Anomalías bioquímicas y hematológicas en la intoxicación grave por organofosforados. Estudio prospectivo en un solo centro.

Biochemical and haematological abnormalities in severe organophosphorus poisoning. A single centre prospective study.

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ABSTRACT

Background: Among all poisons organophosphorus poisoning is considered one of the commonest causes of morbidity and mortality worldwide. Severe organophosphorus poisoning can lead to multiple sometimes lethal metabolic and haematological abnormalities.
Methods: A total of 141 organophosphorus poisoning patients were admitted during the study period and their blood samples were collected on admission and analysed for the biochemical abnormalities.
Results: Out of 141 patients 76 were males (53.9%) and 65 were females (46.1%). Bradycardia with Pulse rate of less than 60 was seen in 21 patients (14.7). Hypoxemia with oxygen saturation of less than 94% was seen in 32 (22.7%). Leucocytosis with total leucocyte count of 11000 or more was seen in 19 patients (13.5%). 101 patients (83.5%) had low serum choline esterase levels less than 1.5 kU/L. Hypokalaemia with K+ of less than 3.5 was seen in 16 patients (9.9%). Five patients died out of 141 (3.5%). Hypoxemia Spo2 of less than 90% was seen in 3 (60%) patients who died and hypoglycaemia with blood glucose of less than 70mg/dl was seen in 2 out of 5 patients (40%).
Conclusions: Low choline esterase levels less than 1.5 kU/L was the most common abnormality indicating severe poisoning followed by hypoxemia. Hypoxemia, hypoglycaemia and low acetylcholine esterase levels are bad prognostic signs and result in high mortality in organophosphorus poisoning.

Keywords: Organophosphorus Poisoning, Hypoxemia, Choline Esterase, Hypokalaemia, Hypoglycaemia.

RESUMEN

Introducción: De entre todos los procesos de intoxicación, el envenenamiento por organofósforados se considera una de las causas más comunes de morbilidad y mortalidad en todo el mundo. La intoxicación grave por organofósforo puede provocar múltiples anomalías metabólicas y hematológicas, a veces letales.
Métodos: Un total de 141 pacientes intoxicados por organofósforados fueron ingresados durante el periodo de estudio y sus muestras de sangre fueron recogidas al ingreso y analizadas para detectar las anomalías bioquímicas.
Resultados: De los 141 pacientes, 76 eran varones (53,9%) y 65 mujeres (46,1%). Se observó bradicardia con una frecuencia de pulso inferior a 60 en 21 pacientes (14,7). Se observó hipoxemia con una saturación de oxígeno inferior al 94% en 32 (22,7%). Leucocitosis con un recuento total de leucocitos de 11.000 o más en 19 pacientes (13,5%). 101 pacientes (83,5%) tenían niveles bajos de colina esterasa sérica inferiores a 1,5 kU/L. Se observó hipopotasemia con K+ inferior a 3,5 en 16 pacientes (9,9%). Cinco pacientes fallecieron de un total de 141 (3,5%). Se observó hipoxemia Spo2 inferior al 90% en 3 (60%) pacientes que fallecieron e hipoglucemia con glucemia inferior a 70 mg/dl en 2 de 5 pacientes (40%).
Conclusiones: Los niveles bajos de colinesterasa inferiores a 1,5 kU/L fueron la anomalía más frecuente que indicaba intoxicación grave, seguida de hipoxemia. La hipoxemia, la hipoglucemia y los niveles bajos de acetilcolinesterasa son signos de mal pronóstico y dan lugar a una elevada mortalidad en la intoxicación por organofosforados.

Palabras clave: Intoxicación por Organofósforados, Hipoxemia, Colinesterasa, Hipopotasemia, Hipoglucemia.

BACKGROUND

Organophosphates (OPs) are chemical substances originally produced by the reaction of alcohols and phosphoric acid. They function as cholinesterase inhibitors, thereby affecting neuromuscular transmission. Worldwide, an estimated 3,000,000 people are exposed to organophosphate or carbamate agents each year, with up to 300,000 fatalities[1-3]. Organophosphate compounds avidly bind to cholinesterase molecules and share a similar chemical structure. In human beings, the two principal cholinesterase's are red blood cell (RBC) or true cholinesterase (acetylcholinesterase), and serum cholinesterase (pseudocholinesterase)[4]. Acetylcholinesterase (Ach E) is the enzyme responsible for hydrolysis of acetylcholine to choline and acetic acid, and inhibition of this enzyme leads to an overabundance of acetylcholine at the neuronal synapses and the neuromuscular junction[5,6]. After some period of time dependent on the chemical structure of the organophosphorus agent, the acetylcholinesterase-organophosphorus compound undergoes a conformational change, known as "aging," which renders the enzyme irreversibly resistant to reactivation by an antidotal oxime[7]. Organophosphate insecticides, such as diazinon, chlorpyrifos, disulfoton, azinphos-methyl, and fonofos, have been used widely in agriculture and in household applications as pesticides. Several organophosphate agents are being tried therapeutically. Medical applications of organophosphates and carbamates include reversal of neuromuscular blockade (neostigmine, pyridostigmine, edrophonium) and treatment of glaucoma, myasthenia gravis, and Alzheimer disease (echothiophate, pyridostigmine, tacrine, and donepezil).

Biochemical and metabolic abnormalities are commonly seen in critically ill patient, in poisoning it results due to its effects on various metabolic pathways or as a result of poison-induced organ dysfunc-

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tion. The management of biochemical abnormalities is an essential part of the supportive care of poisoning patients. There have been many studies looking into biochemical abnormalities in OP poisoning patients however most of these studies had a smaller number of patients usually 50 to 60 patients. Our study is one among the largest observational studies with 141 patients with most of them having severe OP poisoning.

OBJECTIVES

The objectives of the study were to find out the Biochemical and Haematological abnormalities of organophosphate poisoning at presentation to emergency room.

METHODS

This study was conducted in Medical Emergency unit of SMHS hospital Government Medical College Srinagar from December 2020 to January 2022. All the patients who presented with alleged history of OP poisoning with age more than 16 years and duration of less than 6 hrs from time of ingestion were included in this study. During the study period of two years 141 patients with organophosphorus poisoning were admitted. A blood sample for baseline investigations including complete blood count, serum sodium, potassium, blood glucose, choline esterase, lipase, amylase was drawn and oxygen saturation, blood pressure and pulse rate was noted, simultaneously patients were resustated and started on treatment. All the patients had consumed (ingested Poison) with suicidal intent except the one who had accidental ingestion. The results of these investigations and basic vital parameters were entered in Microsoft Excel once the reports of investigations were available and all these parameters were then tabulated. Mean, Standard deviation, frequency and additional statistical analysis was obtained using IBM SPSS 25 software.

RESULTS

During the period of two years 141 patients with organophosphorus poisoning were admitted, the results of basic emergency parameters were recorded. Among 141 patients 76 were males (53.9%) and 65 were females (46.1%) (Table 1).

The minimum age was 15 years and maximum 60 years with mean age of 23.4 years. Three patients were more than 40 years old rest 138 patients had age less than 40 years. Out of 141 patients, 130 (92.2%) had no underlying comorbidity while as 11 patients a had underlying comorbid conditions (Table 2).

Hypoxemia with oxygen saturation of less than 94% was seen in 32 (22.7%) patients. The minimum oxygen saturation was seen as 67% and severe hypoxemia with oxygen saturation less than 90% was in 10 patients (7.1%) (Table 3).

Bradycardia with pulse rate of less than 60 was seen in 21 patients (14.7), pulse rate of >60 and less than 90 in 80 patients (57%) and tachycardia with pulse rate more than 90 was seen in 40 patients (18.4%). The minimum pulse rate was 44, maximum 126, with the mean of 80.7 beats/min. Out of 141 the report of Choline esterase level was done for 133 patients while as that of 8 patients wasn't send as these patients had already received atropine or PAM before reaching to our hospital ER. Out of 133 patients, 22 (16.5%) patients had normal or near normal levels of Choline esterase that is more than 1.5kU/L, while as 101 patients (83.5%) had low choline esterase levels. The minimum choline esterase level was 0.1 kU/L and mean was 0.97kU/L (Table 4).

Total leucocyte count (TLC) of less than 4000 was seen in 4 patients (2.8%). Normal TLC (4000-11000) was seen in 118 patients (83.4%) and leucocytosis with TLC of 11000 or more was seen in 19 patients (13.5%). The minimum blood glucose level was 58 mg/dl and maximum 402 mg/dl. Low blood glucose of less than 70 was seen in 11 patients (6.5%), normal blood glucose of 70-200 mg/dl was seen in 126 patients (91%) and more than 200mg/dl was seen in 4 patients (2.8%). Serum potassium abnormalities were also noted during the study. Hypokalemia with K+ of less than 3.5 was seen in 16 patients (9.9%) and Hyperkalaemia with Serum K+ of more than 4.5 was seen in 45 patients (31.9%). Serum sodium abnormality hyponatremia with Na+ level less than 135 was noted in 12 patients (8.5%) and Hypernatremia with serum sodium more than 145 was seen in 15 patients (10.6%). Serum amylase was done in 135 patients out of 141. Hyperamylasemia with serum amylase of more than 125 was reported in 9 patients (6.7%). Lipase levels were done in 134 patients, hyperlipasemia with serum lipase of more than 78 (Normal range 8 to 78) was found in 14 patients (9%).

Out of 141 patients, 5 patients died (3.5%). 3 patients died during the first week of hospitalisation, one died on 22nd day and other on 16th day of hospitalisation, both of them had autonomic dysfunction and died of cardiac arrythmias in intensive care unit. Among the three patients who died during first week of hospitalisation one died of aspiration pneumonia, one died of hospital acquired sepsis and one patient had ARDS-like picture at presentation and died with 24hrs of hospitalisation and was hepatitis B positive detected first time.

Out of 5 patients who died, 3 (60%) had oxygen saturation less than 90% at presentation, one patient had SPO2 of 92% and one had 99%. The minimum choline esterase level was 0.3 kU/L and maximum was 0.8kU/L which means all the patients who died had low Ache Levels. Two out of five patients who died (40%) had blood glucose less than 70mg/dl, however we did not find any correlation between mortality and any other studied biochemical parameter except Hypoxemia and low blood glucose as described above.

DISCUSSION

The study was conducted to find out basic metabolic and vital parameter abnormalities in patients with organophosphorus poisoning at presentation to emergency room which could help for future triaging and management of OP poisoning patients. In our study random blood glow blood glucose of less than 90 was seen in 50 patients (35.5%), however true hypoglycaemia with random blood sugar of less than 70 was seen in only 4 patients (2.8%). A prospective analytical study of 100 patients of acute organophosphate poisoning has reported low blood glucose levels at the time of presentation in 37% of patients Euglycemic (52%), hyperglycaemic (11%)[8], however in our study blood glucose of 90-200 mg/dl was seen in 83 patients (61.7%) and more than 200mg/dl was seen in 4 patients (2.8%). The reason

Table 1. Showing gender distribution of studied patients

GENDER	FREQUENCY	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
Males	76	53.9	53.9	53.9
Females	65	46.1	46.1	100.0
Total	141	100.0	100.0	

Table 2. Showing comorbid conditions of studied patients

COMORBID CONDITIONS	FREQUENCY	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
No comorbidities	130	92.2	92.2	92.2
Depression	4	2.8	2.8	95.0
Hypothyroid	5	3.5	3.6	98.6
Past suicide attempt	1	.7	.7	99.3
Young Hypertension	1	.7	.7	100.0
Total	141	100.0	100.0	

Table 3. Oxygen saturation of studied patients

OXYGEN SATURATION		FREQUENCY	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
Valid	67	1	.7	.7	.7
	76	2	1.4	1.4	2.1
	88	5	3.5	3.5	5.7
	89	2	1.4	1.4	7.1
	90	3	2.1	2.1	9.2
	91	1	.7	.7	9.9
	92	6	4.3	4.3	14.2
	93	12	8.5	8.5	22.7
	94	8	5.7	5.7	28.4
	95	17	12.1	12.1	40.4
	96	27	19.1	19.1	59.6
	97	14	9.9	9.9	69.5
	98	32	22.7	22.7	92.2
	99	10	7.1	7.1	99.3
	110	1	.7	.7	100.0
	Total	141	100.0	100.0	

Table 4. showing choline esterase level of studied patients

	N	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
Cholinesterase	133	.10kU/L	1.60kU/L	.9683	.40529
Valid N	133				

for low prevalence of hypoglycaemia in our study could be due to the infusion of glucose while these patients are getting referred from primary care to tertiary care during transportation. Many reasons have been attributed to glycaemic variability in acute OP poisoning which include the effect of stress hormones, overproduction of proinflammatory cytokines, pancreatic insufficiency, altered hepatic metabolism due to depletion of enzymes by the toxin that play major role in glucose metabolism, and the prior nutritional status of the patient. [9-12]

The second abnormality found in our study was Hyperkalaemia with Serum K+ of more than 4.5 and was seen in 45 patients out of 141 (31.9%). There is very little data available about the hyperkalaemia in patients with organophosphorus poisoning as few studies have reported Hypokalaemia as bad prognostic factor in OP poisoning[13]. Mohit *et al.* in his study of 50 patients reported 24 patients (48%) had hypokalaemia, however in our study only 16 patients (9.9%) had Hypokalaemia. The reason for low prevalence of Hypokalaemia could be the number of patients in our study was almost three times than that of Mohit *et al.*[14]. In our study, 22 out of 133 patients (16.5%) had normal or near normal levels of Choline esterase, while as 101 patients (83.5%) had very low choline esterase that is less than 1.5kU/L (Normal Range 4.62 to 11.5 kU/L), levels which are significantly higher than that reported. Honnakatti V *et al.*[15] in their study reported 48% of patients had serum ChE levels more than 50%, normal range. Twenty-nine (29%) percentage of patients had mild poisoning with serum ChE levels between 20 and 50% and only 7% of cases had severe poisoning (<10%). In our study severe poisoning with very low levels of choline esterase was seen in 83% patients which is very high compared to Honnakatti V *et al*. The reason for such high prevalence of severe poisoning is almost all the patients in this study had consumed poison with suicidal intent (intent to end life) in addition to that the availability of organophosphorus compounds in households in large quantities as it is being routinely used in apple orchards in our part of the state.

Respiratory failure with oxygen saturation of less than 94% was seen in 32 (22.7%) patients at presentation to emergency department. Respiratory failure has been reported in as a part of severe acute organophosphate (OP) poisoning[16]. The mechanism of respiratory failure is attributed through two mechanisms: central apnea and pulmonary dysfunction. The vagus nerve is involved in both the central control of respiratory rhythm as well as the control of pulmonary vasculature, airways and secretions[17]. Experimental studies support the idea that OP-induced respiratory failure results from local effects of OPs acting on brainstem circuits underlying respiratory rhythmogenesis, and on lung tissues underlying pulmonary secretory, airway and vascular function. Application of acetylcholine or OP compounds to brainstem sites in medullary slice preparations results in a disruption of respiratory associated rhythmic activities[18]. In our study, Hyperamylasaemia with serum amylase of more than 125 was reported in 9 patients (6.7%) and hyperlipasemia with serum lipase of more than 78 (Normal range 8 to 78) was found in 14 patients (9%). High lipase and Amylase levels has been reported as a bad prognostic marker in OP poisoning and predictor of mortality[19]. Leucocytosis with a WBC count of more than 11000/microlitre was seen in 20 patients (14.2%), again leucocytosis has been mentioned as a bad prognostic factor in OP poisoning in one of the studies[20].

CONCLUSIONS

To conclude, the severity of OP poisoning in Kashmir seems to be very high compared to other studies reported from different places as reflected by very low levels of cholinesterase in high percentage of cases likely due to availability of this poison in every household as it being used commonly in apple orchards as insecticide. We found a barrage of biochemical and haematological abnormalities seen in patients with severe OP poisoning which includes Leucocytosis, respiratory failure, hypokalaemia, hyperkalaemia, hyperlipasemias, hyperamylasaemia, glucose variability including both hypoglycaemia and hyperglycaemia. Hypoxemia and hypoglycaemia at presentation had significant correlation with mortality in these patients. Identifying these parameters early in patients with OP poisoning will help in triaging and management of these critically ill patients.

Abbreviations

OP=organophosphorus, RBC=Red blood cells, ACh E= acetylcholinesterase.

DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All the authors unanimously certify the statement that the protocols described in the Helsinki Declaration and current legislation in our country have been followed for writing and publication of this study.

CONSENT FOR PUBLICATION

All the authors unanimously give consent for publication

AVAILABILITY OF DATA AND MATERIAL

All the data is digitally available when ever needed will be provided.

COMPETING INTERESTS

The authors declare no conflict/competing interests.

FUNDING

Not applicable.

CONSENT

The study was an observational one and did not involve any non-routine procedures just the investigations were observed and recorded so a consent of participants was not needed.

AUTHORS' CONTRIBUTIONS

All authors have read and approved the manuscript for publication.
AP designed the study and monitored the research and was involved in writing the paper and analysing the data.
BK was key in collecting and analysing the data
AA was involved in collecting the data and registering it.
MI, MK, MA and IS were involved in collecting the data.

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