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Original Article

Plasma Cholinesterase Activity and Clinical Course in Geriatric Organophosphate Poisoning

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SUMMARY

Background: This study is aimed at evaluating the characteristics of plasma cholinesterase level in geriatric organophosphate (OP) poisoning patients and clinical courses associated with the plasma cholinesterase level.
Method: We conducted a retrospective study of 135 patients who had ingested organophosphate insecticides between Jan 2000 and Dec 2015. Patients were dichotomized into age ≥ 65 (geriatric group) and < 65 years (non-geriatric group). Clinical course and serial plasma cholinesterase level were investigated.
Results: Age was associated with higher incidence of hypotension and central nervous system depression (geriatric group vs. non-geriatric group: 38.6% vs. 21.1% [p = 0.032]; 37.8% vs. 19.1% [p = 0.019], respectively. The plasma cholinesterase level recovered more rapidly in the non-geriatric group than in the geriatric group (p = 0.022). Regarding outcomes, hospital survival rate was lower in the geriatric group than the non-geriatric group (73.3% vs. 91.1% respectively, p = 0.006).
Conclusions: In OP poisoning patients, even though the presenting symptoms and plasma cholinesterase level were similar, the incidences of shock and CNS depression during admission were higher in the geriatric group than in the non-geriatric group. Given these findings, physicians should beware of deterioration of geriatric OP poisoning patients even their initial presentation is mild.

1. Introduction

Organophosphates are widely used pesticides. Organophosphate poisoning (OP) is an increasing worldwide problem because of their acute toxicity.[1] The mortality resulting from OP is reported to be 10% to 20%, which is higher than that from poisoning due to other drugs despite advances in toxicology.[2,3]

Recently, as the world's population is aging, the number of geriatric patients with poisoning is increasing.[4,5] Physiology changes at the structural, functional, and molecular levels as people age, and every major organ system experiences physiologic change with time. The nervous system suffers cognitive decline and volume loss. The cardiovascular system changes result in lower cardiac output and higher blood pressure, leading to significant changes to the structure and function of the heart. The respiratory system changes lead to impaired oxygenation and diminished ventilation/perfusion matching. The gastrointestinal system experiences delayed gastric emptying and reduction of hepatic metabolism, and the renal system experiences a diminished glomerular filtration rate.[6] Given these changes, we could expect geriatric patients to show higher mortality and morbidity than younger patients.

Several studies revealed that geriatric patients showed higher mortality than non-geriatric patients in organophosphate poisoning.[7–10] There have been no reports, however, regarding changes in plasma cholinesterase level and the clinical course associated with it in geriatric patients. So, we aimed to investigate the characteristics of plasma cholinesterase levels in geriatric OP poisoning patients and of clinical courses related to the plasma cholinesterase level in the present study.

2. Methods

2.1. Design

This retrospective study included patients who presented with OP poisoning to a university hospital emergency department between Jan 2000 and Dec 2015. Poisoning with OP was confirmed by patient or guardian statements, and an emergency physician verified the poisoning agent. This study was approved by the institutional committee of our hospital.

2.2. Subject and data collection

OP poisoning patients were identified from toxicology registry of our hospital. Data were retrospectively collected from medical records by one researcher and reviewed by two emergency physicians.

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Poisoning with organophosphate was confirmed by patient or guardian statements, and verification of the agent was performed by an emergency physician who transcribed the bottle label into patient records.

Patients with any of the following conditions were excluded from this study: (1) younger than 18 years of age; (2) an uncertain history of exposure; (3) combined drug exposures; (4) terminal malignancy; (5) patients concurrent with sepsis of any origin; and (6) missing data. Patients were divided into the geriatric group (aged > 65 years) and the non-geriatric group (aged < 65 years). The severity of intoxication was classified by the Namba's Classification (Table 1).[11]

Data were retrospectively collected from medical records and review. The following parameters were assessed: age, sex, poisoning characteristics (e.g., the cause of ingestion, amount, place), and clinical characteristics (e.g., emergency treatment, physical examination and symptoms, laboratory data (including plasma cholinesterase level), clinical outcomes, and mental status with the Glasgow Coma Scale [GCS]). Central nervous system (CNS) depression was classified as mild: GCS of 14–15; Moderate: GCS 9–13; Severe: GCS 3–8.[12]

Regarding plasma cholinesterase, we routinely check serial plasma cholinesterase level in treating OP poisoning patients by our hospital's protocol. Cholinesterase level is one of the important markers for assessing OP poisoning patients' state however it is quite expensive in Korea. Considering the economics and efficiency, the protocol was made as checking plasma cholinesterase level at admission day, 3rd and 5th day of admission, and 5 days interval after 5th day of admission. Resultingly, serial plasma cholinesterase level at presentation and days 1, 3, 5, 10, 15, and 20 were investigated.

The amount of toxin ingested was calculated by the number of mouthfuls (1 mouthful = 20 mL), as stated by the patient and/or calculated from the remaining amount in the chemical bottle.[13] If there were any questions or controversies, one toxicologist answered and resolved those questions and controversies.

2.3. Data analysis

Statistical analyses were performed using SPSS software for Windows (V.20.0K, SPSS, Chicago, IL, USA). Nominal data are presented as frequencies and percentages, and continuous variables are presented as means and standard deviations (SD) and as medians and interquartile ranges (IQR). The Chi-square test or Fisher's exact test was used for a comparison of nominal variables while the two-sample t-test and Mann-Whitney U test were used to compare continuous variables. P-values < 0.05 were considered statistically significant.

3. Results

3.1. General patient characteristics

Between Jan 2000 and Dec 2015, 171 patients were admitted to the emergency department with OP poisoning. Thirty-six patients were excluded because of being < 18 years old (6 patients), an uncertain history of exposure (12 patients), multiple drug exposure (12 patients), a history of terminal malignancy (2 patients), and missing data (6 patients). Finally, a total of 135 patients (45 geriatric and 90 non-geriatric) were included in this study (Fig. 1). The average age of the geriatric patients was 72, and that of the non-geriatric patients was 48. Sex distribution between groups was not significant (geriatric group, 32 men [71.7%]; non-geriatric group, 61 men [67.8%]; p = 0.844). There was no difference between groups in terms of vital signs, clinical symptoms on presentation, initial plasma cholinesterase level, the severity assessed with Namba's classification, Acute Physiology, and Chronic Health Evaluation (APACHE) II score (Table 2).

Attempted suicide appeared to be the most common reason for ingesting pesticides in both geriatric patients (26 [57.8%]) and

Table 1
Assessment of Namba's severity of acute organophosphate poisoning.

	Severity		
	Mild	Moderate	Severe
Clinical manifestations	Able to ambulate Fatigue Headache Dizziness	Unable to ambulate Dysarthria Miosis General weakness	Unconscious Reduced PLR Severe miosis Rale Cyanosis
Serum cholinesterase level	20~50%	10~20%	< 10%

PLR : prompt light reflex.

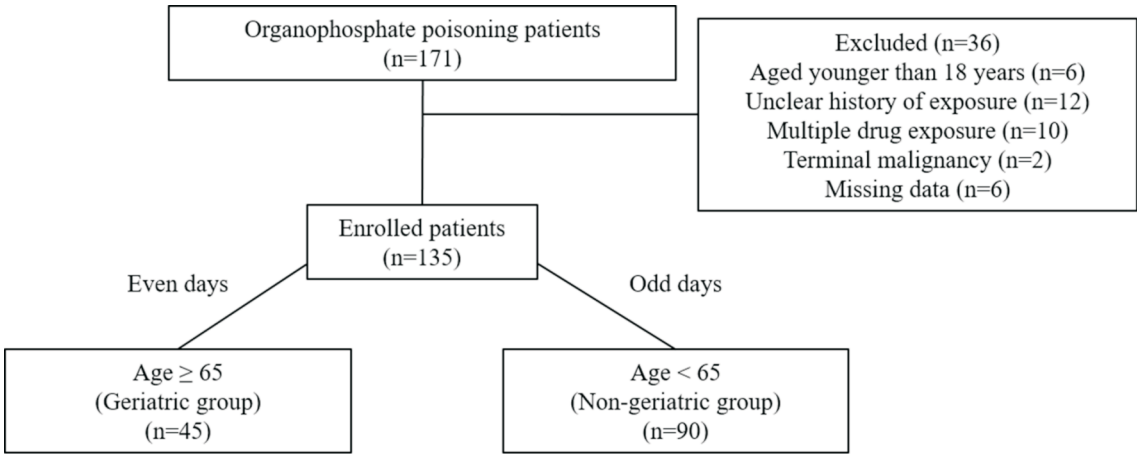

Fig. 1. Study population.

Table 2
General characteristics and laboratory findings

	Non-geriatric patients (N = 90)	Geriatric patients (N = 45)	*p*-value
Male	61 (67.8%)	3 2(71.7%)	0.844
Intentional poisoning	65 (72.2%)	26 (57.8%)	0.119
Amount (mL)	150 (65-300)	100 (80-140)	0.137
Systolic BP (mmHg)	137 ± 33	144 ± 45	0.416
Diastolic BP (mmHg)	82 ± 21	81 ± 22	0.781
Pulse (beats per minute)	99 ± 21	91 ± 22	0.093
Respiratory rate (breaths per minute)	20 ± 4	20 ± 5	0.782
Body temperature (°C)	36.2 ± 0.7	35.9 ± 0.8	0.055
Chief complaint			
CNS symptoms	58 (64.4)	33 (73.3)	0.533
Pulmonary symptoms	11 (12.2)	5 (11.1)	
GI symptoms	21 (23.3)	7 (15.6)	
Namba's classification			
Mild poisoning	18 (20.0)	11 (24.4)	0.074
Moderate poisoning	23 (25.6)	4 (8.9)	
Severe poisoning	49 (54.4)	30 (66.7)	
APACHE II	15.8 ± 5.2	17.5 ± 5.8	0.189
Laboratory findings			
Lactate (mmol/L)	4.80 ± 3.18	5.71 ± 3.62	0.189
Initial plasma cholinesterase (U/L)	864.6 ± 1792.7	751.6 ± 1355.5	0.710
AST	53.6 ± 42.7	45.4 ± 37.7	0.653
ALT	29.1 ± 22.2	27.4 ± 17.0	0.279
BUN	13.8 ± 5.2	15.4 ± 4.6	0.079
Creatinine	0.89 ± 0.3	0.87 ± 0.2	0.725

OP: organophosphate, SBP: systolic blood pressure, DBP: diastolic blood pressure, CNS: central nervous system, GI: gastrointestinal, APACHE: Acute Physiology and Chronic Health Evaluation.
CNS symptoms:mental confusion, headache, dizziness, seizure, coma; Pulmonary symptoms: dyspnea, bronchorrhea; Gastrointestinal symptoms: diarrhea, abdominal pain.
The results are expressed as Number(percentage), Median(Quartile 1 – Quartile 3) or Mean +/- Standard Deviation.

non-geriatric patients (65 [72.2%]). The amount of OP ingested was comparable in both geriatric patients and non-geriatric patients (100 ml [IQR 80-140] vs. 150 ml [IQR 65-300], p = 0.137) (Table 2).

3.2. Recovery rate of plasma cholinesterase level

The recovery rate of plasma cholinesterase level was assessed with repetitive tests over a period of 20 days (day 1, 3, 5, 10, 15, 20). Both groups showed a linear increase, but the recovery rate was slower in the geriatric group than in the non-geriatric group (p = 0.022) (Fig. 2).

3.3. Clinical course during admission

The incidence of pneumonia and intubation rate showed no significant difference in geriatric patients and non-geriatric patients (32 [61.1%] vs. 55 [71.1%], p = 0.253; 12 [30.8%] vs. 14 [19.2%], p = 0.166; respectively). However, a significantly higher proportion of geriatric patients (17 [38.6%]) experienced hypotension than did non-geriatric patients (19 [21.1%]; p = 0.032). Furthermore, geriatric patients were more likely to have severe CNS depression (GCS < 8) than were non-geriatric patients (17 [37.8%] vs. 17 [19.1%], p = 0.019). The overall survival of geriatric patients was lower than that of non-geriatric patients, with 73.3% and 91.1%, respectively (p = 0.006) (Table 3).

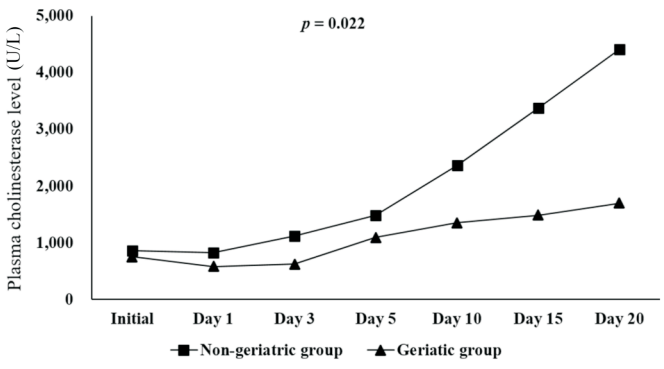

Fig. 2. Time-course analysis of plasma cholinesterase levels.

4. Discussion

Agricultural organophosphate pesticide is commonly used worldwide. It is mostly used in rural areas, but recently, it has been used in urban centers to eradicate harmful insects. Therefore, an increasing number of cases of human poisoning have been reported, mainly from occupational exposure and deliberate or accidental ingestion.

The mortality rate due to the ingestion of this pesticide is higher than that of other poisonings. In this study, the overall mortality rate was 14.8%, which is similar to other studies.[2,3] Also, similar to Huang HS et al.'s report,[14] the mortality rate was higher in the geriatric

Table 3
Clinical course characteristics (treatment, severity, complications, and prognosis)

Category	Non-geriatric patients (N = 90)	Geriatric patients (N = 45)	p-value
Intubation, n (%)	55 (61.1)	32 (71.1)	0.253
Pneumonia, n (%)	14 (19.2)	12 (30.8)	0.166
Hypotension, n (%)	19 (21.1)	17 (38.6)	0.032
GCS < 8, n (%)	17 (19.1)	17 (37.8)	0.019
Survival, n (%)	82 (91.1)	33 (73.3)	0.006

GCS: Glasgow coma scale.

group than the non-geriatric group (26.7% vs. 0.9%, p = 0.006 respectively) even though the presenting clinical characteristics were not different, i.e., the amount of pesticide ingested, initial presenting symptoms, and initial plasma cholinesterase level. Nevertheless, during admission, hypotension (systolic blood pressure < 90 mmHg) was seen in 19 (21.1%) vs. 17 (38.6%) patients, p = 0.032, and CNS depression was seen in 17 (19.1%) vs. 17 (37.1%) patients, p = 0.019, in the geriatric and non-geriatric groups, respectively.

Symptoms of organophosphate poisoning include decreased cholinesterase activity in the neuromuscular system, CNS, and parasympathetic nerve endings and accumulation of acetylcholine in synapses.[15,16] Excessive accumulation of acetylcholine paralyzes cholinergic stimulation in the CNS, autonomic ganglion, parasympathetic nerve endings, sympathetic ganglia and could also cause thyroid dysfunction.[15,17] In patients with organophosphate poisoning, cholinesterase levels decrease but recover by 25–30% within 7–10 days after exposure and return to pre-morbid levels after 4–6 weeks.[18–20]

Oh et al. reported that the prognosis was better when cholinesterase levels recovered over time,[21] and Chen et al. reported that plasma cholinesterase recovery rates in OP poisoning patients were -0.26 mU/mL per hour and 73.34 mU/mL per hour in non-surviving patients and surviving patients, respectively.[22] Likewise, in this study, the geriatric group that showed a higher mortality rate also showed a lower recovery rate of plasma cholinesterase levels than those of the non-geriatric group.

Further insight into the impact of aging on OP poisoning was obtained from the time-course analysis of plasma cholinesterase levels. In both groups, the initial plasma cholinesterase level was below 1000 U/L, which is at least twofold lower than the normal values reported in the literature,[23] and the plasma cholinesterase levels of the geriatric group showed recovery from 3 days after admission whereas the non-geriatric group showed it 1 day after admission. This is consistent with Ali's study that reported the mortality rate in pesticide poisoning was associated with the absence of an increase in plasma cholinesterase activity within 48 h of poisoning.[23] Kang et al. reported that plasma cholinesterase levels were higher in patients who survived than in patients who died, which agrees with the results of the current study.[10,24] These studies suggest that geriatric patients had a poor prognosis because of delayed recovery of cholinesterase activity.

There are some limitations in this study. First, it was a retrospective study and involved only one hospital. As a result, not all relevant assessment parameters were included. Especially, no symptoms could be investigated but the chief complaint.

Second, we measured serum cholinesterase levels but did not measure red blood cell (RBC) cholinesterase levels. RBC cholinesterase level is a better reflection of the functional state of the nerve endings. If the RBC cholinesterase level had been measured, the results would have been different. Further studies are required to clarify these details.

5. Conclusions

The geriatric group showed a lower recovery rate of plasma cholinesterase level compared to the non-geriatric group. In OP poisoning patients, even though presenting symptoms and plasma cholinesterase level were similar, the incidences of shock and CNS depression during admission were higher in the geriatric group than in the non-geriatric group.

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