Role of Serial Serum Cholinesterase Levels in Clinical Outcomes of Patients with Organophosphorus Compound Poisoning: A Cohort Study

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ABSTRACT

Introduction: Poisoning is caused, when a poisonous material is consumed, inhaled, or comes into contact with the skin, eyes, or mucous membranes like the mouth or nose. Poisoning by pesticides has long been considered a serious public health issue. The majority of poisoning cases reported to hospitals involve either an unknown type and quantity of Organophosphorus (OP) poisoning taken by the patient, which makes repeated serum Acetylcholinesterase measurements. Few studies have done the serial Serum Cholinesterase(SChE) tests in the early stages of poisoning.

Aim: To evaluate the prognostic value of measuring serial SChE levels in patients with OP poisoning to predict clinical outcomes.

Materials and Methods: This cohort study was conducted in the Department of Biochemistry and Therapeutics at Hassan Institute of Medical Sciences, Karnataka, India. Medical records of OP poisoning cases admitted during September 2023 and December 2023. A total of 40 patients were included in the study. Detailed demographic and clinical data, along with serial SChE levels at admission, day 2, and day 4, were recorded in the case record forms.

Results: The mean age of the patients was 43.38±16.46 years. There was a significant decrease in serum SChE levels from day 1 to day 4 (p<0.0001). Furthermore, the mean SChE levels at admission in patients who survived were significantly higher (p<0.00001) than those in the group that expired.

Conclusion: Significantly higher SChE levels were found to be associated with improved clinical outcomes, as indicated by improvements in mechanical ventilation and lower fatality rates after acute OP poisoning.

INTRODUCTION

Consumption or inhalation of a poisonous material, or contact with the skin, eyes, or mucous membranes like the mouth or nose, can cause poisoning. Pesticide poisoning has long been considered a serious public health problem. One common way people harm themselves is by poisoning, especially in developing nations [1]. Three million cases of pesticide poisoning occur worldwide every year, with the majority occurring in Asia, and atleast half being caused by OP poisoning as stated by World Health Organisation research [2].

Given that India is an agricultural nation, OP compounds are among the most widely used agents for suicidal poisoning due to their accessibility [3]. OP compounds are the main cause of self-poisoning mortality in South and Central India [4-6]. These issues are particularly common in India's rural communities. According to Chintale KN et al., OP poisoning is common in central and southern India, leading to a higher death toll [7]. They are often used for self-harm or suicide due to the ease of access and widespread availability of pesticides in poor countries where regulatory bodies are less severe than in industrialised countries with strictly enforced regulations [8]. The percentage range of people in India who commit suicide by poisoning themselves with OPs is 10.2% to 43.87% [9].

Organophosphate insecticides primarily function by inhibiting carboxyl ester hydrolases, especially AChE. The enzyme AChE breaks down the neurotransmitter ACh into choline and acetic acid. ACh is found in Red Blood Cells (RBCs), neuromuscular junctions, and the central and peripheral neurological systems. By phosphorylating the serine hydroxyl group in the AChE active site, organophosphates render AChE inactive. Phosphorylation occurs by forming a covalent link with AChE and losing an organophosphate leaving group. Once AChE is deactivated, ACh accumulates throughout the nervous system, overstimulating muscarinic and nicotinic receptors. This leads to activation of the central nervous system, the autonomic nervous system, and the nicotinic receptors in skeletal muscle, resulting in clinical symptoms [10-12]. Serial estimation of SChE levels can be used to identify persistent enzyme inhibition.

According to the Proudfoot criteria, the degree of enzyme inhibition has been estimated using SChE levels to determine the severity of poisoning. Persistent inhibition of the enzyme can be identified by serial estimation of SChE levels. The majority of poisoning cases involve an unknown type and quantity of OP poisoning eaten by the patient, making repeated serum AChE measurements [13]. Few studies have estimated serial SChE levels in the early stages of poisoning, when there is a significant risk of life-threatening consequences. When determining the best course of action for early care in severe instances of OP poisoning in terms of mortality and the requirement for mechanical ventilation, SChE levels will prove to be an excellent diagnostic tool in the laboratory [12,14]. There are not many studies on SChE levels and the clinical outcome of OP poisoning cases in South India [15,16]. Considering the null hypothesis that SChE levels in patients with OP poisoning play no role in predicting clinical outcomes, the present study was conducted to evaluate the prognostic value of measuring serial SChE levels in patients with OP poisoning for predicting the clinical outcome.

MATERIALS AND METHODS

Methodology: A retrospective cohort study was done in the Department of Biochemistry, Central Laboratory, at Hassan Institute

of Medical Sciences, Karnataka, India, from September 2023 to December 2023. The study was approved by the Institutional Ethics Committee (IEC/HIMS/RR543/29-02-2024). Medical records of OP poisoning cases admitted during September 2023 to December 2023 were retrieved from the medical records department.

Inclusion criteria: Records of OP poisoning cases aged more than 18 years were included in the study.

Exclusion criteria: Patients with a history of poisoning with double insecticide, multiple poisoning with other drugs such as opioids, diazepam, barbiturates, etc., malnutrition, and patients with chronic hepatic illness were excluded.

Estimation of sample size: In a study done Mittal C et al., the proportion of OP poisoning in South India was 65.9%, with a 95% confidence interval and 15% absolute precision [17]. The minimum sample required is 39 cases. 40 cases were included in the study after doing records from the Medical Records Department.

Procedure

Demographic details, AChE levels on the day of admission, 2nd day, and 4th day were recorded. SChE levels were determined by measuring the rate of hydrolysis of the substrate (benzyl choline) catalysed by SChE using the Abott Architect ci 4100 integrated chemistry and immunoassay analyser (Impact Laboratory Supplies, Mangalore, Karnataka, India). The normal reference range for Cholinesterase is 4850-12000 U/L [18]. Details of mechanical ventilation were noted, details regarding patient outcomes (i.e., death/discharge) was recorded.

STATISTICAL ANALYSIS

Data were entered into Microsoft excel, and statistical analysis was performed using the tabulated data from the case record forms of patients with OP poisoning. The data were presented as mean±Standard Deviation (SD). The serial SChE levels at various time points were analysed using a paired t-test to compare significance between the groups at serial time points. The level of significance was set at $p < 0.05$ with a power of 80%. The clinical outcome was assessed using a paired t-test. All statistical analyses were performed using SPSS software version 26.0.

RESULTS

The mean age of the patients was 43.38±16.46 years. Poisoning cases were more common in males (n=25, 62.5%) [Table/Fig-1]. Among the 40 subjects, 19 were dead and 21 were discharged.

Variables		Frequency	Percentage
Age (years)	<30	12	30%
	31-50	15	37.5%
	51-70	13	32.5%
Gender	Male	25	62.5%
	Female	15	37.5%

[Table/Fig-1]: Demographic variables of study participants.

The serial SChE levels (U/L) estimated at days 1, 2, and 4 for the group of patients were 3727.13±3574.5, 3664.65±3527.7, and 3629.6±3511.8 U/L, respectively [Table/Fig-2]. The SChE levels among those who survived on days 1, 2, and 4 were significantly more than in the non-survivors (p<0.001). SChE levels were significantly lower in patients who required mechanical ventilation (p<0.001). So higher SChE levels were associated with better outcomes among OP poisoning patients [Table/Fig-3,4].

A patient with SChE levels > 10000 did not require mechanical ventilation and survived poisoning. Nineteen patients with SChE levels < 455 required mechanical ventilation but couldn't survive [Table/Fig-5,6]. In patients, with SChE levels less than 455, the
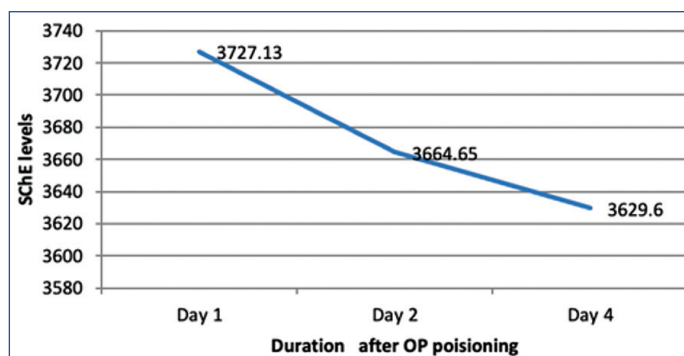
[Table/Fig-2]: Line diagram showing Serial mean SChE levels.
Paired t-test value with p-value <0.0001 between day 1 and day 2, p-value of <0.0001 between Day 1 and Day 4 levels

Day	Mean SChE levels		p-value
	Death	Discharge	
Day 1	453	6687.62±2354.02	**<0.001**
Day 2	453	6568.62±2371.91	**<0.001**
Day 4	457.63±20.18	6501.75±2410.85	**<0.001**

[Table/Fig-3]: Mean and SD values of SChE in death and discharged patients.

Day	Mean SChE Levels		p-value
	On MV	Not on MV	
Day 1	453	6687.62±2354.02	**<0.001**
Day 2	453	6568.62±2371.91	**<0.001**
Day 4	457.63±20.18	6501.95±2410.85	**<0.001**

[Table/Fig-4]: Mean and SD values of SChE in Patients on MV and not on MV.

SChE levels	Not on MV	On MV
<455	0 (0%)	19 (100%)
456-5000	3 (100%)	0
5001-10000	17 (100%)	0
>10000	1 (100%)	0
Total	21 (52.5%)	19 (47.5%)

[Table/Fig-5]: SChE levels on day 1 and Mechanical Ventilation (MV).
Chi-square test 40, p-value <0.00001

SChE levels	Death	Discharged
<455	19	0
456-5000	0	3
5001-10000	0	17
>10000	0	1
Total	19 (47.5%)	21 (52.5%)

[Table/Fig-6]: SChE levels on day 1 and clinical outcome.
Chi-square test 40, p-value <0.00001

mean duration of hospital stay was 6.42±4.1 days. With higher SChE levels, the duration of stay was less [Table/Fig-7].

SChE levels	Mean duration of stay	SD
<455	6.42	4.1
456-5000	4.0	1.0
5001-10000	2.71	1.1
>10000	2	Only one case

[Table/Fig-7]: Duration of stay and SChE levels on day 1.

DISCUSSION

In developing countries like India, where most people work in agriculture and live in rural regions with unfettered access to highly toxic OP chemicals, OP poisoning is a serious medical issue. The majority of the time, there is insufficient knowledge about the specific type of poisoning, type taken with the intention of

S. No.	Authors/ Year	Place of study				
1	Hundekari IA et al., 2013 [16]	Karnataka, India	150 Cases 30 controls	To assess the oxidative damage, haemoglobin level and leukocyte count in acute organophosphorus pesticide poisoning.	Plasma cholinesterase, serum Malondialdehyde (MDA) levels, plasma Total Antioxidant Capacity (TAC), erythrocyte Superoxide Dismutase (SOD), Catalase (CAT) and glutathione peroxidase (GPx) levels.	Cholinesterase levels decreased in cirrelation to the grades of OP poisoning. Significant increase in MDA levels were seen in all grades of OP poisoning cases when compared to controls.
2.	Manu MS et al., [15]	Mysore	37 Cases	A Retrospective Analysis of Serial Measurement of Serum Cholinesterase in Acute Poisoning with Organophosphate Compounds	Serial AChE Levels	AChE Levels below 870IU/L, 1,110IU/L, 1,020IU/L and 885IU/L on day two, three, four indicate poor prognosis and mortality
3.	Goswamy R et al., 1994 [23]	Bombay, India	52	Study of respiratory failure in organophosphate and carbamate poisoning	AChE Levels	Respiratory failure in patients with low AChE
4.	Present study	Hassan, India	40	To evaluate the prognostic value of measuring serial SChE levels in patients with OP poisoning for predicting the clinical outcome	Acetylcholinesterase levels in the serum	Significantly higher SChE levels were found to be associated with improved clinical outcomes, as indicated by improvements in mechanical ventilation and low fatality after acute OP poisoning.

[Table/Fig-8]: Comparative evaluations of previous studies with Present study. [15,16,23, Present study].

suicide attempts, which is frequently made worse by the scarcity of tertiary care services. These variables result in a high death rate and serious, potentially fatal consequences. Acetylcholine builds up at the synapses as a OP drugs irreversibly inhibit the neuropathy target esterase, SChE, and AChE, which causes their toxic symptoms. Cholinergic crisis has thus been caused by hyperstimulation of the central and peripheral nervous systems, resulting in a cholinergic crisis. It may take days or even months for the ensuing muscarinic and nicotinic symptoms to subside before the cholinesterase enzyme is restarted. Cholinesterase levels estimation of OP exposure aids medical practitioners make an early diagnosis and subsequently in starting a treatment plan right away [15,16].

To evaluate the relationship between the serial estimation of SChE levels and the clinical outcome in OP poisoning patients, the present study was undertaken. In the younger age group, the incidence of OP poisoning was more predominant in the 35-50 years age range, while in other studies, it was more common in the 15-35 years age group [16,19]. There was a male predominance with 62.5% of total patients in our study, which is consistent with studies by Arup KK and Kavya ST et al., [20,21].

A single measurement of SChE at admission may not have any predictive value, but serial SChE activity may more accurately predict the patient's clinical fate and help in selecting better treatment alternatives, such as the necessity for mechanical breathing. For these reasons, we examined SChE levels at serial time points. Furthermore, as day 4 is when oximes ideally achieve their optimum activity and reduce the requirement for mechanical ventilation in patients with severe respiratory distress, the levels were examined three times in a row from the time of admission [22]. In this study, the authors observed better SChE levels in those patients who didn't require mechanical ventilation and had a good clinical outcome compared to those on mechanical ventilation. Apart from clinical indicators, low SChE levels have the greatest predictive value for mechanical ventilation in OP poisoning as concluded by another study by Goswamy R et al., [23]. However, Nouira S et al., did not find any statistically significant difference in mean SChE levels in those mechanically ventilated and those not needing ventilator support [24]. Similar studies from the literature have been compared in [Table/Fig-8] [15,16,23].

Limitation(s)

Liver function tests, kidney function tests, and body surface area, which could have added value to the study, were not considered during the planning of the study.

CONCLUSION(S)

Significantly higher levels of SChE were found to be associated with improved clinical outcomes in the current investigation, as evidenced by enhancements in mechanical ventilation and fatality rates after acute OP poisoning. Future studies in this area may benefit from employing a prospective study design, more frequent monitoring of SChE, LFT, RFT, and more clinical outcomes.

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