



GLYCEMIC STATUS IN ORGANOPHOSPHORUS POISONING-A PROSPECTIVE ANALYTICAL STUDY.

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ABSTRACT **Background:** Organophosphorus(OP) poisoning, in addition to its cholinergic manifestations shows metabolic derangements leading to hyperglycemia. Apart from inhibiting acetylcholinesterase it also induces oxidative stress to exhibit this manifestation. The present study aims to assess the glycemic status of OP poisoned patients and its association with various factors in OP poisoning like oxidative stress and dose of atropine.
Methods: This is a prospective study which recruited 350 patients above 18 years of age with history of OP poisoning. They were categorized into 3 grades-mild, moderate and severe based on the Peradeniya Organophosphorus Poisoning Scale.
Results: A prospective analytical study of 350 patients of acute organophosphate poisoning was done and on the basis of blood glucose levels at the time of presentation were further categorised into euglycemics (64%) and hyperglycaemics (36%). The outcome in terms of complication rate was 22.1% and 77.9% in the respective groups. The ventilator requirements among the two groups were 6 and 12 patients respectively. Chi-square test to study the association between the presentation Random Blood Glucose (RBG) and the established Peradeniya Organophosphorus Poisoning Scale (POP) and Poisoning Severity Scale (PSS) revealed the study to be statistically significant (p value < 0.005) indicating that the extreme of glycemic status was associated with higher clinical severity and poorer outcomes.
Conclusion: We conclude that the glycemic status at the time of presentation in acute organophosphate poisoning patients is a simple, cheap, reliable marker in guiding the clinical severity and outcome when considered with clinical severity scores.

KEYWORDS : Atropine; hyperglycemia; organophosphorus; oxidative stress; random plasma glucose.

INTRODUCTION

Organophosphorous (OP) poisoning is a major health problem all over the world, particularly in a predominantly agrarian country like India. Organophosphate insecticide exposure is a toxicological threat that may affect human and animal health because of their various toxicities such as neurotoxicity, endocrine toxicity, immunotoxicity, reproductive toxicity, genotoxicity and ability to induce organ damage, alterations in cellular oxidative balance and disrupt glucose homeostasis.

The results of various studies in critically ill-patients have shown that stress-induced hyperglycaemias as well as hypoglycemia are strong predictors of increased mortality and adverse clinical outcome (1, 2, 3). Extremes in glycemic status is found to be associated with increased risk of infectious complications and septic shock, reduced immune response, dehydration and electrolyte imbalances and lethal multiple organ failure in traumatic and acute ischaemic events(4,5). Although poisoning is one of the important causes of significant morbidity and mortality, and appropriate management is very important in critically ill poison patients (6). Acute poisoning induced hyperglycaemia has not been previously studied in these patients, the rising mortality despite adequate poisoning management forces us to investigate for other possible contributory factors. The glycemic status is one such variable that affects the outcome in critical illness. Thus, this study was done to assess the Glycemic status at the time of presentation in acute organophosphorous poisoning and its correlation with clinical severity and outcome.

MATERIAL AND METHODS

Material

Source of data-- Data was collected from patients fulfilling the inclusion and exclusion criteria Admitted to Medicine Department of GMC Jammu. Informed written consent was obtained from patient or a responsible attendant before including the patient in the study.

Study design: Prospective Analytical study

Data collection: 1 year period-Nov 2016 to Nov 2017

Patients fulfilling following inclusion and exclusion criteria were enrolled for the study.

Inclusion criteria- 1. Patients who are above 18 years of age. 2. Patient with alleged history of organophosphorous poisoning (ingestion / inhalational / contact) and diagnosed to have organophosphorous poisoning.

Exclusion Criteria - 1. Patients with age less than 18 years. 2. Patients with history of Diabetes Mellitus. 3. Patients who had consumed alcohol, drugs, mixed poisoning that could affect the glycemic status of the patients. 4. Pregnancy 5. Patients on steroids 6. High serum HbA1C

Methods

This prospective analytical study was done in GMC Jammu. Patients aged over 18 years with a diagnosis of acute organophosphorous poisoning were included in the study. The diagnosis was based on history of short term exposure or contact, characteristic clinical signs and symptoms. Subjects where in the exact nature of the poisoning could not be established and known diabetics were excluded from the study. A detailed history including particulars regarding age sex, type of compound consumed, time-lag between consumption and initiation of treatment was taken followed by a thorough clinical examination. The severity of the poisoning was graded by POP scaling and PSS. Severity of Poisoning: Mild (score 0-3), Moderate (score 4-7), Severe (score 8-11) Hyperglycemia was defined as random blood glucose of more than 200 mg/dL. Glycosuria was detected using ketodiastix strips. The presence of hyperglycemia or glycosuria or ketosis was correlated with the severity of the poisoning with respect to the nature of the compound consumed, the time lag between consumption and initial treatment, the clinical grade of poisoning, the serum pseudocholinesterase level and the requirement of assisted ventilation and outcome. Following investigations were carried out in each patient.

Investigations 1. Random blood glucose level at the time of admission. 2. Pseudocholinesterase levels at the time of admission if affordable (in selected cases). 3. Complete blood count. 4. Liver function tests. 5. Serum creatinine and blood urea. 6. Urine analysis. 7. HbA1C. (if hyperglycemia documented) 8. ECG. Other relevant investigations if required. For the study purpose, on the basis of on presentation, Random blood glucose (RBG) levels, patients were grouped into two categories, euglycemics (101-200mg/dL) and hyperglycemics (>200mg/dL).

RESULTS

The demographic and clinical characteristics of 350 patients revealed a male preponderance (62.9%) and females (37.1%) as depicted in Table 1. The mean age of the study population was 25.5±8 (range 18-65 yrs). The overall incidence was higher in married group and the most common cause of poisoning was suicidal (83%) followed by accidental (16%) and unknown (1%). Ingestion (88%) was the most common mode of poisoning followed by inhalational (12%).

The percentage of population in grade 1, 2, 3 of POP scale were 48.6%, 30.3%, and 21.1% respectively. Out of 350, 18 patients developed respiratory failure necessitating ventilator requirement. The overall mortality was 5 patients and remaining were discharged. The ventilator requirement and mortality was higher with higher grades of and POP (Table 3 and 6). As per on presentation RBG, 64% were euglycemic and 36% were hyperglycemics. The ventilator requirement in the two groups was 6 and 12 patients respectively (Table 5). Hence a very strong correlation between the glycemic status, ventilator requirements and mortality was established. Further, the RBG was compared with POP and PSS to look for statistically significant association between the extremes of glycemic status and higher grades of these clinical severity scores using Chi-square test in MedCalc. The association between hyperglycemia and the grades of POP is statistically significant ($P < 0.0001$).

TABLE 1-SHOWS SEX DISTRIBUTION OF PATIENTS

SEX	NUMBER (N)	PERCENTAGE (%)
MALE	220	62.9
FEMALE	130	37.1
TOTAL	350	100

TABLE 2-SHOWS AGE DISTRIBUTION OF PATIENTS

AGE (YRS)	NUMBER (N)	PERCENTAGE (%)
18 -30	36	10.3
31-40	126	36
41-50	78	22.3
51-60	76	21.7
61-70	26	7.4
More than 80	8	2.3
TOTAL	350	100

Table 3-glycemic Pattern At The Time Of Admission

Grade (pop Scale)	Total Number Of Patients (n) (%)	Patients With Hyperglycemia (n) (%)	Patients With Glycosuria (n) (%)
1(MILD)	170(48.6)	30(23.8)	20(23.8)
2(moderate)	106(30.3)	41(32.5)	28(33.3)
3(SEVERE)	74(21.1)	55(43.7)	36(42.9)
TOTAL	350(100)	126(100)	84(100)

TABLE 4- MEAN RANDOM PLASMA GLUCOSE AT TIME OF ADMISSION AND DISCHARGE.

POP SCALE	RPG IN mg/dl (on admission)	Final RPG in mg/dl (on date of discharge)
MILD (0-3)	108.3+ 28.2	94.3+ 23.8*
MODERATE(4-7)	121.6+ 33.8	103.9+ 15.9*
SEVERE(8-11)	144.2+ 34.2	110.2+ 18.3*

* $P < 0.001$

TABLE 5- ASSOCIATION BETWEEN BLOOD GLUCOSE LEVELS ON DAY OF ADMISSION AND COMPLICATIONS.

Blood Sugar	Number Of Patients N (%)	Complication Present	P- Value
Hyperglycemic	126(36)	46(77.9)	<0.005
Normoglycemic	224(64)	13(22.1)	
Total	350(100)	59(100)	

TABLE 6- ASSOCIATION OF HYPERGLYCEMIA AND NEED OF VENTILATOR.

Blood Glucose	Ventilator Needed	P-value
Hyperglycemia	12	$P < 0.05$
Normoglycemia	6	
Total	18	

DISCUSSION

Among 350 patients studied, the poisoning was more common among males, age group of 18-40 years. The most common cause was suicidal and the most common mode was ingestion. The mean time lag between the consumption and medical attention seeking was 5 ± 2.6 hrs. Vomiting, abdominal pain, altered sensorium and breathlessness were the most common symptoms. In emergency department, most patients had POP grade 1 and on further follow up in critical care unit, the majority developed grade 2 and 3 PSS. Respiratory failure necessitating the need for ventilator was the most lethal and most common complication. Of the study group, the glycemic status on presentation was in the following order of decreasing frequency-

euglycemia (64%) followed hyperglycemia (36%) whereas the study by Ali Mohammad Sabzghabee et al.(7) showed 62% and 23% respectively. The ventilator requirements was 6 and 12 patients among euglycemics and hyperglycemics respectively. The study by Preeti G Pendkar et al.(8) showed the incidence of complications to be 73% in hyperglycemics, 27% in normoglycemics and hypoglycemics were not included in the study. Understanding the mechanism of glycemic variability in OP poisoning and its burden on the clinical outcomes are of importance as our study shows a significant association between the extremes of the the glycemic status and complications and outcome. Although the studies enlightening the mechanisms of glycemic variability in acute OP poisoning are few, the following possible reasons could be attributed.(9-12) 1. The effect of stress hormones, 2. Overproduction of proinflammatory cytokines, 3. Pancreatic insufficiency, 4. Altered hepatic metabolism due to depletion of enzymes by the toxin that play major role in glucose metabolism and 5. The prior nutritional status of the patient. Hyperglycemia and fluctuation in the glycemic status are known to be deleterious in critical illness as they increase the overall complications, morbidity, hospital stay and mortality. (13-15)

CONCLUSION

We conclude that the extreme of glycemic status at presentation in acute Organophosphate poisoning is strongly associated with the severity, complications and the mortality hence can be used as a cheap, simple, reliable marker of prognosis along with the S. ChE, and other clinical scores like POP and PSS in a resource limited country like India.

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