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Epidemiology of organophosphate intoxication and predictors of intermediate syndrome

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Aim: To evaluate the usefulness of plasma glucose and serum cholinesterase levels as predictors of organophosphate-induced intermediate syndrome.

Materials and methods: Seventy-one organophosphate poisoning patients who were admitted to our emergency department during a 4-year period were evaluated retrospectively. Four patients were excluded from the study due to a lack of medical records. Categorical variables were analyzed using the chi-square test and nonparametric variables were analyzed using the Mann–Whitney U test.

Results: Thirty-five (52.2%) patients were male and 32(47.8%) were female. Patients had a mean age of 39.4 ± 15.9 years and 70.1% of the patients were married. Oral intake (68.7%) was the most common method of intoxication, and attempted suicide (67.2%) was the most common cause. The most common organophosphates were methamidophos (20.8%), dichlorvos (19.4%), parathion (7.5%), and methyl parathion (7.5%). Fifty-seven (85%) patients were treated in the emergency observation unit and 10 (15%) patients were admitted to the intensive care unit. Eleven (16%) patients developed intermediate syndrome and had significantly lower levels of serum cholinesterase ($P < 0.01$) and higher blood glucose levels ($P = 0.037$).

Conclusion: Initial serum cholinesterase and glucose levels measured in the emergency department may be a useful marker in predicting organophosphate-induced intermediate syndrome.

Key words: Intoxication, organophosphate, hyperglycemia, intermediate syndrome, cholinesterase

1. Introduction

Organophosphates (OPs) are widely used in agriculture and OP intoxication is a global public health problem (1–3). OP intoxication can occur by accidental occupational exposure or suicide attempts. Intermediate syndrome (IMS) is a clinical syndrome characterized by respiratory muscle paralysis, proximal muscle weakness, and motor cranial nerve involvement (4–8).

Many theories have been proposed to explain IMS, including the severity of intoxication, methamidophos and dimethoate intoxication, and late or insufficient oxime therapy (5,6). IMS has been reported in patients treated with early treatment doses of oxime, as recommended by the World Health Organization (9). IMS occurs frequently and it is a major factor of OP-related mortality. The aim of the present study was to evaluate the usefulness of plasma glucose and serum cholinesterase levels as predictors of IMS (9).

2. Materials and methods

Seventy-one OP poisoning patients admitted to our university hospital's emergency department (ED) during a 4-year period were evaluated retrospectively. Four patients were excluded from the study due to a lack of medical records. Age, sex, occupation, marital status, cause of poisoning, method of poisoning, laboratory and electrocardiographic findings, specific treatments, intensive care unit (ICU) admission, and mortality were obtained from the patient files.

Patients with a history of contact with or exposure to OPs, typical signs and symptoms of OP poisoning, low levels of serum cholinesterase, and symptomatic responses to atropine and oximes were diagnosed with OP intoxication. Those with weakness of proximal limb muscles, neck flexors, respiratory muscles, and motor cranial nerves in the interval between acute cholinergic crisis and organophosphate-induced delayed neurotoxicity were diagnosed with IMS (9,10).

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Patients having any chronic diseases and those who were pregnant, less than 18 years old, or lacking medical records were excluded from the study.

Patient data were analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Results were expressed as mean ± standard deviation (SD). Categorical variables were analyzed using the chi-square test and nonparametric variables were analyzed using the Mann–Whitney U test. A level of statistical significance was established at $P < 0.05$ for all analyses.

3. Results

Thirty-five (52.2%) patients were male and 32 (47.8%) were female. Patients had a mean age of 39.4 ± 15.9 years and 70.1% of the patients were married. The most common OPs were methamidophos (20.8%), dichlorvos (19.4%), parathion (7.5%), and methyl parathion (7.5%).

Oral intake (68.7%) was the most common method of intoxication. Other methods of exposure were inhalation in 13 patients (19.3%), dermal exposure in 2 patients (3%), and combined dermal exposure and inhalation in 6 patients (9%). Attempted suicide (67.2%) was the most common cause of intoxication (Table 1).

Vomiting (79.1%) was the most common clinical finding upon admission to the ED. At admission, mean serum cholinesterase levels were 2292.73 ± 1420.21 U/L. Laboratory values on admission to the ED are shown in Table 2.

Eleven (16%) patients developed IMS and had significantly lower levels of serum cholinesterase ($P < 0.01$). Similarly, the IMS group had significantly higher blood glucose levels ($P = 0.037$; Table 3).

Thirty-nine patients (58.3%) were treated with oxime therapy in the ED. Oxime therapy was administered to 28

Table 1. Causes of organophosphate exposure.

	Oral, n (%)	Inhalation, n (%)	Dermal, n (%)	Dermal and inhalation, n (%)	Total, n (%)
Suicide attempt	45 (67.2%)	0	0	0	45 (67.2%)
Occupational	0	1 (1.5%)	1 (1.5%)	6 (9%)	8 (11.9%)
Accidental	1 (1.59%)	12 (17.9%)	1 (1.5%)	0	14 (20.9%)
Total	46 (68.7%)	13 (19.4%)	2 (3%)	6 (9%)	67 (100%)

Table 2. Initial laboratory findings.

Laboratory findings	Mean ± SD	Normal ranges
White blood cells (U/L)	11,627.95 ± 3900.06	4000–11,000
Creatine kinase (U/L)	183.81 ± 103.47	35–195
Glucose (mg/dL)	144.7 ± 85.3	70–110
Aspartate aminotransferase	28.86 ± 17.01	8–46
Serum cholinesterase (U/L)	2292.73 ± 1420.21	3600–12,900

Table 3. Differences of IMS patients.

Laboratory findings	Patients without IMS (n = 56)	IMS patients (n = 11)	P-value
Glucose (70–110 mg/dL)	138.55 ± 71.34	186.63 ± 57.31	0.039
Serum cholinesterase (3600–12,900 U/L)	2651.72 ± 1266.68	465.11 ± 302.63	0.001
Creatine kinase (35–195 U/L)	189.81 ± 110.73	153.26 ± 44.61	0.928
Aspartate aminotransferase (8–46 U/L)	29.55 ± 17.82	22.66 ± 2.08	0.067
Leukocytes (4000–1100 U/L)	11409.36 ± 3659.45	12740.78 ± 5010.53	0.09

(41.7%) patients in other hospitals. Fifty-seven patients (85%) were treated in the emergency observation unit and 10 patients (15%) were hospitalized in the ICU. Sixty-one patients (91%) were discharged, 3 patients (4.5%) were discharged in a vegetative state, and 3 patients (4.5%) died.

4. Discussion

Poisoning due to OPs is a major public health problem in developing countries. OP intoxication can be observed in all age groups (11–13). The average age of the patients in the present study was 39.4 years, which was consistent with that described in the literature (12,14,15). Many studies have reported a female predominance with respect to OP intoxication. However, several

other studies have reported a male predominance (16–18). In the present study, OP intoxication

was more common in men. OP intoxication is also more common in married people (16–21). Forty-seven patients (70.1%) in the present study were married. OP compounds are highly toxic and can be easily obtained. OP compounds are commonly preferred for suicide attempts (19,20,22,23). In our study, oral intake was the most common way of intoxication and suicide attempt was the most common cause.

Symptoms of OP intoxication vary according to the type of OP and duration of exposure. Recent

studies have reported that the most common clinical findings are vomiting and myosis (12,17,20,24,25). In our study, vomiting (79.1%) and myosis (50.7%) were also the most common clinical findings. In previous studies, the most common OP compounds were dichlorvos, fenitrothion, and malathion (12,17,18,26,27). In our study, common causes were methamidophos (20.8%) and dichlorvos (19.4%). Studies have reported that glycogenolysis-related hyperglycemia in OP intoxication is due to increased sympathetic activity (28–30). In our study, the mean glucose level of patients was 144.7 ± 85.3 mg/dL. IMS is related to permanent inhibition of acetylcholinesterase and severe intoxication. Early aggressive decontamination, appropriate antidote therapy, and adequate respiratory support reduce the incidence of IMS (9). The incidence of IMS in OP intoxication studies varies between 7.7% and 65% (19,31,32). In the current study, IMS occurred in 16% of patients. A lower IMS incidence may be related to the effective management of organophosphate poisoning.

In the present study, lower serum cholinesterase levels and hyperglycemia predicted the

occurrence of IMS. Aygun et al. reported that IMS incidence increased in patients with lower serum cholinesterase levels (33). In previous studies, the relationship between hyperglycemia and IMS was not evaluated (1–33). Hyperglycemia commonly occurs in critically ill patients and impacts outcome. It is associated with the severity of the disease (34). Hyperglycemia may occur due to a sympathetic nerve system activation-related metabolic response in severe OP intoxication.

An increased severity of OP poisoning is also associated with increased risk of IMS (33). Therefore, hyperglycemia may predict the occurrence of IMS. In our study, the IMS group had significantly higher blood glucose levels ($P = 0.037$).

Initial serum cholinesterase and glucose levels measured in the emergency department may be a useful marker in predicting organophosphate-induced IMS. However, our study possessed some limitations. It was a retrospective, single-center study with a small number of IMS patients. Thus, further research is required to analyze the predictors of IMS.

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