HYPOKALAEMIA IN ORGANOPHOSPHOROUS COMPOUND POISONING

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ABSTRACT

BACKGROUND

Inhibition of cholinesterase plays a key role in organophosphate (OP) toxicity. There are other factors which contribute to the severity of poisoning. One of them is electrolyte imbalances such as hypokalaemia. The aim of our study was to find out the value of hypokalaemia in association with plasma cholinesterase (PChE) levels in assessing the morbidity and mortality of OP poisoning.

MATERIALS AND METHODS

In this cross-sectional study, patients with definitive history of OP poisoning were taken as subjects. Pre-interventional clinical features were observed and noted with severity assessment as per Proudfoot's classification along with measurement of serum potassium ion ([K+]) concentration and PChE level.

RESULTS

Fifty OP poisoned patients (32 men, 18 women) were enrolled with median age of 30 years. The most common clinical manifestation was Respiratory distress (50%) followed by fasciculation and neck muscle weakness (44%) followed by diaphoresis (30%) and others. A total of 28 cases presented with one or more severe clinical features according to Proudfoot classification, among them 56% of cases (20 out of 28) developed hypokalaemia. Muscle weakness or fasciculation developed with mean serum [K+] of 3.39 ± 0.60. Ventilatory support was required at the mean serum [K+] of 3.47 ± 0.66 mmol/L. No fatality was noted. Correlation of the severe clinical features and serum [K+] was significant ($P < 0.05$). We also noted that severe clinical features were associated with marked suppression of PChE (> 50%).

CONCLUSION

Serum [K+] and PChE level are greatly reduced in patients with OP poisoning with severe clinical features. Hence, these biochemical markers can be considered predictors of outcome in OP poisoning. Physicians should consider hypokalaemia associated with reduced PChE level as alarming signs of poor prognosis in OP poisoned patients and the need for ICU admission and ventilatory support.

KEYWORDS

Organophosphorous compound (OP), Acetylcholinesterase (AchE), Pseudocholinesterase (PchE).

HOW TO CITE THIS ARTICLE: Narasimhamurthy DT, Hegde SV. Hypokalaemia in organophosphorous compound poisoning. J. Evolution Med. Dent. Sci. 2017;6(84):5832-5834, DOI: 10.14260/jemds/2017/1267

BACKGROUND

Organophosphorous compounds (OP) are one of the most commonly used insecticides in India and Asia.[1] They are the most commonly used agents for poisoning in India due to their easy availability. In some instances, severe poisoning may occur as an occupational hazard.[2] It is not a common health issue in developed nations, because access to poisons are restricted. Insecticides being used as suicidal agents, especially OP compounds, is an important public health problem worldwide and its incidence keep raising.[2]

Mechanism of action of OP compound is by inhibiting acetylcholinesterase (AchE) at muscarinic and nicotinic receptors. The commonly measured cholinesterases are butyrylcholinesterase (BuChE) and red cell cholinesterase. BuChE is produced in the liver. It is secreted into blood to metabolise xenobiotics. The latter is found in RBCs (PchE). Inhibition of these enzymes serves as the marker of poisoning.[3,4] Enzyme inhibition in RBCs will predict AchE inhibition at synaptic levels in acute poisoning. Hence, determination of PchE level is used for screening as well as for the diagnosis of OP poisoning so that proper and immediate intervention is possible.[5]

Although, we have understood the mechanism of OP toxicity as a result of cholinesterase inhibition, various health effects following exposure to OP are yet to be completely understood. It is apparent that although inhibition of cholinesterase plays a key role in OP toxicity, there are other factors which are important like individual susceptibility and direct effects of OP on tissues.[6] Electrolyte imbalances are one among the contributing factors for the severity of OP poisoning. In acute OP poisoning, the most common cause of mortality is respiratory failure as a result of respiratory muscle paralysis.[6] Hypokalaemia is also a frequent finding in OP poisoning either due to GI loss or through excessive secretions. Associated hypokalaemia increases muscle weakness. Hence, hypokalaemia can be considered as an important factor in the poisoning.[7]

'Financial or Other Competing Interest': None.
Submission 29-08-2017, Peer Review 07-10-2017,
Acceptance 12-10-2017, Published 19-10-2017.
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MATERIALS AND METHODS

Following ethical clearance, a cross-sectional study was conducted in Department of Medicine, Victoria and Bowring and Lady Curzon Hospitals attached to Bangalore Medical College and Research Institute from February 2016 to June 2017. Patients with definitive history of OP poisoning were taken into the study. Patients with kidney disease, Heart disease and patients who are already on diuretics are excluded from the study. As soon as the patient is received, clinical features were observed and noted with severity assessment as per Proudfoot classification[8] (Table 4) along with measurement of serum potassium ion ([K+]) concentration and PChE level. The serum [K+] levels of less than 3.5 mmol/L were considered as hypokalaemia.[9] The PChE level was measured. The normal values of PChE range from 5320 to 11700. Data were analysed using descriptive statistics and unpaired student 't' test. Data were analysed using SPSS software (version 17).

RESULTS

Demographic Features

In this study, 50 OP poisoned patients (32 men, 18 women) were enrolled with median age of 30 +/- 0.56 years in men and 30 +/- 0.12 years in women. Chlorpyrifos was the commonest type (26%) of OP compound consumed followed by dichlorvos (24%), quinalphos (14%), methyl parathion (8%) and others (Table 2).

Baseline Clinical Features

Clinical manifestations of the patients are summarised in Table 3. The most common clinical manifestation was respiratory distress (50%) followed by neck muscle weakness/ fasciculations (44%), miosis (40%) and diaphoresis (30%). A total of 28 cases presented with one or more severe clinical features according to Proudfoot's classification (Table 4).

Gender	No. of Patients	Mean Age
Male	32(64%)	30 +/- 0.56 yrs.
Female	18(36%)	30 +/- 0.12 yrs.

Table 1. Demographic Features

Compound Name	No.	Percentage %
Chlorpyrifos	13	26
Dichlorvos	12	24
Quinalphos	7	14
Methyl Parathion	4	8
Monocrotophos	3	6
Parathion	3	6
Phorate	3	6
Dimethoate	2	4
Diazinon	1	2
Pantothenate	1	2
Profenofos	1	2

Table 2. Type of Compounds Consumed

Clinical Manifestations	No.	%
Diaphoresis	15	30
Salivation	14	28
Bronchorrhoea	10	20
Vomiting	6	12
Neck muscle weakness	22	44
Fasciculations	22	44
Respiratory distress	25	50
Miosis	20	40
Seizures	1	2

Table 3. Clinical Manifestations of OP Poisoning Patients (n= 50)

	Mild	Moderate	Severe
Clinical Manifestations	Fatigue, Headache, Paraesthesia Nausea and Vomiting, Diaphoresis, Salivation, Abdominal pain Diarrhoea, Able to ambulate	Symptoms of Mild poisoning + Miosis, General weakness, Dysarthria, Fasciculations, Unable to ambulate	Generalised Fasciculation, Marked Miosis, Flaccid paralysis, Respiratory distress, Unconsciousness
Decline in Serum PchE	<10%	10-50%	>50%

Table 4. Proudfoot Classification- Assessment of Severity of Acute OP Poisoning[8]

Serum Potassium Alterations in Severe Cases

Among severe cases, 56% (20 out of 28) developed hypokalaemia. Among all patients, 44% (22 cases) had muscle weakness or fasciculation with mean serum [K+] of 3.39 ± 0.60 showing that as the serum [K+] level decreases below 3.5 mmol/L, these alarming signs can be recognised. The ventilatory support was required at the mean serum [K+] of 3.48 ± 0.61 mmol/L. No Fatality was noted. For these conditions, the correlation of the clinical effects and serum [K+] was significant ($P < 0.05$).

Plasma Cholinesterase Levels in Severe Cases

Among the cases with severe clinical features, the PChE level was remarkably reduced except in two cases. The relation between PChE and clinical manifestations was assessed independently at the time of presentation. As it is shown in Table 5, muscle weakness, fasciculation and respiratory distress were associated with marked suppression of PChE (>50%). For those patients with severe clinical effects, considerable reduction in serum [K+] was also evident (Table 5). Among those who required ventilatory support had the lowest PChE levels (1187 +/- 0.15 IU/L).

Clinical Features		Mean K+	Mean PChE
Muscle weakness/ fasciculations	Yes	3.391+/- 0.60	958.73+/- 801.17
	No	3.84+/- 0.43	3192.44+/- 2927.01
	P value	0.003	0.001
Respiratory Distress	Yes	3.472+/- 0.66	1006.17+/- 836.04
	No	3.82+/-0.35	3413.04+/- 3007.49
	P value	0.025	0.001
Miosis	Yes	3.635+/- 0.54	1597.50+/- 2039.598
	No	3.653+/- 0.56	2617.68+/- 2721.184
	P value	0.910	o.160

Ventilatory support	Yes	3.48 ± 0.61	1187.24+/- 1525.83
	No	3.895+/- 0.32	3743.15+/- 3743.15
	P value	0.008	0.001

Table 5. Mean Potassium and Mean PChE Levels in association with Severe Clinical Features of OP Poisoning

DISCUSSION

OP compounds bind to acetylcholinesterase (AChE), preventing hydrolysis of acetylcholine and resulting in its accumulation in muscarinic and nicotinic receptors. Accumulation at nicotinic receptors results in muscle fasciculation and flaccid paralysis. Decrease in serum [K+] may alter neuromuscular junction activity by hyperpolarising the muscle and impairing their ability to develop the depolarisation necessary for muscle contraction. Balali-Mood et al revealed that hypokalaemia may aggravate muscular weakness due to inhibition of AChE by OP compounds.[10] We also found that reduction in serum [K+] aggravate the OP toxicity induced muscle weakness and paralysis. The patients in the present study developed severe signs and symptoms of nicotinic effects of OP as the [K+] reduced. More than 98% of total body potassium is intracellular, chiefly in the muscle; buffering of extracellular potassium by this large intracellular pool plays a crucial role in the regulation of plasma K+ concentration.[11] Changes in the exchange and distribution of intra- and extra-cellular K+ can thus lead to hypo- and hyperkalaemia. The resting membrane potential and functional activity of electrically excitable cells undergo significant alteration even due to minute change in extracellular potassium concentration.[11] In acute cases of OP poisoning due to strong nicotinic actions, respiratory distress, muscle weakness and paralysis sets in. In such conditions, hypokalaemia acts as an add-on to the clinical severity of OP poisoning.

It is a well-known fact that Hypokalaemia and Hyperkalaemia can cause muscle weakness and periodic paralysis.[12,13] Hypokalaemia manifests with lassitude, muscular weakness, loss of deep tendon reflexes, paralysis and death (which is usually due to cardiac arrhythmias and respiratory distress).[11]

Cause of death in both acute OP poisoning and hypokalaemia is usually muscular weakness and respiratory distress.[13,14,9,15,16] Hypokalaemia and paralysis are potentially reversible medical emergencies[12,13]; however, when these features were coupled with reduction of PChE, higher chance of morbidity were observed. Hence, the level of PChE and serum [K+] can be proposed as OP poisoning predictive markers.

CONCLUSION

Serum [K+] and PchE level are greatly reduced in patients with OP poisoning with severe clinical features. Hence, these biochemical markers can be considered predictors of outcome in OP poisoning. Physicians should consider hypokalaemia associated with reduced PchE level as alarming signs of poor prognosis in OP poisoned patients and the need for ICU admission and ventilatory support.

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