Original Research Article

Severity and clinical outcome of OPC poisoning and its association with glycemic status

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Abstract

Background: Organophosphorus compound (OPC) poisoning is one of the common medical emergencies among rural population in India due to suicide attempts. Its toxicological threat may affect human and animal health because of their various toxicities such as neurotoxicity (cholinergic toxicity, Organophosphorus ester-induced delayed neurotoxicity (OPIDN) and Organophosphorus ester-induced chronic neurotoxicity (OPICN)), endocrine toxicity (pancreatic insufficiency), immunotoxicity, reproductive toxicity, genotoxicity and ability to induce organ damage, OPC induced oxidative stress and disrupted glucose homeostasis. Among the various factors contributing to the mortality of the OPC poisoning, extremes and fluctuation in the glycemic status is a well documented parameter affecting the outcomes of these patients. The purpose of this study was to investigate the relationship between the glycemic status of the patients with the severity and clinical outcome of the OPC poisoning. **Aims and Objectives :** 1.To assess the glycemic status by estimating random blood glucose (RBS) level at the time of admission in cases of acute OPC Poisoning 2.To assess severity of the poisoning with Peradeniya organophosphorus poisoning scale (POP scale) 3.To determine the relation between glycemic status at admission with the severity and clinical outcome in organophosphorus poisoning. **Method:** A prospective analytical study of 100 patients with diagnosed acute OPC poisoning, above the age of 18 years and fulfilling the inclusion and exclusion criterias was done and the patients were grouped according to their glycemic status into hypoglycemic [<100mg/dL], euglycemics [RBS of 100-200] and hyperglycemics [RBS of more than 200 mg/dL] and the same was correlated with the severity and clinical outcome using descriptive statistics, association and test of significance **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 in a resource limited country like India.
Key Word: OPC poisoning.

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INTRODUCTION

Organophosphorus (OP) compounds are employed for pest control worldwide. In developing countries like India due to rampant use of pesticides, short term organophosphorus compound poisoning (OPC Poisoning) is one of the common medical emergencies and is not only a leading cause of mortality but also increases the morbidity in recovered patients. They represent an important source of suicidal poisoning among rural population in India in present days because of its easy accessibility and availability. OPC compounds are lipophilic in nature therefore they are quickly absorbed through the respiratory system, skin and gastrointestinal tract mucosa. Phosphate radicals of OP compounds bind to cholinesterase active sites by covalent binding. This binding makes them inert resulting in overstimulation of muscarinic and nicotinic receptors at the synaptic junctions within the central and peripheral nervous system. This produces an array of symptoms like miosis, bradycardia, increased gastrointestinal motility, emesis, sweating, tachypnoea, salivation, lacrimation, altered sensorium, fasciculation, bronchospasm, blurred vision,

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urination and defecation. If unattended it leads to complications that include acidosis, respiratory paralysis, acute renal failure, seizures, arrhythmia, aspiration etc and finally death due to combination of these complications. In addition to increased cholinergic manifestation, biochemical alterations like hypokalemia, hyperglycemia, and acute renal failure, transient elevation of liver enzymes, abnormal arterial blood gas analysis, and dearranged calcium and phosphorus parameters occur in OP poisoning. OPC Poisoning induces oxidative stress leading to pancreatic damage thereby exhibiting glucose intolerance. Apart from oxidative stress, glucocorticoid receptor activation and adrenergic receptor activation causes hyperglycemia via induction of liver gluconeogenesis. 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. The purpose of this study was to investigate the relationships between the Glycemic status at the time of presentation in acute organophosphorous poisoning and its correlation with clinical severity and outcome.

MATERIALS AND METHODS

A prospective analytical study was done at the Department Of General Medicine, Kanyakumari Medical College and a sample of 100 Patients with organophosphate poisoning admitted to emergency care room were included in the study.

All OPC Poisoning cases of both genders aged >18 yrs were included in the study and their datas were collected. Patients other than OPC Poisoning and known diabetic mellitus were excluded from the study.

- The severity of the poisoning was graded by POP scaling; Severity of Poisoning: Mild (score 0-3), Moderate (score 4-7), Severe(score8-11)
- The glycemic status was graded into
  - Hypoglycemia [RBS of <100mg/dL],
  - Euglycemica[RBS of 100-200] and
  - Hyperglycemics [RBS of more than 200 mg/dL]

The presence of hyperglycemia or hypoglycemia was correlated with the severity of the poisoning. The mortality and ventilator requirement in each group were compared with another in terms of descriptive analysis and chi square test was applied to look for the statistically significant association between the glycemic status and the POP clinical score.

Inclusion criteria

1. Patients or the relatives who have given informed written consent.
2. Patients who are above 18 years of age.
3. Patient with alleged history of organophosphorous poisoning (ingestion/inhalational/contact) within previous 24 hours with characteristic clinical manifestations of organophosphorus compound poisoning.

Exclusion Criteria

1.Patients with age less than 18 years.
2. Patients with history Diabetes Mellitus.
3. Patients already treated at other centres and referred to our centre for further management with no details available at the time of first presentation.
4. Patients who had consumed alcohol, drugs and mixed poisoning that could affect the glycemic status of the patients.

Peradeniya organophosphorus poisoning scale (POP scale)

Parameters	Criteria	Score
Pupil Size	≥2mm	0
	<2 mm	1
	Pinpoint	2
Respiratory Rate	<20/min	1
	≥20/min	2
	≥20/min with central cyanosis	3
Heart Rate	>60/min	0
	41-60/min	1
	<40/min	2
Fasciculation	None	0
	Present, generalized/ continuous	1
	Both generalized and continuous	2
Level of Consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No response to verbal commands	2
Seizures	Absent	0
	Present	1

RESULTS

100 cases of OPC poisoning admitted to Kanyakumari Medical College were considered. Commonest age group involved were between 26 to 35 years. Males were the most common victims (65%).Suicide was the most common motive of poisoning (90%) and ingestion was the most common mode of poisoning (90%). Majority of patients admitted within 5 hours of exposure. Chlorpyrifos was the most common compound in poisoning. The percentage of population in 0 to 3(mild), 4 to 7(moderate) and 8 to 11(severe) POP scores were 55% ,42% and 3% respectively. Our study showed that the Hyperglycemic patients had more severe poisoning followed by the hypoglycemic patients and the majority of euglycemics had mild (0 to 3) poisoning. The ventilator requirements were 92.5%, 52% and 100% among hypoglycemics, euglycemics and hyperglycemics respectively. The mortality in hypoglycemics, euglycemics and hyperglycemics where 55.6% ,11.3% ,65% respectively. Further, the RBS was compared with the scores POP scale to look for statistically significant association between the extremes of glycemic status and higher grades of these clinical severity scores using Chi-square test.. The results were statistically significant (p=0.0001, Chisquare=18.643, DF=2 for POP scale.

Table 1: Age Distribution Of Study Subjects

Age	No.Of.Patients (n=100)
18-25	25
26-35	27
36-45	19
46-55	13
56-65	10
>65	6

Table 2: Gender Distribution Of Study Subjects

Sex	Number (n=100)	Percentage
Male	65	65
Female	35	35

Table 3: Glycemic status (RBS) at presentation - severity and its relation to ventilator support requirement and mortality

RBS	VENTILATORY SUPPORT	EXPIRED
<100 (n=27)	25	15
100-200 (n=53)	28	6
>200 (n=20)	20	13

Table 4: POP score at the time of presentation - Severity and its relation to ventilator support and mortality

POP	No. of patients	Ventilator support	Expired
0 to 3 (Mild)	55	27	10
4 to 7 (Moderate)	42	42	23
8 to 11 (Severe)	3	3	3

Table 5: Association of glycemic status (RBS) of patients with different grades of POP score

POP	NO OF PATIENTS	<55*88 mg/dl	101 to 200	>200 mg/dl
0 to 3 (Mild)	55	13	39	3
4 to 7 (Moderate)	42	13	14	15
8 to 11 (Severe)	3	1	0	2

DISCUSSION

In addition to neurotoxicity and oxidative stress, alterations in glucose homeostasis often culminating hyperglycemia is increasingly being reported as characteristic outcome of OPC poisoning. Numerous experiments have been conducted with experimental animals that reveal hyperglycemia as a characteristic outcome of OPC poisoning. Acute exposure of rats to malathion resulted in hyperglycemia with peak increase occurring at 2.2h after administration followed by decrease after 4h. This reversible phase of hyperglycemia was associated with increased glycogen deposition in liver, indicating that glucose may have come from gluconeogenesis. Malathion induced hyperglycemia was associated with AChE inhibition in pancreas.

- **Pancreatic dysfunctions :** OPC possess propensity to elicit structural and functional alterations in pancreatic milieu that may be associated with

disruptions in euglycemic conditions. From the animal studies, it may be argued that OPC may present a great threat to pancreatic functions in human beings and such threats may have far-reaching consequences on gluco-regulation in human beings.

- **HPA AXIS DYSFUNCTION** : Acetylcholine exerts strong influence on functioning of hypothalamus-pituitary-adrenal (HPA) axis. Acetylcholine has been found to increase corticotrophin releasing hormone (CRH) activity of hypothalamus *in vitro* as measured by effect on corticosteroidogenesis, an effect that was antagonized by atropine.Given the importance of ACh in excitation of HPA axis, assessment of cholinergic stress in activation of HPA axis in monocrotophos treated rats becomes important.
- **Adrenal involvement:** Adrenals are an important part of the endocrine system and play a key role in glucose homeostasis by secreting glucocorticoid and amine hormones. Glucocorticoid hormones (GCs) (mainly cortisol in man and corticosterone In rodents) are secreted by the adrenal cortex under the control of hypothalamic pituitary-adrenal axis. Glucocorticoid hormones, along with other key hormones, act to maintain blood glucose levels within narrow limits. **GCs, glucagon and epinephrine** raise blood glucose by inhibiting glucose uptake in the periphery and stimulating hepatic glucose release. **Increased glycogenolysis and gluconeogenesis** appear to be the two chief mechanisms underlying OPC-induced hyperglycemia. OPC and other AChE inhibiting organophosphate compounds exert strong influences on functioning of hypothalamic-pituitary-adrenal (HPA) axis, leading to increased circulating levels of corticosteroid hormones in vivo. Further, hypercorticosteronemia was associated with decrease in adrenal cholesterol pools, which is the precursor for corticosterone synthesis. Depletion in adrenal cholesterol pools may therefore be attributable to increased synthesis and secretion of corticosterone. Interestingly, both OPC did not cause depletion in hepatic glycogen content. At time points that represented normalization of blood glucose levels, there was phenomenal increase in liver glycogen levels. The data presented above clearly demonstrates co-existence of hypercorticosteronemia and induction of liver gluconeogenesis enzyme activities with hyperglycemia in OPC treated rats, indicating that OPC may trigger induction of liver gluconeogenesis machinery as result of hypercorticosteronemia , leading to hyperglycemia.
- **RISK FOR DIABETES:** Oxidative stress in pancreatic milieu and glucose intolerance, up regulated gluconeogenesis machinery and hyperglycemia are critical factors in diabetes etiology. With the ability to induce the above-mentioned dysregulations, OPC may have far reaching consequences on diabetic outcomes.
- Likewise,hypoglycemia is an independent marker of severity and mortality in critical illnesses . The FOUR cause death categories in patients with critical illness and hypoglycemia are 1. Neurologic 2. Cardiovascular 3. Hypoxic respiratory failure and 4. Liver related .
- Individual hypoglycemic episodes are associated with biologic toxicity by increasing the systemic inflammatory response, inducing neuro-glycopenia, inhibition of corticosteroid stress response and cerebral vasodilation. Hence we urge that the management of both the extremes of glycemic status and their fluctuation is of prime importance in acute OPC poisoning like any other critical illness for better outcomes.

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