slurred speech, ataxia, generalized weakness, coma, convulsions, depression of respiratory and cardiovascular centers.
Intermediate	Ptosis, diplopia, facial palsy, paralysis of ocular, bulbar, neck, proximal and respiratory muscles, absent deep tendon reflexes.
Delayed	Delayed motor/sensory polyneuropathy, Landry Guillain Barre syndrome (rare), pyramidal tract generation.

Methodology

The study was conducted at MGM medical college and hospital, navi mumbai, over a period of two years between January 2017 and October 2018. 30 patients presenting in the emergency room with alleged history of Organophosphorus poisoning and features of respiratory failure (requiring ventilatory support), who fulfilled the proposed inclusion and exclusion criteria were included in the study. Prior ethical approval for the study and the protocol was obtained from the institution ethics committee. After explaining the possible prognosis in the course of organophosphorus poisoning, consent from a responsible attendant / informant of the patient was obtained before the actual study was initiated.

Inclusion Criteria for the study were as follows:

Patients who had allegedly consumed organophosphate poison and admitted to hospital within 24 hour of ingestion, irrespective of age / sex.

Exclusion Criteria for the study were as follows:

1. Patients with dual insecticide / multiple poisoning with other drugs such as opioids, diazepam, barbiturate etc.,
2. Patients with history of respiratory diseases including bronchial asthma, cardiac diseases, neuromuscular diseases like myasthenia gravis or muscular dystrophy or other concomitant illnesses.
3. All conditions causing of hypokalemia-alkalosis, diuretic use, beta agonist use, high aldosterone levels, insulin overdose, laxative abuse, corticosteroids,

Each of the patients with Organophosphorus poisoning were assessed clinically with detailed history and thorough physical examination.

Features correlating to: (a) Severity of organophosphorus poisoning and (b) Respiratory failure requiring mechanical ventilation was assessed.

(a) **Criteria for grading of severity of organophosphorus poisoning:**

- The grading of clinical severity of organophosphate poisoning

Grade	Symptoms	Signs
Mild	Dizziness, anxiety, headache, tightness of breath	Rhinorrhea, sweating, salivation, nausea, weakness, coughing, lacrimation, mild bradycardia and hypotension
Moderate	Restlessness, confusion, dyspnea, disorientation, abdominal pain, vomiting, diarrhea, drowsiness	Pallor, miosis/mydriasis, bradycardia/ tachycardia, hypotension/ hypertension, muscle twitching, fasciculation, respiratory depression, bronchorrhea, bronchospasm, loss of consciousness
Severe		Convulsions, respiratory failure, pulmonary edema, flaccid paralysis, involuntary micturation/defecation cyanosis, deep coma
Fatal		Coma, convulsions, hypersecretions and apnea within a few minute after exposure

- Based on various factor which influence on ventilator support the severity of organophosphate poison was classified in mild, moderate and severe.

Grades of poisoning	Level of consciousness	Pupil size	Fasciculation score
Mild	Normal GCS 12-15	≥ 4mm.	0-1.
Moderate	slightly decreased. GCS 8-11	2-3mm.	2-4.
Severe	Coma GCS <7, history of convulsion	< 1mm.	>5,

Fasciculation grading was done by giving 1 for each fasciculation to the anterior chest, back of chest, anterior and posterior side of abdomen, right and left arm, right and left leg. Total sum of this is called fasciculation score

(a) Criteria for diagnosis of respiratory failure: The patients who have features suggestive of severe poisoning as stated above are then assessed for ventilatory support based on following:

- Apnoea
- Obvious Hypoventilation
- Persistent Cyanosis inspite of 02 supplementation
- Persistent Tachypnoea - Respiratory rate (per minute) > 24
- Persistent Sp02 < 90% with Oxygen supplementation by non invasive means.
- Active use of accessory muscles of respiration.

Immediately after clinical assessment, blood samples were withdrawn and sent for investigations including Haemoglobin level, Total and Differential Blood Count (DC), serum electrolytes and Serum Cholinesterase levels, arterial blood gas analysis. (More investigations as necessary were done after institution of treatment and ventilation).

Immediate Management: Patients were given gastric wash, body wash and intravenous cannulation done. Injection Pralidoxime, bolus dose — 2 gm. I.V. and Inj. Atropine bolus 5-10 mg. IV every 5 mins were given till signs of atropinisation was achieved. Patients were reassessed for respiratory failure, and if so, intubated and shifted to Medical Intensive Care unit by Ambu ventilation. On arrival in the Medical Intensive Care Unit, the patients were immediately connected to ventilator and supportive therapy was initiated along with definitive therapy.

The Definitive Therapy for Organophosphorus poisoning: Protocol followed was:-20% of total atropine required for atropinisation as Inj Atropine Infusion with 1 mg bolus IV when required, till signs of atropiniiation were achieved - Inj PAM infusion at 50 - 100 mg / hr administered for the initial 48 hrs. depending upon the severity.(following the initial bolus 2 gm. given on arrival at emergency ward).

Supportive Therapy (as required): ■ Maintenance of intravascular volume by IV fluids. ■ Antibiotics to prevent and treat infections. ■ Inotropic support for cardiac functions. ■ Regular and thorough endotracheal and oral suction. ■ Chest and limb physiotherapy. ■ Nutritional support by enteral feeding when indicated. ■ Measures to reduce gastric acidity and secretions.

Ventilator Management: The patients were put on Drager Savina ventilator with the following initial settings-Mode - CMV with pressure support Tidal volume - 8-10 ml/kg body wt, Respiratory rate - 10-12 bpm, Fi02 -0.4-0.6, PEEP - 2 to 5 cm H2O. Increments were used as indicated. Weaning Technique consisted of SIMV with PS • CPAP T-Piece

Investigations: Repeat and / or additional investigations as required by the patient's status were ordered.

Serum cholinesterase: The reference values and Interpretations / definitions are as follows:

The serum cholinesterase activity was measured by kinetic/ DGKC calorimetric method, of Zydus Pathline Limited. EDTA samples were sent to the laboratory. The results are expressed in KU / L which is U / L x 1000. The laboratory reference range used in the present study for serum cholinesterase: 5100 to 11700 IU / Ltr. Based on the Serum Cholinesterase values, the severity of

poisoning may be defined as per (Proudfoot classification) with above normal range:

■ Mild poisoning: SCE. level 20 - 50 % of normal / >2001 IU / L
■ Moderate poisoning: SCE. level 10 – 20 % of normal /1001 -2000 IU / L
■ Severe poisoning: SCE. level < 10 % of normal / < 1000 IU / L

Statistical Analysis

All the collected data was entered in Microsoft Excel sheet and then transferred to Statistical Package of Social Sciences (SPSS Inc., Chicago, IL, USA) software ver. 17 for analysis. Data are presented with median or mean and standard deviation (SD) for continuous variables and frequency and percentage for categorical variables and analysed using chi-square test. One-way ANOVA test was used to compare the means of serum [K+] between different clinical features. P-value < 0.05 was taken as level of significance.

Results

In the study, Hypokalemia was observed in 63.3% of OPC poisoning cases.

Table no 1 Incidence of Hypokalemia

Hypokalemia	Frequency	Percent
Absent	11	36.7
Present	19	63.3
Total	30	100.0

Table no 2 Type of OPC compound vs Hypokalemia

			Hypokalemia		
			No	Yes	Total
type of OPC compound	Dichlorphos	Count	1	0	1
		%	9.1%	0.0%	3.3%
	Dimethoate	Count	1	1	2
		%	9.1%	5.3%	6.7%
	Parathion	Count	0	1	1
		%	0.0%	5.3%	3.3%
	Phorate	Count	8	13	21
		%	72.7%	68.4%	70.0%
	Unknown	Count	1	4	5
		%	9.1%	21.1%	16.7%
Total		Count	11	19	30
		%	100.0%	100.0%	100.0%

P value -0.545

As seen in the above table, hypokalemia was observed most commonly in phorate OPC poisoning cases (68.4%) followed by parathion (5.3% and dimethoate (5.3%) though the difference was statistically insignificant.

Table no 3 Convulsion vs Hypokalemia

			Hypokalemia		
			No	Yes	Total
Convulsion	No	Count	10	14	24
		%	90.9%	73.7%	80.0%
	Yes	Count	1	5	6
		%	9.1%	26.3%	20.0%
Total		Count	11	19	30
		%	100.0%	100.0%	100.0%

P value -0.256

As seen in the above table, Convulsion was observed in 26.3% of Hypokalemic OPC poisoning cases as compared to 9.1% of normokalemic OPC poisoning cases and the difference was statistically insignificant.

Table no 4 Respiratory Distress RR> 24 vs Hypokalemia

			Hypokalemia		
			No	Yes	Total
Respiratory Distress RR> 24	No	Count	8	9	17
		%	72.7%	47.4%	56.7%
	Yes	Count	3	10	13
		%	27.3%	52.6%	43.3%
Total		Count	11	19	30
		%	100.0%	100.0%	100.0%

P value -0.177

As seen in the above table, Respiratory distress (RR> 24) was observed in 52.6% of Hypokalemic OPC poisoning cases as compared to 27.3% of normokalemic OPC poisoning cases and the difference was statistically insignificant.

Table no 5 Requirement of ventilator vs Hypokalemia

			Hypokalemia		
			No	Yes	Total
Requirement of ventilator	No	Count	10	10	20
		%	90.9%	52.6%	66.7%
	Yes	Count	1	9	10
		%	9.1%	47.4%	33.3%
Total		Count	11	19	30
		%	100.0%	100.0%	100.0%

P value -0.03

As seen in the above table, ventilator requirement was observed in 47.4% of Hypokalemic OPC poisoning cases as compared to 9.1% of normokalemic OPC poisoning cases and the difference was statistically significant.

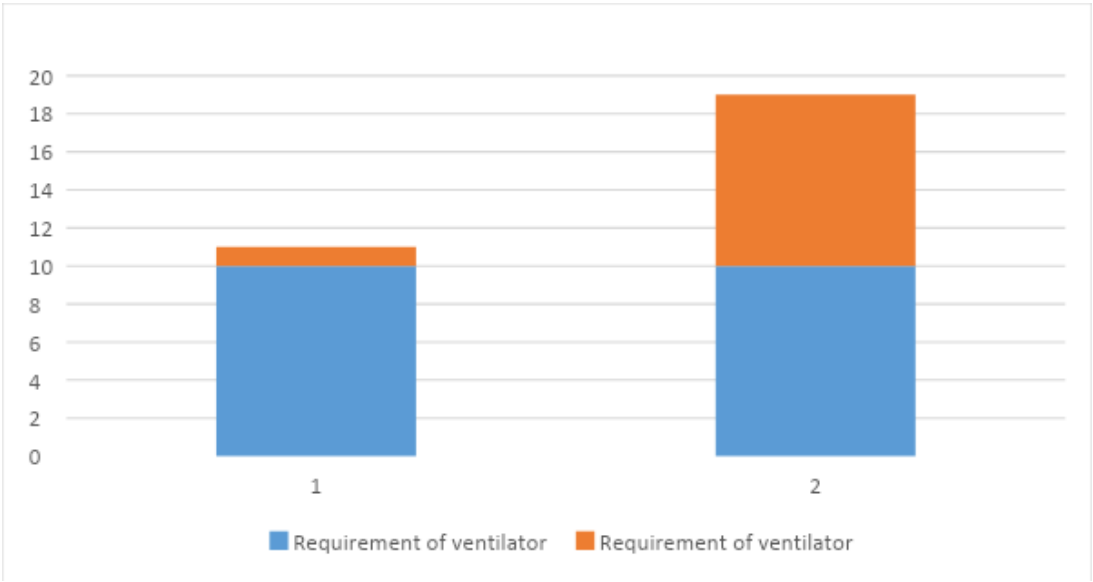

Table no 6 Apache Score vs Hypokalemia

	Hypokalemia				
	No		Yes		P value
	Mean	SD	Mean	SD	
Apache Score	7.5	6.4	14.1	9.0	.044

As seen in the above table, mean Apache Score was significantly higher in hypokalemic OPC poisoning cases as compared to normokalemic OPC poisoning cases.

Table no 7 Mortality vs Hypokalemia

			Hypokalemia		
			No	Yes	Total
Death	No	Count	11	13	24
		%	100.0%	68.4%	80.0%
	Yes	Count	0	6	6
		%	0.0%	31.6%	20.0%
Total		Count	11	19	30
		%	100.0%	100.0%	100.0%

P value -0.03

As seen in the above table, death was observed in 31.6% of Hypokalemic OPC poisoning cases as compared to 0 % of normokalemic OPC poisoning cases and the difference was statistically significant.

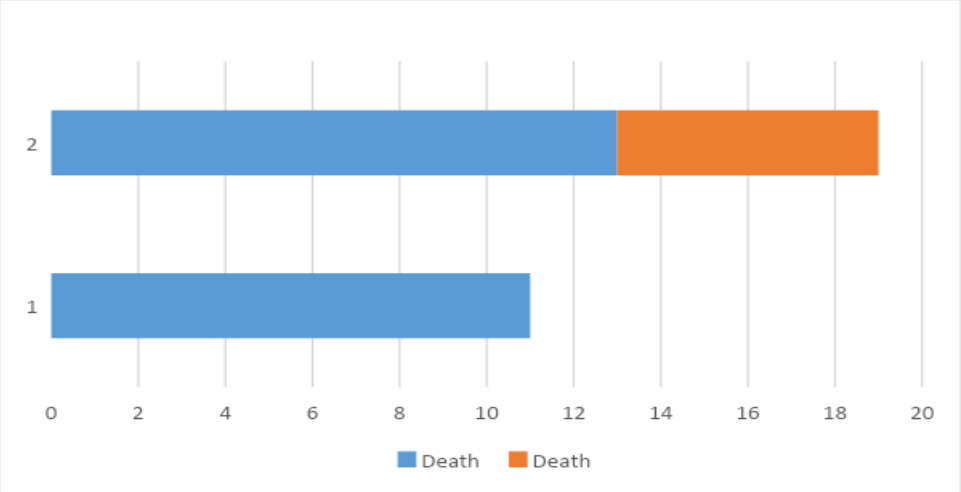

Table no 8 Duration of hospital stay vs Hypokalemia

			Hypokalemia		
			No	Yes	Total
Duration of hospital stay	less than 10 days	Count	9	13	22
		%	81.8%	68.4%	73.3%
	more than 10 days	Count	2	6	8
		%	18.2%	31.6%	26.7%
Total		Count	11	19	30
		%	100.0%	100.0%	100.0%

P value -0.624

As seen in the above table, more than 10 days was observed in 31.6% of Hypokalemic OPC poisoning cases as compared to 18.2% of normokalemic OPC poisoning cases and the difference was statistically insignificant.

Discussion

In the present study, there was male predominance (73.3%) as compared to female (26.7%). Similarly in the study conducted by Tanveer Hassan Banday et al., the female to male ratio is 1:3.2. The incidence of poisoning was higher in males than in females (76.6% Vs. 23.3%).[1] Similar trend was also observed by Safdar *et al.*, and Aziza *et al.*[2,3] However, the female to male ratio given by Ather *et al.*, is 1:1 and Tall *et al.*, is 1:1.8 which is quite different from present study. [4,5]

In the present study, Hypokalemia was observed in 63.3% of OPC poisoning cases. Similarly in the study conducted by Tanveer Hassan Banday et al., hypokalemia were found in 15.03% of cases respectively.[1]

In the present study, phorate (70%) was the most common type of OPC poisoning followed by dimethoate (6.7%), dichlorphos (3.3%) and parathion (3.3%)

In the present study, mean Apache Score was significantly higher in hypokalemic OPC poisoning cases as compared to normokalemic OPC poisoning cases.

In the present study, hypokalemia was observed most commonly in phorate OPC poisoning cases (68.4%) followed by parathion (5.3% and dimethoate (5.3%) though the difference was statistically insignificant.

In the present study, hypokalemia was observed most commonly in severe grade of OPC poisoning cases (42.2%) followed by moderate grade (36.8%) and mild (21.1%) though the difference was statistically insignificant. Similarly in the study by Syed M Ahmed et al., out of 86 patients, 14 (16.3%) had mild, 30 (34.9%) had moderate and 42 (48.8%) had severe grade of poisoning. In the present study, Respiratory distress (RR> 24) was observed in 52.6% of Hypokalemic OPC poisoning cases as compared to 27.3% of normokalemic OPC poisoning cases and the difference was statistically insignificant.[6]

Ventilatorrequirementwas observed in 47.4% of Hypokalemic OPC poisoning cases as compared to 9.1% of normokalemic OPC poisoning cases and the difference was statistically significant. This findings is in agreement with the study conducted by Banday, et al., in which Ventilator requirement was observed in 39.8% of OPC cases.[1]This findings is in agreement with the study conducted by Mahadeshwara Prasad et al in which both respiratory distress and mechanical ventilation taken together and statistically significant(p value < 0.001).[7]

In the present study, hypokalemia was observed most commonly in severe proud foot grade of OPC poisoning cases (68.4%) followed by mild (26.3%) and moderate grade (5.3%) though the difference was statistically insignificant.

In the present study, Convulsion and Fasciculation was observed in 26.3% and 15.8% of Hypokalemic OPC poisoning cases and the difference was statistically insignificant. This findings is in agreement with the study conducted by Indranil Banerjee et al., Fasciculation was observed in 10% of OPC poisoning cases.[8]

In the present study, death was observed in 31.6% of Hypokalemic OPC poisoning cases as compared to 0 % of normokalemic OPC poisoning cases and the difference was statistically significant. In D.R. Mahadeshwara Prasad et al study, death occurred in patients with a mean potassium levels of 2.90 +/- 0.057 meq/dl (p value < 0.001). In Lyzhnikov EA et al study, severe arrhythmia and cardiac arrest leading to death occurred in 29 patients who are found to have hypernatremia and hypokalemia.[7,9]

In the present study, more than 10 days was observed in 31.6% of Hypokalemic OPC poisoning cases as compared to 18.2% of normokalemic OPC poisoning cases and the difference was statistically insignificant.

Conclusion

The ease of access to OPCs in developing countries like India has made this compound the main tool for suicidal poisoning. Present study was conducted keeping in mind the paucity of studies for OPC-Poisoning and the relation of electrolyte derangements with it. From the study conducted, it was found that Hypokalemia increases both morbidity and mortality in organophosphorus compound poisoning significantly. Hence Hypokalemia can be used as a reliable and a cost effective marker of morbidity and mortality in organophosphorus compound poisoning. Early hospitalization and correction of hypokalemia can be life saving in OPC-Poisoning.

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Conflict of interest: None

Ethical approval: The study was approved by the institutional ethics committee.

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