European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 05, 2022

Original Research Article

To evaluate glycemic status at the time of admission as a prognostic indicator and to assess it correlates with pseudo-cholinesterase levels and severity of organophosphorus compound poisoning: A prospective study

[1]Harshith Suresh, [2]Radha A, [3]Nagesh HN

[1]General Medicine, Registrar, Apollo Health City, DNB, Bengaluru, Karnataka, India
[2]Assistant Professor, Department of Pharmacology, St Peter's Medical College, Hospital and Research Institute, Bengaluru, Karnataka, India
[3]Associate Professor, Department of Pharmacology, SABVMCRI, RGUHS, Bengaluru, Karnataka, India

Corresponding Author:
Nagesh HN (nagu728@gmail.com)

Abstract

Background: Acute Organophosphorus poisoning (OP) is prevalent in the world and its numbers are constantly on the rise. It is more common in developing countries. Health Organisation (WHO) has estimated that nearly 2 lakh die from pesticide poisoning in the world. So, it has high inpatient mortality. All OP poisoning patients cannot be managed in ICU. So, it is important to know prognostic indicators at initial assessment. Few studies showed Serum Pseudo-cholinesterase levels and hyperglycemia were used in the initial assessment to know prognosis and severity in acute organophosphorus poisoning. The present study aims to evaluate the glycemic status at the time of admission and its correlation with pseudo-cholinesterase levels and severity in acute OP compound poisoning.

Objectives:

1. To assess the glycemic status by estimating random blood glucose level at the time of admission in cases of acute organophosphorus poisoning.
2. To assess the pseudo-cholinesterase level at the time of admission in cases of acute organophosphorus poisoning.
3. To correlate hyperglycemia with pseudo-cholinesterase levels and severity or clinical outcome of OP poisoning.

Methodology: The prospective study was conducted in tertiary care hospital. After obtaining informed written consent, 100 confirmed acute OP compound poisoning patients were enrolled for the study, underwent a detailed clinical examination as per the proforma. The Random Blood Glucose level and pseudo-cholinesterase levels at the time of admission were measured and patients were monitored closely and continuously for severity of clinical signs and symptoms. The data obtained were statistically analysed by using SPSS 21.0 Version. Results were presented as Mean (Median) ± SD, counts and percentages and diagrams. Association of Categorical variables was found using Chi square test. $p<0.05$ will be considered statistically significant.

Results: The study showed hyperglycemia in 32% of the patients and decreased pseudo-cholinesterase level in 71% of patients. Out of 100 study samples, 42 patients developed

ISSN 2515-8260 Volume 09, Issue 05, 2022

complications and 25 patients needed ventilator, in that 54.8% and 64% were hyperglycemic and 97.6% and 96% were had low pseudo-cholinesterase level respectively. 28 out of 32 patients who presented with hyperglycemia had reduced Pseudo-cholinesterase which was highly significant, out of 9 deaths 55.5% were hyperglycemic and 66.6% were had low pseudo-cholinesterase level.

Conclusion: Hyperglycemia and low levels of Pseudo-cholinesterase in acute OP compound poisoning correlates with complications, requirement of ventilator support and poor prognosis. To conclude, hyperglycemia along with low levels of pseudo-cholinesterase at the time of admission can be considered as a prognostic factor in predicting the morbidity and mortality of organophosphorus poisoning.

Keywords: Glycemic status, organophosphorus poisoning, pseudo-cholinesterase, random blood sugar

Introduction

Acute Organophosphorus poisoning (OP) is prevalent in the world and its numbers are constantly on the rise [1]. OP pesticide poisoning is common in developing countries. In India, it is the most common poisoning and exposure to OP compounds in the form of nerve agents and pesticides poses an ever-ending threat. Health Organisation (WHO) has estimated that nearly 2 lakh die from pesticide poisoning in the world [2]. OP poisoning has high inpatient mortality and many patients have cardiorespiratory arrests after admission (40% of patients requiring intubation) [3]. All patients cannot be managed in ICU, there is a need to identify prognostic indicators at initial assessment. Few studies showed Serum Pseudo-cholinesterase levels and hyperglycemia were used in the initial assessment to know prognosis and severity in acute organophosphorus poisoning. Previous studies associating the severity or prognosis of organophosphorus poisoning with the estimation of plasma cholinesterase have been contradictory [4].

The present study aims to evaluate the glycemic status at the time of admission and its correlation with pseudo-cholinesterase levels and severity in acute OP compound poisoning.

Objectives of the study

1. To assess the glycemic status by estimating random blood glucose level at the time of admission in cases of acute organophosphorus poisoning.
2. To assess the pseudo-cholinesterase level at the time of admission in cases of acute organophosphorus poisoning.
3. To correlate hyperglycemia with pseudo-cholinesterase levels and severity or clinical outcome of OP poisoning.

Materials and Methods

The prospective study was carried out in Shri B.M. Patil's medical college hospital and research centre, Vijayapura from October 2018 to June 2020 after obtaining ethical committee clearance. After obtaining informed written consent from patients or relatives, patients over 18 years of age with alleged history, clinical signs and symptoms with diagnosis of organophosphorus poisoning were included in the study.

Patients of age less than 18 years, with history of Diabetes Mellitus, who had consumed alcohol, drugs, mixed poisons and already treated at other centres and referred to our centre for further management with no details available at the time of first presentation were excluded from the study.

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By using purposive sampling method, 100 patients were studied over the period of 20 months.
Each patient enrolled for study underwent a detailed clinical examination as per the proforma, specially designed for the study, which included examination for presence of respiratory failure, detailed assessment of CNS and cardiovascular examination.
The patients were given stomach wash, body and eye wash, in patients who had exposure via uncovered skin and/or eyes. This was followed by 1 gm bolus dose of PAM (Pralidoxime) by slow IV injection. Thereafter, a bolus dose of atropine (2 mg iv push) was administered after correcting cyanosis, till signs of atropinization (clear lungs, dry axilla, dry mucosa, heart rate ≥ 120 bpm, and dilated pupils). All patients were monitored closely and continuously and all clinical signs assessed 12^{th} hourly till complete recovery and were followed till discharge from hospital.
Ventilator support was provided if patient had persistent cyanosis, hypoventilation, apnoea, persistent tachypnoea or deranged ABG ($PaO_2 < 60$ mm Hg, $PaCO_2 > 50$ mm Hg, pH < 7.2).
All patients underwent biochemical investigations such as Blood routine: Hb%, TC, DC, ESR; blood sugar, blood urea, serum Creatinine, Urine: albumin, sugar, microscopy, ECG, Serum Pseudo-cholinesterase levels, Serum electrolytes, ABG (arterial blood gas) analysis, Liver function tests were performed at the time of presentation and whenever required.
The glycemic status on the day of admission was compared with day of discharge. Random plasma glucose >140mg/dl was taken as hyperglycemia [5, 6].
S-butyryl thiocholine iodide was used to estimate Pseudo-cholinesterase level and Dibucaine as inhibitor.

Statistical analysis: The data obtained were entered in a Microsoft Excel sheet, and statistical analysis was performed using statistical package for the social sciences (SPSS 21.0 Version). Results were presented as Mean (Median) ±SD, counts and percentages and diagrams. Association of Categorical variables was found using Chi square test. $p<0.05$ will be considered statistically significant. All statistical tests will be Performed two tailed.

Results

100 patients of OP compound poisoning were studied. Out of which maximum incidence of poisoning was among 20-29 years of age group (39%) and Females were the more common victims (Table-1). The present study showed hyperglycemia in 32% of the patients and decreased pseudo-cholinesterase level in 71% of patients (Table-2). Out of 100 study samples, 42 patients developed complications, in that 54.8% were hypoglycemic and 97.6% were had low pseudo-cholinesterase (Table-3). And 25 patients needed ventilator, in that 64% were hyperglycemic and 96% were had low pseudo-cholinesterase level (Table-4). 28 out of 32 patients who presented with hyperglycemia had reduced Pseudo-cholinesterase which was highly significant (Table-5).
9 patients were died out of which 55.5% were hyperglycemic and 66.6% were had low pseudo-cholinesterase level. Out of 5 hyperglycemic deaths, 4 patients had low pseudo-cholinesterase levels (Table-6).

Table 1: Demographic parameters of studied acute OP compound poisoning patients. (n=100)

Demographic Parameters		Number of patients	Percentage
Age distribution (Years)	18 - 20	17	17.0
	20 - 29	39	39.0
	30 - 39	28	28.0
	40 - 49	10	10.0
	>50	6	6.0

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Gender	Female	59	59.0
	Male	41	41.0
Occupation	Agriculture	34	34.0
	House wife	37	37.0
	Student	19	19.0
	Self Employed	10	10.0
Marital status	Married	77	77.0
	Unmarried	23	23.00

Table 2: RBS (Random Blood Sugar) values of OP compound Poisoning patients at the time of admission (N=100)

		No of Patients	**Percentage**
Glycemic status	Hypoglycemic	05	05
	Euglycemic	63	63
	Hyperglycemic	32	32
Pseudo-cholinesterase levels	<3500	63	63
	3500-5000	08	08
	>5000	29	29

Table 3: Association of Glycemic status and Pseudo-cholinesterase levels with Complications (n=100)

		Complications			**Chi square test**	**"p- value"**
		No	**Yes**	**Total**		
Glycemic status	Hypoglycaemia	1	4	5	X^2=23.246	"p=0.001"*
	%	1.7%	9.5%	5.0%		
	Normoglycemia	48	15	63		
	%	82.8%	35.7%	63.0%		
	Hyperglycemia	9	23	32		
	%	15.5%	54.8%	32.0%		
	Total	58	42	100		
Pseudo-cholinesterase levels	< 3500	22	41	63	X^2=37.262	"p=0.001"*
	%	37.9%	97.6%	63.0%		
	3500 - 5000	8	0	8		
	%	13.8%	0.0%	8.0%		
	5001	28	1	29		
	%	48.3%	2.4%	29.0%		
	Total	58	42	100		
*Highly significant						

Table 4: Association of Glycemic status and Pseudo-cholinesterase levels with Ventilator support (n=100)

		Ventilator support			**Chi square test**	**P value**
		No	**Yes**	**Total**		
Glycemic status	Hypoglycaemia	2	3	5	X^2=21.981	P=0.001*
	%	2.7%	12.0%	5.0%		
	Normoglycemia	57	6	63		
	%	76.0%	24.0%	63.0%		
	Hyperglycemia	16	16	32		
	%	21.3%	64.0%	32.0%		
	Total	75	25	100		
Pseudo-cholinesterase levels	< 3500	39	24	63	X^2=15.612	P=0.001*
	%	52.0%	96.0%	63.0%		

	3500 - 5000	8	0	8		
	%	10.7%	0.0%	8.0%		
	5001+	28	1	29		
	%	37.3%	4.0%	29.0%		
	Total	75	25	100		
*Highly significant						

Table 5: Association of Glycemic status and Pseudo-Cholinesterase levels in OP poisoning (n=100)

Glycemic status	Pseudo-Cholinesterase				Chi square test	"p-value"
	< 3500	3500-5000	5001+	Total		
Hypoglycaemia	3	1	1	5	X^2=17.435	"p=0.004"*
%	4.8%	12.5%	3.4%	5.0%		
Normoglycemia	32	4	27	63		
%	50.8%	50.0%	93.1%	63.0%		
Hyperglycemia	28	3	1	32		
%	44.4%	37.5%	3.4%	32.0%		
Total	63	8	29	100		
*Highly significant						

Table 6: Association of Glycemic status and low-level pseudo-cholinesterase with mortality (n=9)

Outcome	Expired	Low pseudo-cholinesterase level
Hypoglycemic	2	1
Normoglycemic	2	1
Hyperglycemic	5	4

Discussion

Organophosphorus poisoning has been diagnosed as a prime problem in developing countries like India because of its predominant use in pest control and crop protection. The diagnosis of OP poisoning is mainly based on the history of ingestion or exposure, clinical features, low serum cholinesterase levels and therapeutic response to atropine [7, 8]. Two major forms of cholinesterase are present which hydrolyze acetyl choline. One is Pseudo/Butyryl Cholinesterase found in plasma, liver (main), pancreas and intestinal mucosa. Second one is True/Specific Cholinesterase found in nervous tissue, erythrocytes, lung, spleen and grey matter [9]. Butyryl cholinesterase levels are easy to measure. Butyrylcholinesterase shows any prior cholinesterase inhibition even after recovery of acetylcholinesterase activity by pralidoxime. Decreased cholinesterase levels are confirmatory and are expressed as % of normal levels in healthy adults [10].

Organophosphorus (OP) compounds in addition to its cholinergic manifestations shows metabolic derangements leading to hyperglycemia. Apart from inhibiting acetylcholinesterase it also induces oxidative stress to exhibit hyperglycemic manifestation [11].

Previous studies associating the severity or prognosis of organophosphorus poisoning with the estimation of plasma cholinesterase have been contradictory. Goswamy R *et al.* [12], in their study concluded that apart from clinical indicators, low plasma cholinesterase levels were of greatest predictive value in organophosphorus poisoning. However Aygun D *et al.* [13] found that plasma cholinesterase level estimations are useful in diagnosis of organophosphorus poisoning in acute phase but show no relation to severity of poisoning and also regarding morbidity and mortality of case.

In this study, maximum incidence of poisoning was among 20-29 years of age group (39%) which is consistent with the studies done by Shankar PS *et al.* [14] and Lograj M *et al.* [15].

Female were the more common victims in the present study in contrast to male predominance

in findings of Goel *et al*. [16], Vikram P *et al*. [17], Shobha TR *et al*. [18] but consistent with findings by Karki P *et al*. [19] and Panda S *et al*. [6].

Hyperglycemia was detected in 32% of the patients in this study which is comparable to findings in the study by Sungur M *et al*. [20], Ravindra K.R *et al*. [21]. And it was observed that on complications associated with on admission hyperglycemia (RBS>160 mg/dl) was 54.8% as compared to 35.7% in normoglycemics. This is highly significant (p=0.001). In addition hyperglycemia also showed a significant association with need for ventilator support (p=0.001).64% of patients with hyperglycemia were found to need ventilator support as compared to 24% with normoglycemia.

In our study, 61% had reduction of Pseudo-cholinesterase levels with 46 of them having severe depression which is comparable to Rao R *et al*. [22] The mean Pseudo-cholinesterase levels were 2701.23 IU/L which is comparable to findings by Jeong Mi Moon *et al*. [23] (2736.0 IU/L). In our study it was noted that Pseudo-cholinesterase values<3500U/L (p=0.001) was associated with complication in 97.6% of the cases and ventilator support in 96% (p<0.001), these observations were statistically significant.

The present study showed an overall mortality of 9% comparable with Bardin PG *et al*. [24], Singh S *et al*. [25] Out of 9 patients who expired, 5 patients had hyperglycaemia at presentation with 3 of them having RBS > 200 mg/dl. Mortality rate of 9%, 55.5% was in patients with hyperglycemia and 66.6% was in low pseudo-cholinesterase patients, which were highly significant (p<0.05).

The above results indicate RBS value >160mg/dl is a good marker for predicting the mortality and also for assessing the need for ventilator support. Admission RBS was comparable to the drop in Pseudo-cholinesterase levels, with a p=0.004 which was highly significant.

These observations suggest that admission hyperglycemia is a prognostic indicator in OP compound poisoning and it is comparable to Pseudo-cholinesterase. Further studies are needed in this area.

Conclusion

Hyperglycemia can occur in moderate to severe organophosphorus poisoning and it correlates with complications, requirement of ventilator support and poor prognosis. Hyperglycemia is also correlated with low levels of Pseudo-cholinesterase in predicting mortality and ventilator support.

So, hyperglycemia along with low levels of pseudo-cholinesterase at the time of admission can be considered as a prognostic factor in predicting the morbidity and mortality of organophosphorus poisoning.

References

1. Eddleston M. Pattern of deliberate self-poisoning in the developing world. QJM. 2000;93:715-16.
2. Singh S. Organophosphorus poisoning: an evidence-based approach. MJAFI. 2004;60:2-4.
3. Eddleston M, Mohamed F, Davies JO, Eyer P, Worek F, Sheriff MH, *et al*. Respiratory failure in acute organophosphorus pesticide self-poisoning. QJM. 2006;99:513-22.
4. Ravi BN, Manmohan US, Bharadwaj BSP, *et al*. Study of hyperglycemia and its association with pseudocholinesterase levels and severity of organophosphorus poisoning. Int J Health Sci Res. 2018;8(9):20-26.
5. Fauci AS, Hauser SL, Loscalzo J. Harrison's principles of internal medicine. 20th edition. New York: McGraw-Hill Education, 2018.

6. Panda S, Nanda R, Mangaraj M, Rathod PK, Mishra PK. Glycemic Status in Organophosphorus Poisoning. J Nepal Health Res Counc. 2015 Sep-Dec;13(31):214-9.
7. Raghavan P, Amar R, Nayak VC, Bakkannavar SM. Profile of organophosphorus insecticides poisoning in Kasturuba Hospital, Manipal South India. Journal of Pharmaceutical & Scientific Innovation. 2014;3(1):73-77.
8. Kumar SV, Fareedullah Md, Sudhakar Y, Venkateswaralu B, Ashok Kumar E. Current review on organophosphorus poisoning. Arch. Appl. Sci. Res. 2010;2(4):199- 215.
9. Ganong FW. Review of medical physiology. 21s' edn. McGraw Hill Medical Publication Division, 2003.
10. Midtling JE, Bernett PG, Coye MJ, *et al*. Clinical management of field worker organophosphate poisoning. West J Med. 1985;142:514-18.
11. Singh S. Blood glucose changes following Anticholinesterase insecticide poisoning. JAPI. 2000;48;1145-46.
12. Goswamy R, Chaudhuri A, Mahashur AA. Study of respiratory failure in organophosphorus and carbamate poisoning heart lung. The Journal of Critical Care. 1994 Nov;23(6):466-72.
13. Aygun D, Doganay Z, Altintop L, Guven H, Onar M, Deniz T, *et al*. Serum acetylcholinesterase and prognosis of acute organophosphorus poisoning. J Toxicol 2002;40(7):903-10.
14. Shankar PS. Pulmonary edema in diazinon poisoning. India J Chest Dis. 1967;9:106-10.
15. Logaraj M, Ethirajan N, Felix JW, Roseline FW. Suicidal attempts reported at amedical college hospital in Tamil Nadu. Indian J Comm Med. 2005;30(4):136-137.
16. Goel A, Joseph S, Dutta TK. Organophosphate poisoning: predicting the need for ventilatory support. JAPI. 1998;46(9):786-790.
17. Vikram P, Arun M, Saralaya KM, Bhoopendra S. Spectrum of organophosphorus poisoning in Manipal. Ind Medica-Medicolegal Update. 2005;5(2):55-57.
18. Shobha TR, Prakash O. Glycosuria in organophosphate and carbamate poisoning. JAPI, 2000, 48(12).
19. Karki P, Hansdak SG, Bhandari S, Shukla A, Koirala S. A clinic epidemiological study of organophosphorus poisoning at a rural based teachinghospital in eastern Nepal. Trop Doct. 2001;21(1):32-4.
20. Sungur M, Guven M. Intensive care management of organophosphate insecticide poisoning. Crit Care. 2001;5(4):211-5.
21. Raveendra R, Chandana V. A prospective study to assess glycemic status as a possible prognostic marker in non-diabetic acute organophosphate poisoning patients. International Journal of Advances in Medicine. 2020 Mar;7(3):464.
22. Rao R, Raju G. Random blood sugar levels and pseudocholinesterase levels their relevance in organophosphorus compound poisoning. Int J Community Med Public Health. 2016 Dec;3:2757-61.
23. Moon JM, Chun BJ, Cho YS. Hyperglycemia at presentation is associated with in hospital mortality in non-diabetic patient with organophosphate poisoning. Clinical toxicology. 2016 Mar;54(3):252-8.
24. Bardin PG, Vaneeden SF, Joubert JR. Intensive care management of acuteorganophosphate poisoning. A 7 yr experience in the western cape. S Afr Med J. 1987;72(9):593-7.
25. Singh S, Wig N, Chaudhary D, Sood NK, Sharma BK. Changing pattern of acute poisoning in adults: Experience of a large north west Indian hospital (1970-1989). JAPI 1997;45(3):194-197.