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(RESEARCH ARTICLE)

Study of acid base imbalance in organophosphorus poisoning in intensive care patients of eastern Gujarat tribal region

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Abstract

Organophosphorus (OP) pesticides poisoning can result from occupational, accidental or intentional exposure. The compounds can be absorbed through skin, conjunctiva, oral mucosa, GI tract or respiratory tract. This study aimed to analyze arterial blood gas (ABG) analysis and serum cholinesterase (SC) activity in OP poisoning, to study clinical correlation of OP poisoning with the help of ABG analysis and SC and to compare factors of OP poisoning patients and control group. A total, 156 OP poisoning cases and 156 control participants were included in this study. The ABG and SC sample was processed at Central Clinical Biochemistry Laboratory, Medical College and Hospital, in a tertiary health care in eastern Gujarat. Most of the OP poisoning cases were young people 80% (<50 years of age) with mean±SD age as 26.41±11.28 years (range: 11-80). Among these 90(57.69%) and 66(42.31%) were females and males respectively. While control participants with mean±SD age as 29.97±15.75 (range: 15-85) and male were 103(66%) and 53(34%) were females. Significant difference was found out between the age, Electrolytes: Na^+, K^+, Cl^- and SC ($p<0.001$), mean SC level in patients with the latent grade of poisoning was 1363.24±1326.76 IU/L, which is clinically significant ($p<0.001$), no significant difference found between pH, pCO_2, pO_2, HCO_3act and HCO_3std ($p>0.05$). This study concluded that mortality is directly proportionate to the amount of OP substances consumed, clinical severity of poison, SC levels, ABG analysis and electrolytes level in blood. This study can be improving survival or reduces mortality in patients with organophosphorus insecticide poisoning.

Keywords: Organophosphorus; Poisoning; Arterial Blood Gas analysis; Serum Cholinesterase

1. Introduction

Organophosphorus (OP) compounds have been employed as pesticides, petroleum additives and chemical warfare nerve agents. The organophosphates have been used as pesticides for more than 50 years and are still used in most developing countries including India [1]. Poison is anything that kills or injures the live stocks through its chemical actions. In regard to poisoning, chemicals can be divided into different/diverse broad groups: agricultural and industrial chemicals, drugs and health care products and biological poisons i.e., plant and animal sources. The four main classes of insecticides are organophosphates, carbamates, chlorinated hydrocarbons, and insecticides derived from plants. OP insecticides have become increasingly popular for both agricultural and home use because their unstable chemical structure leads to rapid hydrolysis and little long-term accumulation in the environment. It was observed from literature survey that malathion, azinphos-methyl, tetrachlorvinphos, chlorpyrifos, diazinon, dichlorvos, fenitrothion, parathion and are frequently used compounds have encompassed. OP pesticides poisoning can result from occupational, accidental or intentional exposure. The commonly used OP insecticides are chlorpyrifos, dichlorvos, diazinon,

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dimethoate, fenitrothion, methyl parathion, phenthoate, phorate, quinalphos, etc. These compounds can be absorbed through skin, conjunctiva, oral mucosa, GI tract or respiratory tract where concentration of acetylcholine (ACh) increased in the cholinergic synapses to inhibit acetylcholinesterase (AChE) activity leads to altered signaling in these synapses, result various pathological effects. Lipid solubility makes easy access to CNS and fat stores. which intermittently released from fat stores to blood circulation or secreted to the stomach and have been incriminated for the sudden deterioration in a stable patient [2].

OP pesticides poisoning may lead to occupational, accidental or intentional exposure. Scientist, Von Hoffman, synthesized organophosphorus compound from methyl phosphorus chloride which is utilized for the amalgamation of various insecticides. Higher mortality rate found in the developing countries where OP pesticides are readily available and may be used for suicide. They are estimated to cause 300,000 fatalities annually. The OP warfare agents called "nerve agents" which is more toxic than pesticides [3,4]. The replacement of an oxygen atom in the organophosphorus structure by sulphur leads to the formation of organothiophosphorus compounds such as malathion and parathion, which have a lower lethal potential but in vivo metabolization to the oxon metabolite enhances their toxicity. Most organophosphates can be divided into two types: diethyl may include chlorpyrifos, diazinon, parathion, phorate and dichlofenthion and dimethyl such as dimethoate, dichlorvos, fenitrothion, malathion and fenthion [4].

One of the lethal complications following OP poisoning is the development of respiratory failure. This may occur due to many reasons, including aspiration of gastrointestinal contents, excessive secretions, neuromuscular involvement, intermediate syndrome, septicemia and adult respiratory distress syndrome. Early recognition of respiratory failure, early endotracheal intubation, and mechanical ventilation are life-saving in severe OP poisoning [5,6]. These patients need intensive care management for respiratory and close hemodynamic monitoring due to above-mentioned reasons. The SOFA scoring system is a widely used means to track a patient's organ failure status during ICU stay by determining the extent of a patient's organ function or rate of failure [4,7].

Aims and Objectives of study

To analyze Arterial Blood Gas (ABG) with electrolytes and serum cholinesterase activity in OP poisoning and to study and observed the clinical correlation of OP poisoning with the help of ABG analysis and SC and to compare various factors of OP poisoning patients and control group.

2. Materials and Methods

2.1. Study Design

A hospital based; retrospective study of tribal population conducted at tertiary care center, Medical College and Hospital of eastern Gujarat. This study based on the factual data records obtained from a tertiary health care while maintaining the confidentiality of the patient's data.

2.2. Sample size

Convenient sampling technique was adopted for sample selection. Total, 156 OP poisoning cases and equally 156 control participants were included in this study of either gender in study duration. Keeping 1:1 ratio of cases and controls.

2.3. Ethical consideration institutional

Study was approved from the institute ethical committee. The consent form was taken before the study from the participant / their relatives.

2.4. Inclusion Criteria

Patients with OP poisoning immediately after admission to hospital and before starting any kind of treatment. Cases were included irrespective of gender.

2.5. Exclusion Criteria

i) Patients with poisoning other than OP, ii) patients who administered pralidoxime and atropine or iii) started treatment before taking sample and iv) the participants denied to consent were excluded from the study.

2.6. Procedures of ABG analysis

ABG test requires the collection of a small sample of blood containing heparin as an anticoagulant. Arterial blood can be obtained from an artery in wrist, arm, or groin, or pre-existing arterial line if you are currently hospitalized. A blood gas sample can also be venous, from a vein or pre-existing IV or capillary, which requires a small prick to the heel.

The blood samples were analyzed within 10 minutes of the procedure to ensure an accurate test result by a portable machine (Cobas b 221. Roche).

2.7. ABG Interpretation

It is especially important in critically ill patients. The following six-step process helps ensure a complete interpretation of every ABG

Step 1: Assess the internal consistency of the values using the Henderson-Hasselbalch equation:

$$[H^+] = \frac{24(PaCO_2)}{[HCO^{3-}]}$$

If the pH and the [H+] are inconsistent, the ABG is probably not valid.

Step 2: Criteria for alkalemia or acidaemia; pH < 7.35 acidaemia and pH > 7.45 alkalemia

Step 3: Is the disturbance respiratory or metabolic? What is the relationship between the direction of change in the pH and the direction of change in the $PaCO_2$ In primary respiratory disorders, the pH and $PaCO_2$ change in opposite directions; in metabolic disorders the pH and $PaCO_2$ change in the same direction.

Step 4: Is there appropriate compensation for the primary disturbance? Usually, compensation does not return the pH to normal

Step 5: Calculation the anion gap (if a metabolic acidosis exists):

$$AG = [Na^+] - ([Cl^-] + [HCO_3^-]) - 12 \pm 2$$

Step 6: If an increased anion gap is present, assess the relationship between the increase in the anion gap and the decrease in $[HCO^{3-}]$. Assess the ratio of the change in the anion gap (ΔAG) to the change in $[HCO^{3-}]$ ($\Delta[HCO^{3-}]$): $\Delta AG/\Delta[HCO^{3-}]$.

This ratio should be between 1.0 and 2.0 if an uncomplicated anion gap metabolic acidosis is present. If this ratio falls outside of this range, then another metabolic disorder is present:

If $\Delta AG/\Delta[HCO^{3-}] < 1.0$, then a non-anion gap metabolic acidosis is likely to be present.

If $\Delta AG/\Delta[HCO^{3-}] > 2.0$, then a metabolic alkalosis is likely to be present [8,9]

2.7.1. Quantitative Determination of Cholinesterase IVD

Accucare cholinesterase-butyrylthiocoline potassium hexacyanoferrate (iii) method [10].

2.8. Statistical Analysis

Data was collected, compiled and analyzed by using Microsoft Excel and SPSS (v-16). Descriptive statistics such as frequencies, percentage and mean ± standard deviation (SD) was used. Pearson's correlation coefficient was used for checking correlations between biochemical parameters, serum cholinesterase of OP poisoning cases and control group respectively. Comparisons of various factors of OP poisoning patients and control group was done using student's t-test. Probability value of $p<0.05$ was considered statistically significant.

3. Results

In this section, results of characteristics were given with frequencies, percentages, appropriate descriptive measures and hypothesis testing. For deciding the size of class interval, formula suggested by H.A. Sturges was used, as follows:

$$i = \frac{R}{1 + (3.3logN)}$$

Where, i = size of class interval; R = Range (i.e., difference between the values of the largest item and smallest item among the given items); N = Number of items to be grouped.

Table 1 Age and gender distribution of participants

Characteristics		**Cases, n (%)**	**Control, n (%)**
Gender	Female	90(57.69)	53(33.97)
	Male	66(42.31)	103(66.03)
Age group (years)	10-19	45(28.85)	52(33.33)
	20-29	70(44.87)	44(28.21)
	30-39	22(14.10)	29(18.59)
	40-49	9(5.77)	9(5.77)
	50-59	6(3.85)	11(7.05)
	60-69	2(1.28)	4(2.56)
	70-79	2(1.28)	4(2.56)
	80-89	0(0)	3(1.92)
Total		156	156

Form table 1, as per OP poisoning cases, females 90(57.67%) were higher as compare to male 66(42.31) whereas among age group distribution maximum patients were 70(44.87%) in 20-29 years followed by 45(28.85%) in 10-19 years and 22(14.10%) in 30-39 years. It was seen that almost 115(73.72%) cases were in the age group of 10-29 years.

Table 2 Comparison of biochemical parameters and Cholinesterase values of OP poisoning (156) and control (156)

Factors	**Case, Mean±SD**	**Control, Mean±SD**	**p**
Age (years)	26.41±11.28	29.97±15.75	0.022
pH	7.42±0.03	7.41±0.03	0.825
pCO_2 (mmHg)	35.43±7.46	34.43±5.24	0.172
pO_2 (mmHg)	132.47±103.58	133.98±99.5	0.896
HCO_3-act (mmol/l)	21.53±2.63	21.38±3.51	0.667
HCO_3-std (mmol/l)	22.48±1.75	21.96±2.93	0.061
Na+ (mmol/l)	141.09±3.83	138.76±2.2	0.000
K^+ (mmol/l)	3.81±0.69	4.27±0.23	0.000
Cl^- (mmol/l)	102.53±3.1	100.89±2.63	0.000
SC (U/ml)	1363.24±1326.33	7943.83±2013.7	0.000

Note: SD: standard deviation; p: Independent Sample t-test; Case: OP patients; pCO2: partial pressure of carbon dioxide; pO2: partial pressure of oxygen; HCO3 act: bicarbonate; HCO3 std: standard bicarbonate; Na+: sodium; K+: potassium; Cl-: Chloride; SC: Serum Cholinesterase.

In table 2, comparison of biochemical parameters and Cholinesterase values of OP poisoning and control was given. Significant difference was found in variable age ($p<0.05$), while biochemical parameters as pCO2, pO2, HCO3-act and HCO3-std not showed any significancy ($p>0.05$) whereas other biochemical variables like, Na+, K+, Cl- and SC were showed significant difference among case and control group ($p<0.0001$).

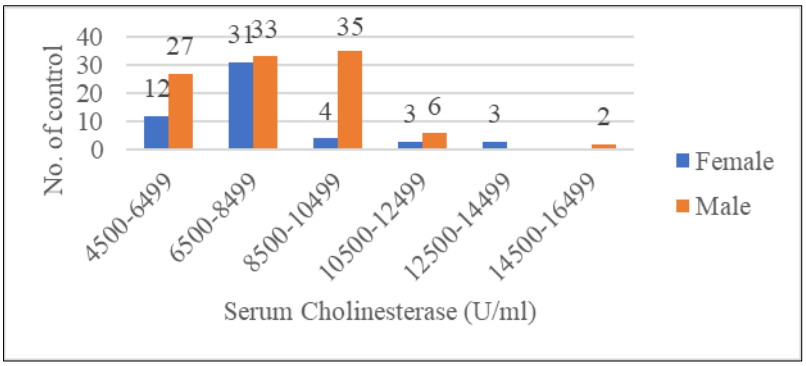

Figure 1 Distribution of SC among gender of control group

From figure 1, it was observed that, SC level almost equal in range and above 4500 U/ml.

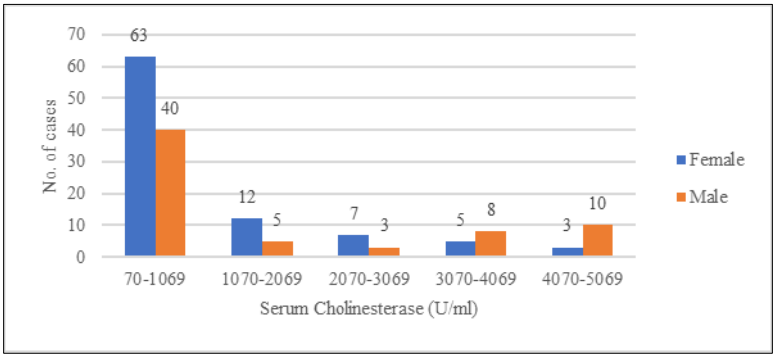

Figure 2 Distribution of SC among gender of cases

From figure 2, it was observed that, SC level very unstable among gender and also highest patients 113(66.03%) has 70-1069 U/ml, followed by 53(33.97%) has 1070-5069 U/ml. It was clearly observed that, in OP poisoning patients the level of SC gradually decreases as compare to control group (figure 1 and 2).

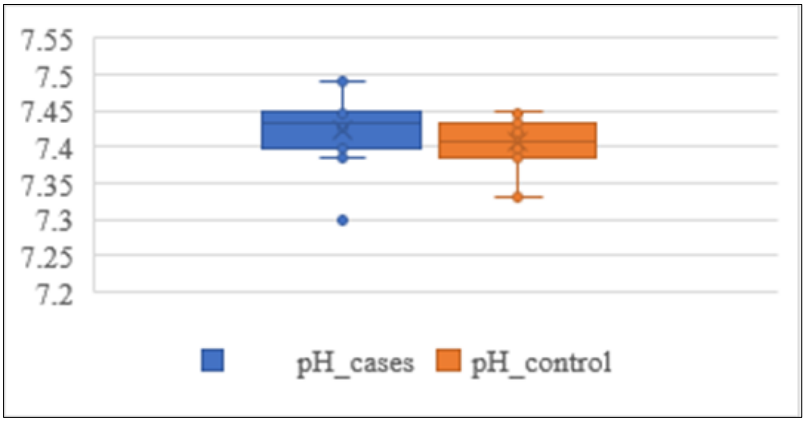

Figure 3 Distribution of pH among control (156) and case (156)

From figure 3, it showed that pH was slightly high in cases as compare to control group.

Table 3 Correlations between biochemical parameters OP poisoning cases (156)

		pCO_2	**pO_2**	**HCO_3 act**	**HCO_3 std**	**Na^+**	**K^+**	**Cl^-**	**SC**
pH	r	**-0.597****	**0.213****	**-0.194***	0.12	-0.07	-0.06	0.06	0.00
	p	**0.000**	**0.008**	**0.015**	0.13	0.36	0.47	0.45	0.97
pCO_2	r	1	**-0.221****	**0.326****	0.13	0.02	0.08	-0.06	0.05
	p		**0.005**	**0.000**	0.11	0.84	0.31	0.46	0.52
pO_2	r		1	-0.10	-0.05	**0.170***	-0.03	0.00	-0.08
	p			0.23	0.55	**0.034**	0.70	0.97	0.32
HCO_3 act	r			1	**0.946****	-0.01	-0.01	-0.01	0.10
	p				**0.000**	0.95	0.95	0.91	0.22
HCO_3 std	r				1	-0.03	-0.03	0.02	0.10
	p					0.73	0.74	0.83	0.20
Na^+	r					1	0.06	0.11	-0.07
	p						0.43	0.17	0.38
K^+	r						1.00	0.05	0.02
	p							0.51	0.80
Cl^-	r							1.00	-0.04
	p								0.65

r: Pearson correlation coefficient; **. Correlation is significant at the 0.01 level (2-tailed).; *. Correlation is significant at the 0.05 level (2-tailed).

Table 4 Correlations between biochemical parameters of control group (156)

		pCO_2	**pO_2**	**HCO_3 act**	**HCO_3 std**	**Na^+**	**K^+**	**Cl^-**	**SC**
pH	r	**0.381****	**0.281****	**0.686****	**0.802****	0.044	0.088	0.109	**-0.280****
	p	**0.000**	**0.000**	**0.000**	**0.000**	0.584	0.276	0.176	**0.000**
pCO_2	r	1	-0.027	**0.787****	**0.809****	**0.292****	0.076	0.029	-0.13
	p		0.736	**0.000**	**0.000**	**0.000**	0.347	0.723	0.107
pO_2	r		1	0.053	0.148	-0.062	-0.089	0.031	0.031
	p			0.512	0.065	0.445	0.268	0.703	0.7
HCO_3 act	r			1	**0.909****	**0.176***	0.111	0.072	**-0.171***
	p				**0.000**	**0.028**	0.167	0.37	**0.032**
HCO_3 std	r				1	.182*	0.127	0.087	**-0.246****
	p					0.023	0.113	0.28	**0.002**
Na^+	r					1	0.057	0.152	0.007
	p						0.48	0.058	0.932
K^+	r						1	-0.109	**-.197***
	p							0.175	**0.014**
Cl^-	r							1	-0.073
	p								0.365

r: Pearson correlation coefficient; **. Correlation is significant at the 0.01 level (2-tailed).; *. Correlation is significant at the 0.05 level (2-tailed).

Table no. 3 and 4 gives correlations between biochemical parameters of OP poisoning cases and control group respectively. In case of OP poisoning group, pH was significant negatively correlated with pCO2 (r= -0.597, p<0.01) and pO2 (r= -0.194, p<0.01) also does not showed any correlation with SC (r=0.00, p>0.05), further pCO2 was significant negatively correlated with pO2 (r= -0.221, p<0.01) and positively with HCO3 act (r=0.326, p<0.01), pO2 positively correlated with Na (r=0.17, p<0.05), HCO3 act positively correlated with HCO3 std (r=0.95, p<0.05).

However, in case of control group, pH was significant positively correlated with pCO2 (r=0.381, p<0.001), pO2 (r=0.281, p<0.001), HCO3 act (r=0.686, p<0.001), HCO3 std (r=0.802, p<0.001) and negatively correlated with SC (r= -0.280, p<0.001). Followed by pCO2 was significant positively correlated with HCO3 act (r=0.787, p<0.001), HCO3 std (r=0.809, p<0.001) and Na (r=0.292, p<0.001), HCO3 act was significant positively correlated with HCO3 std (r=0.909, p<0.001) and Na (r=0.176, p<0.005) and negatively correlated with SC (r= -0.171, p<0.05). HCO3 std and K were negatively correlated with SC (r= -0.246, p<0.005, r=-0.197, p<0.005) respectively (Table 4).

4. Discussion

The first global estimates of the extent of pesticide poisoning were published in 1990 by the World Health Organization [11]. OP poisoning is a complex clinical condition where concentration of acetylcholine (ACh) increased in the cholinergic synapses to inhibit acetylcholinesterase (AChE) leads to altered signaling in these synapses, result various pathological effects. OP actions may be directly or indirectly modified biological functioning of the complex intracellular mechanisms and importantly contribute to the effects of OP poisoning. OP pesticide poisoning and highest incidence is common in all developing worlds including India and suffers mainly males [12,13]. The cases of suicidal and non-suicidal OP poisoning are a major problem in rural areas of India, with rapidly increasing incidence rate [14].

The current study observed, females 90(57.67%) were higher as compare to male 66(42.31) in OP poisoning cases. Maximum patients were 70(44.87%) in 20-29 years followed by 45(28.85%) in 10-19 years and 22(14.10%) in 30-39 years. Similar findings have been reported by Rehiman S et al. The age of the patients ranged from 15-70 years with 70% of them between 15-25 years. In our study, almost 115(73.71%) cases were in the age group of 10-29 years. Also, the incidence of poisoning was higher in females than in males (62% vs 38%) [15].

However, the present study showed, the incidence of OP poisoning, was highest in patients aged less than 40 years and majority of the cases (80%) were young people, predominantly males from the age group 13-40 years, this is comparable to other studies as done by Khan RA, et al. where maximum number of patients were between in the age group of 15-35 years and this age group is to be the most ambitious and more vulnerable to various emotional conflicts that may occur during this phase of life [16]. Our observation was similar to the previous studies that showed the highest incidence of OP poisoning in people aged between 21-39 years [8].

In this study, overall mortality rate was 33.3%, which is higher than shown in a study done by Munidasa UA, et al. and Pandyal BP, et al. [17,18]. However, frequency of mortality due to organophosphates given by Yamashita et al. varied between 4% and 30% and 5.5% in a study by Malik, et al. [19,20]. The reason for higher mortality rates may be due to late arrival, not receiving any treatment at periphery before arrival to the hospital, poverty, illiteracy, unawareness about mortality rate of OP poisoning and unavailability of intensive care unit (ICU) facilities [18].

OP compound present in pesticides which inhibit enzyme cholinesterase irreversibly, specifically acetylcholinesterase (AChE) in synapses and on red cell membranes, and butyrylcholinesterase (Bu-ChE) in plasma results an accumulation of acetylcholine which stimulate of cholinergic receptors at the neuromuscular junctions, in the autonomic and central nervous systems. Clinical effects of OP pesticide poisonings depend on the types of cholinergic receptors stimulated at various sites in the body [21].

Enzyme cholinesterase present in plasma which synthesized by the liver and its true physiological function is unknown, but it may be hydrolyses choline in plasma. activity of cholinesterase is usually measured for liver function and is a sensitive test of exposure to pesticides organ phosphorus and identification of patients with the atypical form of enzyme whose presents high sensitivity to succinyl-choline. Clinical diagnosis should not be made on a single test result; it should integrate clinical and other laboratory data. Butyryl thiocholine is hydrolyzed by cholinesterase to produce thiocoline in the presence of potassium hexacyanoferrate (III), the absorbance decrease is proportional to the cholinesterase activity [22].

OP poisoning is an important cause of morbidity and mortality [17]. Mortality rate associated with OP poisoning was found to be between 28% and 47% [6,23,24] correspondingly various studies conducted have consistently shown mortality rates below 15% [25,26,27]. It was estimated that around 3 million cases of pesticide poisonings occurred

world-wide annually with 220000 deaths, the majority intentional and the fatality rate is rising year by year. Furthermore, a review of poisoning studies reveals that pesticides are the commonest means of self-poisoning in many rural and tribal areas and associated with a high mortality rate and is estimated that there are 258234 (plausible range 233997 to 325907) deaths from pesticide self-poisoning worldwide each year, accounting for 30% (range 27% to 37%) of suicides worldwide. Authenticated data from India probably underestimate the incidence of suicides; applying evidence-based corrections to India's official data, our estimate for world suicides using pesticides increases to 371594 (range 347357 to 439267).

In this study, biochemical parameters as pCO2, pO2, HCO3-act and HCO3-std not showed any significancy ($p>0.05$) while other biochemical variables like, Na+, K+, Cl- and SC were showed significant difference among case and control group ($p<0.01$). In a study done by Alen Binny, et al. (April 2017) was observed similar output regarding potassium (K+). Study also gives electrolytes with outcome of death and live cases. They found that, the mean serum potassium in survived cases is higher as compare to death cases (3.27 vs 3.14) ($p<0.05$) like in this study the mean serum potassium is decreases in cases as compare to control group (3.81 vs 4.27, $p<0.001$) while the mean serum sodium (Na+) in patients who survived and who expired (135.41 vs 134.19) is not statistically significant ($p>0.05$). But, in this study, the mean serum sodium is increases in cases as compare to control group (141.09 vs 138.73, $p<0.001$). As in this study the mean SC is decreases in cases as compare to control group (1363.24 vs 7943.83, $p<0.001$) similar findings was found by Alen Binny, et al. as the mean SC in patients who survived was 2357.34 and in those patients who expired it is 821 ($p<0.05$) [28].

5. Conclusion

Organophosphorus poisoning is most prevalent in the age group of 21-30 years. Incidence is more common in males because they are actually work in agriculture, Chemical industries, Drug Departments etc. as compare to females. Since in tribal region female workers were higher in agriculture field than males. OP poisoning is more common among agricultural laborers and unskilled workers. The most important cause for consumption of OP poison is self-harm. The common route of exposure is ingestion of poison and it is associated with clinical severity.

The quantity consumed has direct proportional relationship with severity of poisoning. The duration of stay in the hospital has significant correlation with clinical severity. The higher the clinical grade of poisoning at initial presentation more the need of ventilatory support and adverse the outcome. The proximal muscle involvement in OP poisoning forms an important indicator in assessment of clinical severity, need of ventilatory support and the outcome. The serum cholinesterase level can be used as a diagnostic marker and a tool to gauge the clinical severity. They reflect skeletal muscle injury and oxidative stress caused by the poison. The blood gas analysis forms an important investigation in OP poisoning in correlation with clinical severity.

This study may improve survival or reduces mortality in patients with OP insecticide poisoning in tribal population from entire tribal belt of India. Further studies of different biochemical parameters like blood lactate, blood sugar, risks of gastric lavage in OP poisoning, BE (B), BE (ECF), act CO2 etc. are required.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There are no conflicts of interest.

Statement of ethical approval

This study involves human participants, but not any kind of intervention on them. Study was approved from the institute ethical committee (IEC). IEC No. 06-2020.

Statement of informed consent

The consent form was taken from participants and in some cases their relatives before the study.

Availability of supporting data

Data pertaining of the original article will be provided to editorial board of Magna Scientia Advanced Research and Reviews (MSARR) Journal if needed by the editorial board.

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