An Analytical Prospective Study of Plasma Pseudo–Cholinesterase Level & its Co-Relation to Mortality in Acute Organo Phosphate Poisoning

Tejas J.[1], Siva Kumar V.[1], Shruthi K.[2], Vishwanathan K.G.[3]

[1]Associate Professor, Dept. of Forensic Medicine & Toxicology, Kmchihsr, Coimbatore, Tn, [2]Assistant Professor, Dept. of Physiology, Rvsims, Chittoor, Ap, [3]Professor and Head, Dept. of Forensic Medicine, Basaveshwara Medical College & Hospital, Ka

Abstract

Background: The Incidence of Poisoning Is Constantly On The Rise In The Modern World With A Gradual Shift Towards The Use of Agricultural Poisons In Suicides With Majority of Cases Using Organophosphate Compounds And In India The Incidence of Ingested Suicidal Poisoning Is High Especially In The Southern States. This Study Is Undertaken With A View To Asses If There Is Any Correlation Between Plasma Levels of Pseudocholinesterase and mortality in cases of acute organophosphate poisoning. Method: The study was conducted on patients of organophosphate poisoning admitted to Bapuji Hospital (J.J.M. Medical College), Davangere during a period of October 2011 to March 2013. Total number of cases studied were 150. Detailed history was obtained regarding the amount of poison, type of poison, quantity of poison, etc from the patient and his/her relatives as well from the police.

Clinical examination of each patient was carried out and according to signs and symptoms, the patients were grouped into 3 grades, mild, moderate and severe according to Dreisbach's criteria. At the time of admission pseudocholinesterase was measured. All patients were followed-up for 3 days to know the outcome and results were compared and analysed.

Conclusion: Our study concludes that there is a very good correlation between the levels of plasma pseudocholinesterase and mortality as well as morbidity

Keywords: *Pseudocholinesterase, organo-phosphate, butyrylcholinesterase, agricultural poisons.*

Introduction

Paracelsus in 16th century expressed the classic toxicology maxim "All things are poison, and nothing is without poison; the dosage alone makes it so a thing is not a poison.". The world health organization defines poisoning as that which occurs when people drink, eat, breathe, inject, or touch enough of a hazardous substance (poison) to cause illness or death[1]. The incidence of poisoning is constantly on the rise in the modern world with a gradual shift towards the use of agricultural poisons in suicides with majority of cases using organophosphate compounds. In India the incidence of ingested suicidal poisoning is high especially in the southern states. This study is undertaken with a view to asses if there is any correlation between plasma levels of pseudocholinesterase and mortality in cases of acute organophosphate poisoning with an aim to develop good prognostic index and mortality predictor in such cases.

Corresponding Author:
Dr. Sivakumar
Assistant Professor, Dept. of Forensic Medicine & Toxicology, Kmchihsr, Coimbatore-641014
Ph: +919739279018
e-mail: sivakumarvarattoor89@gmail.com

Methodology

Study Sample: The study was conducted on patients of organophosphate poisoning admitted to Bapuji Hospital (J. J. M. Medical College), Davangere

during a period of October 2011 to March 2013. Total number of cases studied were 150

Materials Used: 18-gauge needle, 10cc syringe, Colour coded vacutainer tubes, Cobas Integra 400 cholinesterase assay system.

Inclusion Criteria: All patients with Organophosphate poisoning with age more than 14 years belonging to either sex was included in the study.

Exclusion Criteria: All patients with age less than 14 years, poisoning other than organophosphate

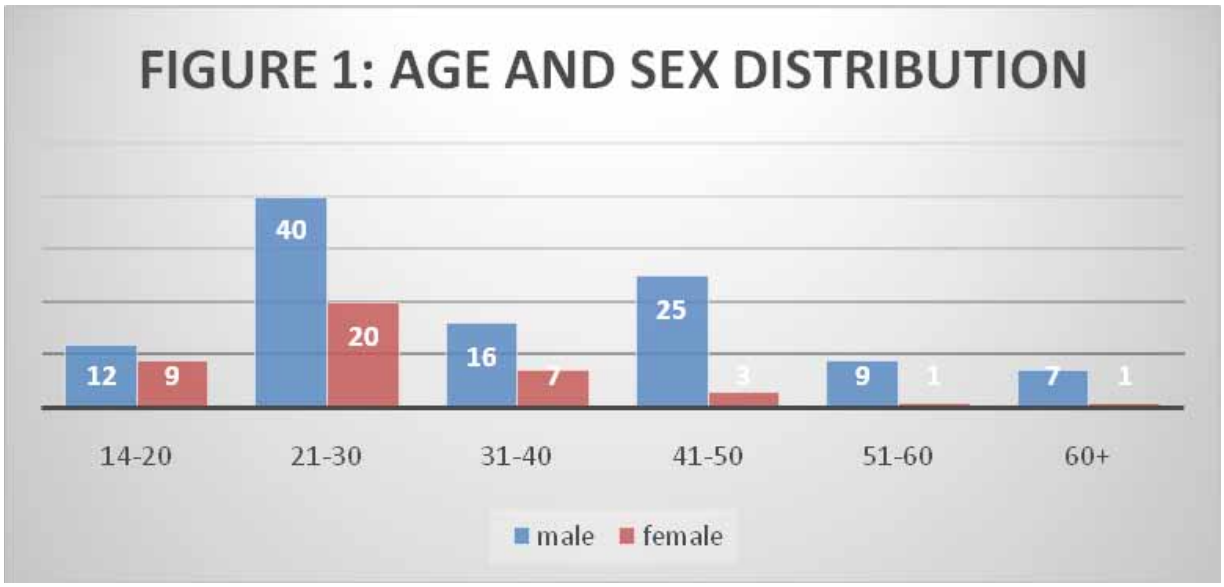
Data Collection: Data was collected from hospital admission records, hospital MLC registers, patient case history & examination and history from eye witness, relatives, friends of deceased & investigating officer. Detailed history was obtained regarding the amount of poison, type of poison, quantity of poison, etc from the patient and his/her relatives as well from the police. Examination of the poison container was also done whenever available. Clinical examination of each patient was carried out and according to signs and symptoms, the patients were grouped into 3 grades, mild, moderate and severe according to Dreisbach's criteria[2].

Grade (Dreisbachs)	Symptom
Mild	1. Nausea 2. Vomiting 3. Diarrhoea 4. Sweating
Moderate	1. Lacrimation 2. Salivation 3. Miosis 4. Fasciculation
Severe	1. Coma 2. Seizures 3. Incontinence 4. ARDS 5. Areflexia

At the time of admission pseudocholinesterase was measured by drawing blood from the patient, collected and forwarded in vacutainer tube with EDTA as preservative and subjected it to analysis by COBAS INTEGRA 400 CHOLINESTERASE ASSAY SYSTEM. The range of values in 3 control patients was found to be 13,400 U/L to 15,600 U/L at room temperature (37ºC). All patients were followed-up for 3 days to know the outcome. Also, in fatal cases the Forensic Science Laboratory was also used for conformation of organophosphorus poisoning. Results were analysed using Microsoft excel 2013 and IBM SPSS statistics 22 software.

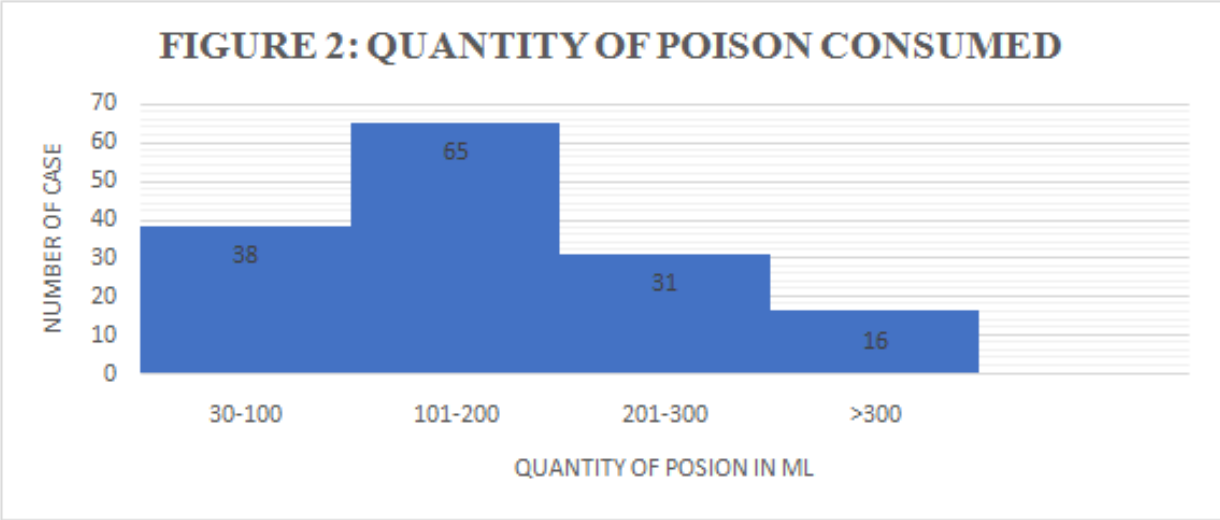
Results

Patient Characteristics: Age and Sex: The age and sex distribution of the study group is shown in figure 1. The maximum number of cases was seen in the 21 to 30 years age group. Youngest patients were 2 females of age 14 years each and oldest patient was a male of age 76 years. Sex distribution of the cases studied had a male predominance in each age group with 109 (73%) male patients to 41 (27%) female patients.

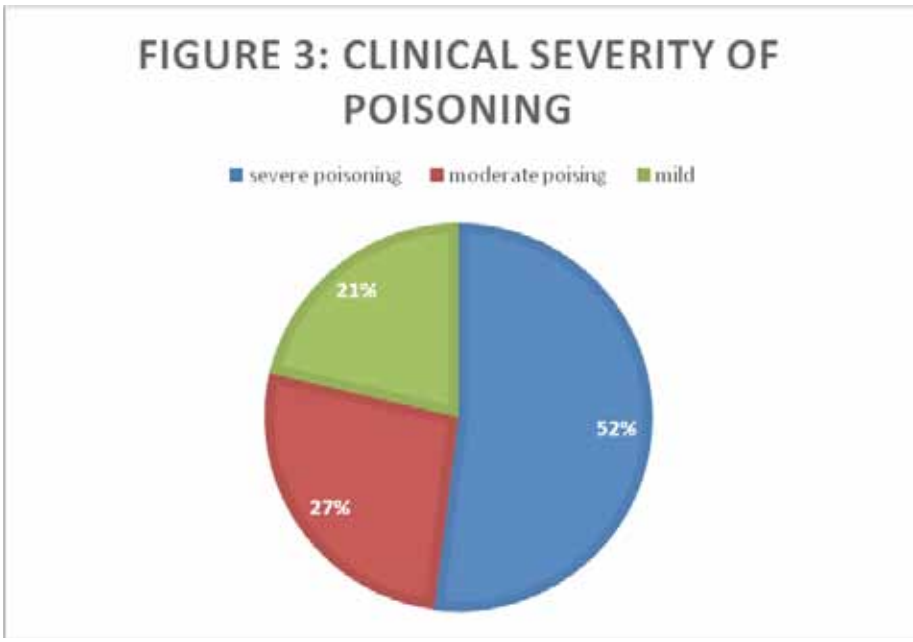


Type of Poison Consumed: The distribution of patients according to type of poison consumed is shown in figure. 2. The commonest poison consumed in the study was Malathion (28 patients, 18.67%). Second commonest was Dimethoate (26 patients, 17.33%), followed by dichlorvos and parathion. All poisons belonged to organophosphorus class.

Approximate Quantity of Insecticide Ingested: 65 patients (43.33%) had consumed 101ml to 200ml of organophosphorus compound. 38 patients (25.33%) had consumed 30ml to 100ml of organophosphorus compound. 31 patients (20.67%) had consumed 201ml to 300ml of organophosphorus compound. Very high doses of consumption i.e. > 300ml were seen in 16 patients (10.67%).



Clinical Severity of Poisoning Based on Clinical Features: The patients were clinically examined and divided into groups using the Dreisbach's criteria [2]. 78 patients (52%) had sever poisoning, 40 patients (26.67%) had moderate poisoning and 32 patients (21.33%) had mild poisoning. Emesis and gastric irritation were seen in >90% of cases followed by defecation, urination, lacrimation and salivation which were seen in >80% cases.



Final Outcome: In the 3-day follow-up 60 patients (40%) had fatal outcome (including coma) and 90 patients (60%) survived with treatment. Of the 60 fatalities, 26 cases (17.33%) died within 24 hours.

All the fatalities were associated with severe poisoning. Among those who survived 18 patients (12%) had severe poisoning.

Plasma Pseudo-Cholinesterase Levels: In the group with severe poisoning the plasma pseudo-cholinesterase levels were found to be range from 912 U/L to 2,490 U/L. (mean value = 1,696.62 U/L and S.D = +/- 438.99 U/L). This group contained all the 60 fatalities (40%) observed in this study. The Plasma Pseudocholinesterase levels of all the 60 fatal cases were compared and found to be statistically highly significant ($p < 0.001$). This amounts to suppression of plasma pseudo-cholinesterase by 84.04% to 93.19%. 18 patients (12%) survived with severe poisoning but no statistically significant difference was found between those who survived and fatalities ($p > 0.5$)

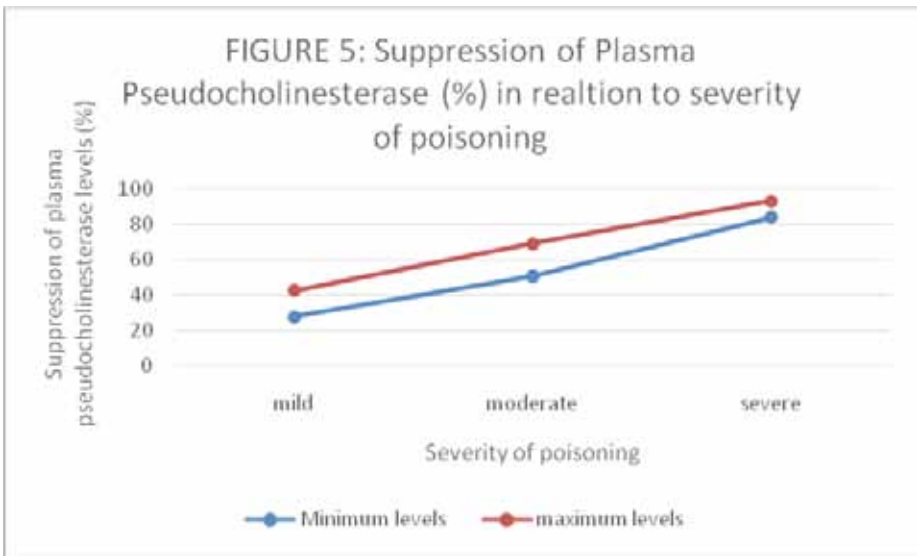
In the 26 patients (17.33%) who died within 24 hours of admission to hospital, the plasma-pseudocholinesterase levels were found to be statistically highly significant ($p < 0.001$) and ranged from 912 U/L to 1,678 U/L (mean value = 1,390.35 U/L and S.D = +/- 200.68 U/L) which amounts to suppression of plasma pseudo-cholinesterase by 89.24% to 93.19%

In the group with moderate poisoning the plasma pseudo-cholinesterase levels were compared and found to be statistically highly significant ($p < 0.001$) ranging from 4,128 U/L to 7,642 U/L (mean value = 5,339.40 U/L and S.D = +/- 1121.33 U/L). This amounts to suppression of plasma pseudo-cholinesterase by 51.01% to 69.19%

In the group with mild poisoning the plasma pseudo-cholinesterase levels were compared and found to be statistically highly significant ($p < 0.001$) ranging from 7,654 U/L to 11,230 U/L (mean value = 9,110.38 U/L and S.D = +/- 927.29). This amounts to suppression of plasma pseudo-cholinesterase by 28.01% to 42.88%

Table 1. Correlation between Severity of Posioning and Plasma Pseudocholinesterase Levels

Clinical grade of poisoning		Plasma Pseudo-Cholinesterase Levels			Percentage suppression of Plasma Pseudocholinesterase level
		Range (U/L)	Mean (U/L)	Standard deviation (U/L)	
Severe	Death within 24 hours (17.33% mortality rate)	912 to 1,678	1,380	200.68	89.24% to 93.19%
	Death over a period of 3 days following admission (40% mortality rate)	912 to 2,490	2,158.15	774.15	84.04% to 93.19%
Moderate		4,128 to 7,642	5,339.40	1121.33	51.01% to 69.19%
Mild		7,654 to 11,230	9,110.38	927.29	28.01% to 42.88%



Discussion

1. **Patient Characteristics: Age and Sex:** In the present study, the sex incidence shows males are more affected (73%) than the females (27%). Similar observations were made by Singh et al.30 [3], consisting of 67.95% males and majority of the cases were adults belonging to the age group of 21 to 30 years. Our study shows that all of the patients admitted were agricultural laborers. This could be due to easy availability and accessibility of poisons, particularly insecticides which are responsible for high incidence of poisoning among the agricultural workers. Similar incidence was reported by Sozmen et al.[4] and Naravaneni & Jamil [5] where in all the patients chosen for the study with exposure to organophosphate insecticide were farmers. In all cases the poisons were consumed via the oral route. Malathion is one of the most commonly used organophosphate insecticide and is commonly available for agricultural use. Even though it has a disagreeable taste, it is most often taken orally because of its easy availability to farmers and also lethality of its action. Other studies also reflect similar findings [3–6].

2. **Type of Poison Consumed:** The commonest poison consumed in the study was Malathion, 28 patients (18.67%). Second common was Dimethoate, 26 patients (17.33%). In all cases the poisons were consumed via the oral route. This finding is in agreement with other studies[6–9]

3. **Approximate Quantity Of Insecticide Ingested:** Majority of the patients in our study had consumed 101ml to 200ml of organophosphorus compound (43.33%). This dose is in excess of the lethal dose for the two most common poisons found to be used in our study i.e Malathion and Dimethoate.

4. **Clinical Severity of Poisoning Based on Clinical Features:** Patients with severe poisoning constituted the major group. This could be attributed partially to the manner of death as most of the cases in this study consumed poison with suicidal intent in which case the amount of poison consumed will be significantly more than accidental or very rarely homicidal consumption.

5. **Final Outcome:** The patients were followed up for 3 days during which 40% had fatal outcome (including coma) and 60% survived with treatment. of the total number of fatalities 17.33% died within 24 hours of admission to the hospital. All the fatalities were associated with sever poisoning and only 12% survived with severe poisoning. A study by Kar[10] found a mortality of 26% patients with suicidal organ phosphorus poisoning which is higher than that found in our study as our study also includes other manners of death. A study by Singh et al. [3] reports a mortality of 17.30% which is in agreement with our 24 hour mortality rate.

6. **Plasma Pseudo-Cholinesterase Levels:** In this study severe poisoning accounted for all the 60 fatalities (40%) observed and only 18 patients (12%) survived. The Plasma Pseudocholinesterase levels of all the 60 fatal cases were compared and found to be statistically highly significant ($p < 0.001$). No statistically significant difference was found between those who survived and those who died with severe poisoning ($p > 0.5$). Therefore, the pseudocholinesterase levels estimated at the time of admission to the hospital serves as a very good prognostic indictor and also helps in dose adjustment of various drugs for treatment. Severe poisoning was associated with suppression of plasma pseudocholinesterase by 84.04% to 93.19% where death occurred over a 3 day duration following admission to hospital. If plasma pseudocholinesterase was suppressed by 89.24% to 93.19% (as seen in those who died within 24 hours of admission) then it is associated with 100% mortality. This shows that there is a direct correlation between plasma pseudocholinesterase and severity of poisoning. And suppression of this enzyme by more than 89.24% (i.e. plasma pseudocholinesterase levels <1,678 U/L) is associated with fatal outcome. This is in agreement with a study by Xu, Zhang, yang and He [11] which states that when the plasma pseudocholinesterase levels reach 10% then severe acute organophosphorus poisoning occurs. A cohort study done by Eddleston and colleagues[12] found plasma pseudocholinesterase activity of <600 U/L on admission was highly sensitive in chlorpyrifos and specific for dimethoate poisoning which is also in agreement with this study. Sunder Ram et al.[13] also states that plasma pseudocholinesterase level below 10% of normal were associated with poor prognosis which is in agreement with this study. Studies reported in Reddy [14], Pillay [15] and by Sozmen and colleagues[16] are all in acceptance with this study. Kukde and colleagues[17] have found no significant difference of pseudocholinesterase levels

between post-mortem samples of brought dead cases and partially treated cases.

Limitations of the Study

1. Patients with age less than 14 years were not included in this study
2. Poisoning other than organophosphate whether taken independently or along with organophosphates (E.g. Alcohol) were not included in this study.
3. Serial monitoring of cases could not be done due to poor patient compliance and also due to economic limitations and only follow-up to know the outcome was performed.

Conclusion

Our study concludes that there is a very good correlation between the levels of plasma pseudocholinesterase and mortality as well as morbidity. This study helps not only in predicting the outcome of the patient with organophosphate poisoning based on plasma pseudocholinesterase levels but also can be retrospectively used to plan the treatment of such patients and dosage calibration of antidotes such as pralidoxime.

Ethical Clearance: Taken from institutional ethics committee, JJMMC, Davangere

Source of Funding: Self

Conflict of Interest: Nil

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