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원 저

유기인계 중독 환자에서 알코올이 사망률에 미치는 효과

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Effect of Alcohol on Death Rate in Organophosphate Poisoned Patients

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Purpose: Many patients who are acutely poisoned with organophosphorus pesticides have co-ingested alcohol. The purpose of this study was to identify the factors that influence mortality in organophosphate intoxication and the differences between alcohol coingested patients and non-coingested patients, looking at vital signs, length of admission, cholinesterase activity, complications, and mortality.

Methods: All patients visiting one Emergency Department (ED) with organophosphate intoxication between January 2000 and December 2012 were reviewed retrospectively. The patients were divided into two groups, alcohol coingested group and non-coingested group.

Results: During the study period, 136 patients (alcohol coingested group, 95 patients; non-coingested group, 41 patients) presented to the ED with organophosphate intoxication. Seventy-one alcohol coingested patients (74.1%) vs. 16 non-coingested patients (39.0%) received endotracheal intubation, with results of the analysis showing a clear distinction between the two groups (p=0.001). Twenty-three alcohol coingested patients (24.2%) vs. 1 non-coingested patient (2.4%) required inotropics, indicating a significant gap (p=0.002). Twenty-eight alcohol coingested patients (29.5%) vs. 2 non-coingested patients (4.9%) died, with results of the analysis showing a clear distinction between the two groups (p=0.002).

Conclusion: In cases of organophosphate intoxication, alcohol coingested patients tended to receive endotracheal intubation, went into shock, developed central nervous system complications, and more died.

Key Words: Organophosphate poisoning, Alcohols, Mortality

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Introduction

Two hundred thousand people die globally every year from organophosphate poisoning, and it represents an important medical problem, with a death rate of 15%~30%[1]. Poisoning by organophosphate agents inhibits acetylcholinesterase, inducing cholinergic

hyperstimulation in the central nervous system, the neuromuscular junction, and the autonomic nervous system, resulting in symptoms such as anxiety, miosis, increased secretion and bradycardia. In serious cases, organophosphate poising may cause death through respiratory failure and shock, requiring intensive ICU care[1]. Respiratory failure reportedly occurs in up to 70 % of organophosphate poisoned patients, and Grmec et al[2]. reported that respiratory failure often occurs in patients with conscious degradation. Eddleston et al[3]. reported a high death rate in response to the combination of organophosphate and alcohol due to the aggravation of conscious degradation and respiratory failure of the central nervous system. However, studies on the effect of alcohol consumption in organophosphate poisoned patients are rare, and the few existing investigations only reported the relationship between organophosphate blood concentration and blood alcohol concentration, but did not consider clinical characteristics.

Therefore, we analysed clinical characteristics in organophosphate poisoned patients who consumed alcohol, and determined its relationship with the death rate.

Methods

1. Study design

This was a retrospective cohort study conducted, for 12 years from January 2000 through December 2012, on organophosphate poisoned patients visiting 5 emergency centres. Organophosphate poisoning was determined through the poisoning registry, and only registered patients poisoned with a single organophosphate agent were included in this study. Patients under the age of 18 with a medical history of cirrhosis, cancer, or deteriorated nutritional status were excluded from the study. A total of 136 patients were selected as subjects.

2. Subject and Data collection

This study targeted patients that visited the ER with organophosphate poisoning, and the data was collected through handwritten charts and electronic medical records. Data regarding general patient characteristics (age, gender, vital signs, poison amount, reason of poisoning, concomitant alcohol consumption and cholinesterase concentration), clinical characteristics (major symptoms, Acute Physiology and Chronic Health Evaluation [APACHE] II score, Namba classification, and aspiration pneumonia), treatment (ICU hospitalization, intubation and inotropics usage, and atropine dosage) and results (length of stay in ICU and hospital and in-hospital death rate) were collected. Patient and guardian statements were used to determine the poison amount, and Gas Chromatography (7694 Series II, HewlettPackard, Avondale, PA, USA) was used to determine the patient' s blood alcohol concentration. Pseudocholinesterase concentration was measured using a colorimetric assay (Cobas c701, Roche, Indianapolis, IN, USA). The first concentration measured at the ER visit was used as a standard.

3. Data Analysis

First, we divided organophosphate poisoned patients into two groups according to concomitant alcohol consumption. Differences in general and clinical characteristics, treatment, and results were compared between the two groups. The difference in the death rate between the two groups was compared as the primary result, and complication and treatment differences were compared as secondary results. The normality of the data was verified through the Kolmogorov-Smirnov test. Chi-square or the Fisher' s exact tests were used for categorical variable analysis, and presented as percentage (%) and frequency. The Mann-Whitney U test was used to analyse continuous variables, which are presented as median and quartile. SPSS 18.0.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis, and its statistical significance was set to 0.05.

Results

1. General and clinical characteristics of the study group

A total of 136 subjects were enrolled in this study (95 in the alcohol coingested group and 41 in the non-coingested group). Further, 93 were male and 43 were female. The median age of the alcohol coingested group was 59 years, and the median age for the non-coingested group was 55 years. All drug addiction routes were through oral administration. Sixty-two (65.3%) in the alcohol coingested group and 29 (70.7%) in the non-coingested group had administered the poison for suicidal reasons; this difference was not significant (p=0.534). Vital signs during the hospital visit, poison amount, and the first pseudocholinesterase concentration were not statistically different. The median serum alcohol level of alcohol coingested group was 161 (IQR 89-209) (Table 1).

Seventy-two (75.8%) in the alcohol coingested group and 19 in the non-coingested group were displayed central nervous system symptoms, with no

Table 1. Baseline characteristics

Variables	Alcohol coingested patients (N=95)	Non-coingested patients (N=41)	*p* value
Male, n	66 (69.5%)	27 (65.9%)	0.667
Age, year	59.0 (47.0-68.0)*	55.0 (38.0-68.0)*	0.307
Vital sign			
Systolic blood pressure, mmHg	142.0 (117.0-159.5)*	132.0 (122.0-148.0)*	0.536
Diastolic blood pressure, mmHg	80.0 (77.0-98.5)*	84.0 (71.0-90.0)*	0.969
Pulse rate, /min	95.0 (80.0-114.7)*	92.0 (85.0-104.0)*	0.290
Respiratory rate, /min	20.0 (18.0-22.0)*	20.0 (18.0-22.0)*	0.211
Body temperature, ˚C	36.0 (36.0-36.4)*	36.5 (36.0-36.8)*	0.054
Cause of ingestion, n			0.534
Suicide	62 (65.3%)	29 (70.7%)	
Accidental	33 (34.7%)	12 (29.3%)	
Serum alcohol level, mg/dL	161 (89-209)*	0	<0.001
Amount of ingestion, mL	100 (77.5-200.0)*	200.0 (50.0-500.0)*	0.217
Pseudocholinesterase level, U/L	171.5 (143.5-697.0)*	274.0 (790-810.0)*	0.738

* Values are expressed as the median and interquartile range or frequencies.

Table 2. Clinical characteristics of organophosphate ingesting patients

Variables	Alcohol coingested patients (N=95)	Non-coingested patients (N=41)	*p* value
Chief complaint, n			
Central nervous system	72 (75.8%)	19 (46.3%)	0.001
Pulmonary	10 (10.5%)	5 (12.2%)	0.771
Gastrointestinal	10 (10.5%)	17 (41.5%)	<0.001
General weakness	3 (3.2%)	0 (0.0%)	0.554
Namba Clinical, n			
Mild poisoning	13 (13.7%)	15 (36.6%)	0.002
Moderate poisoning	19 (20.0%)	9 (22.0%)	0.796
Severe poisoning	63 (66.3%)	17 (41.5%)	0.007
APACHE† II score	15.0 (12.0-19.0)*	16.0 (12.3-21.8)*	0.283
Aspiration pneumonia, n			0.021
Yes	23 (24.2%)	3 (7.3%)	
No	72 (75.8%)	38 (92.7%)	

* Values are expressed as the median and interquartile range or frequencies.

† APACHE: acute physiology and chronic health evaluation

statistical difference between groups. Thirteen (13.7%) in the alcohol coingested group and 15 subjects (36.6%) in the non-coingested group were mild according to the Namba classification, which was significantly different (p=0.002). Sixty-three (66.3%) in the alcohol coingested group and 17 (41.5%) in the non-coingested group were severe according to the Namba classification, indicating a significant difference (p=0.007). No significant difference was observed between the two groups regarding the APACHE II score (p=0.283). Twenty-three (24.2%) in the alcohol coingested group and 3 (7.4%) in the non-coingested group displayed aspiration pneumonia, which was significantly different (Table 2, p=0.021).

2. Treatment modalities and primary outcomes

Intubation was performed on 71 subjects (74.7%) in the alcohol coingested group and on 16 (39.0%) in the non-coingested group, a significant difference (p<0.001). Inotropics application was also significantly different between the two groups (p=0.002). The total atropine dosage used was 452.5 mg (IQR 176.0-1027.5) in the alcohol coingested group and 180.0 mg (IQR 60.0-480.0) in the non-coingested group, representing a significant difference (Table 3, p=0.036).

No significant difference was observed between the two groups for the length of stay in ICU and hospital. Twenty-eight died in the alcohol coingested group and 2 died in the non-coingested group, which was significantly different (Table 4, p=0.002).

Discussion

Here, we compared general/clinical characteristics and prognosis differences in organophosphate poisoned patients according to concomitant alcohol consumption. The organophosphate poison group with concomitant alcohol consumption complained more of central nervous system symptoms and digestive system symptoms compared to the organophosphate agent poisoned group. They also displayed severe Namba severity and frequently displayed aspiration pneumonia. In addition, intubation and inotropics

Table 3. Treatment modalities of organophosphate ingesting patients

Variables	Alcohol coingested patients (N=95)	Non-coingested patients (N=41)	*p* value
ICU† admission, n			0.087
Yes	83 (87.4%)	31 (75.6%)	
No	12 (12.6%)	10 (24.4%)	
Intubation, n			<0.001
Yes	71 (74.7%)	16 (39.0%)	
No	24 (25.3%)	25 (61.0%)	
Use of inotropic agents, n			0.002
Yes	23 (24.2%)	1 (2.4%)	
No	72 (75.8%)	40 (97.6%)	
Total atropine, mg	452.5 (176.0-1027.5)*	180.0 (60.0-480.0)*	0.036

* Values are expressed as the median and interquartile range or frequencies.
† ICU: intensive care unit

Table 4. Outcomes of organophosphate ingesting patients

Variables	Alcohol coingested patient (N=95)	Non-coingested patients (N=41)	*p* value
Length of stay in hospital, day	15.0 (5.0-24.0)*	10.0 (5.0-24.0)*	0.654
Length of stay in ICU†, day	9.0 (3.0-17.0)*	6.0 (1.0-10.5)*	0.054
In-hospital mortality, n	28 (29.5%)	2 (4.9%)	0.002

* Values are expressed as the median and interquartile range frequencies.
† ICU: intensive care unit

were used at a higher frequency in the poison group with concomitant alcohol consumption compared to the poison alone group, and atropine usage and the in-hospital death rate were also significantly increased in the poison and alcohol coingested group.

The general cause of poisoning was suicide. Chun et al[4]. and Lim et al[5]. reported that 63% and 78% of poisoning cases were suicide attempts, respectively. Suicide was reported as the cause of poisoning in 66.9% of subjects in this study, which is similar to that reported in previous studies.

The relationships between concomitant alcohol consumption, poison dosage, and its blood concentration vary between studies. Eddlestone et al[3]. reported higher blood organophosphate concentration due to higher organophosphate poison dosage in the poison group with concomitant alcohol consumption. In contrast, Lee[6] explained the short ICU period of the concomitant alcohol poison group with lower addictive agent poison dose compared to the single addictive agent poisoned group in patients with various agents, including organophosphate. The organophosphate poison dosage in the poison group with concomitant alcohol consumption was lower compared to the single organophosphate agent poisoned group in this study. The blood concentration indicated the opposite, but is thought to be inaccurate because it depends on the statements of the patients and their guardians. However, the poison dosage and blood concentration were not significantly different between the two groups.

In this study, a higher death rate was observed in the poison group with concomitant alcohol consumption compared to the single organophosphate poison group. More severe clinical symptoms were observed in the group poisoned with organophosphate agents with alcohol, as this group displayed more aspiration pneumonia and frequently required intubation. In addition, inotropics was used to increase blood pressure due to more frequent shock in the alcohol group. The death rate likely increased due to these symptoms. Furthermore, more atropine was administered in the alcohol coingested group. Decreased consciousness and respiratory depression may occur with concomitant alcohol consumption. Tachycardia and delirium were the most common withdrawal symptoms in chronic alcoholic patients, leading to increased complication with atropine administration, which is predicted to increase cardiac complications by alcoholic myopathy. It was previously reported that myocardial damage in organophosphate exposed patients increased the death rate[7].

Organophosphate poisoning is fatal due to aspiration pneumonia, shock, respiratory complications, and central nervous system injury. Ryu et al[8]. and Han et al[9]. reported pneumonia as the main cause of death (53% in both studies), similar to the results of our study. According to Kang et al[10]., the APACHE II score was a good predictive indicator of prognosis in organophosphate poisoned patients, but we observed no difference in this parameter between the two groups in our study. Grmec et al[2]. stated that the Glasgow coma scale was a predictor of prognosis. Similar results were observed in this study, demonstrating a higher death rate in the alcohol group, with more central nervous system complications. 1 In agreement with our results, Jin et al[11]. reported that 83% of patients that required mechanical ventilation displayed central nervous system anomaly, whereas this number was 66.6% in severe patients. In addition, they reported a higher death rate in the alcohol group, and more patients in this group required mechanical ventilation due to central nervous system complications and respiratory complications.

Kim[12] reported that the death rate was lower in severe organophosphate poisoning when high doses of atropine were administered, whereas a higher death rate was noted with high doses of atropine were administered to patients with moderate poisoning. In this study, severe organophosphate poisoning was more often seen when alcohol was consumed, and the administration of high doses of atropine resulted in higher death rates. These findings support the hypothesis that the interaction between alcohol and atropine increase the death rate.

Although the death rate was higher in the alcohol

group, there was no difference in the pseudocholinesterase concentration between the two groups. Thus, the different results of the two groups are not due to the effect of alcohol itself on the pseudocholinesterase metabolism, but rather the effect of conscious degradation and acute respiratory failure.

One limitation of this study is that no tests were performed to assess cardiomyopathy. Second, no records were available regarding delirium. Third, this study is a retrospective cohort study. In addition, not enough data could be collected from the 5 hospitals. Thus, no significant relationship between alcohol and death rate was identified in this study. Also, we measured amount of insecticides ingested. But we could not measure exact amount of organophosphate ingested, because contents of insecticide products were varies.

Conclusion

When organophosphate is consumed concomitantly with alcohol, intubation performance rate was higher due to aspiration pneumonia and decreased consciousness. Inotropics and atropine were used more frequently, and there significant difference in the death rate in the poison and alcohol coingested group.

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