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Original article

CLINICAL CRITERIA FOR THE OUTCOME FORECAST OF ACUTE EXOGENOUS INTOXICATIONS WITH ORGANOPHOSPHORUS PESTICIDES

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ABSTRACT

Purpose: The wide-spread use of organophosphorus pesticides (OPP) and their substantial toxicity determine the high frequency of poisoning with them. Despite the modern treatment methods, the acute exogenous intoxications (AEI) continue to exhibit high lethality and are the source of one of the most serious problems in the clinical toxicology. A number of not commonly accepted criteria have been suggested to estimate the gravity of the organophosphorous intoxication. Until now no system of clinical criteria exists that would forecast the outcome of this type of acute poisoning. The aim of this study is to develop an outcome forecast of AEI with OPP with the help of basic clinical criteria.

Materials and Methods: The subjects of the study are 160 patients. We explore the significance of five of the most typical clinical indicators of the acute poisoning with OPP for the outcome of the intoxication and the need of artificial pulmonary ventilation, with the aid of discriminatory statistical analysis. The selected indicators form a discriminatory model with automatically built discrimination function.

Results: The obtained classification coefficients allow us to construct a forecast matrix containing score estimates designed for practical applications.

Key words: organophosphorus pesticides, acute poisoning, prognosis

INTRODUCTION

The organophosphorus pesticides (OPP) are the most often used substances for plant protection in Bulgaria as well as in many other countries. Their popularity and substantial toxicity determine the high frequency of the acute poisoning with them. Despite substituting the highly toxic OPP with less toxic compounds and the integration of modern treatment methods, the acute exogenous intoxications (AEI) continue to exhibit high lethality and are the source of one of the most serious problems in the clinical toxicology [1-8].

A number of not commonly accepted criteria have been suggested to estimate the gravity of organophosphorous intoxication [9]. The large practical importance notwithstanding, so far no system of clinical criteria has been developed to forecast the outcome of this type of acute poisoning [10]. It is known that patients with low values of acetylcholinesterase face a bad forecast. It has been proven that patients with a prolonged corrected QT-interval and low GCS (Glasgow Coma State) more often develop acute respiratory insufficiency and require intubation. For them the forecast is worse, and respectively the lethality is higher [11-15]. Acute Physiology and Chronic Health Evaluation (APACHE) II score and Simplifed Acute Physiology Score (SARS) II may be used to predict the mortality rate in OPP [16-18]. Serum bicarbonate concentration, APACHE II score and pneumonia during haspitalization were the important prognostic factors in patients with OPP [19]. OPP often cause respiratory failure [20, 21]. Systolic blood pressure of <100 mm Hg and FiO2 of >40% to maintain a SpO2 of >92% within the first 24 h were recognized as poor prognostic indicators among mechanically ventilated patients [22]. Hypotension, respiratory failure, coma and QTc prolongation were significant risk factors for mortality [23]. The difference in C-teactive protein value between initial and 24 hours follow-up (D-CRP) was associated with mortality of patients with OPP [24]. Multiple organ insufficiency syndrome (MOIS) and renal failure are relatively rare but correlated with death [25].

Our aim is to develop an outcome forecast of AEI with organophosphorus pesticides with the help of basic clinical criteria.

MATERIAL AND METHODS

The subjects of the study are 160 patients aged between 14 and 86 years (96 male and 64 female) treated during a 10-year period at the Clinic for Intensive Treatment of Acute Intoxications and Toxicoallergies, Naval Hospital – Varna.

We explore the significance of 5 of the most typical clinical indicators of acute OPP poisoning to the intoxication outcome and the need of artificial pulmonary ventilation with the help of discriminatory statistical analysis.

RESULTS AND DISCUSSION

To forecast the outcome of the OPP intoxication we get simplified mathematical expressions in the form of score estimates. The aim is to as quickly and easily as possible, even while checking in the patient, to find an answer to the following questions:

1. Is it sufficiently likely for the patient to be successfully treated, respectively what is the probability of a lethal outcome of the intoxication?

2. What is the probability of requiring an artificial pulmonary ventilation?

Taking into consideration the respective assumptions and requirements of the mathematical statistics and the data volume, 160 cases, leads to the logical conclusion that the target model should contain no more than five indicators (at least 30 patients per indicator). On the other hand, many of the indicators are mutually dependent in a direct fashion and must not be simultaneously present when looking for mathematical functional dependencies. In connection to this, with the help of preliminary analysis we have pre-selected the following most important indicators: presence of spasms; type of conscience; presence of pulmonary edema; presence of a shock; presence of a multiorgan insufficiency syndrome (MOIS).

The indicators we have determined are non-parametric (qualitative) which necessitates the use only of non-parametric statistical models. For the indicators that have more than two possible manifestations (symptoms), in our case "type of conscience" and "spasms", it is necessary to develop scales of well-chosen weight coefficients (Tabl. 1).

Tabl. 1. Weight coefficients for the manifestations of the "type of conscience" and "spasms" for AEI with OPP

Indicator "Type of conscience"	Weight coefficient	Indicator "Spasms"	Weight coefficient
Without change	1	None	1
Obnibulation	1	Miofibrilation	2.5
Somnolence	2.7	Clonic-tonic	4
Stupor	3.0		
Coma	4.25		

In view of the type and features of the indicated variables we propose to use a discriminatory analysis as the solely appropriate statistical method to forecast the outcome of the disease and the need of artificial pulmonary ventilation. The idea of the method we have chosen is to find those indicators that have the largest statistical significance to separate the observed cases into two or more classes (sub-groups). The objective is to achieve this in the most effective manner, i.e. with the lowest number of indicators containing the largest group significance. The latter means that individually they may happen not to display the largest significance, but when viewed together they interact in such a way that mutually compensates their statistical scattering.

The selected indicators form a discriminatory model with an automatically constructed discriminatory function, while their classification is carried out through a "classification function". It constitutes a mathematical expression of the linear polynomial type and is directly related to the auxiliary discriminatory function. Although the selection (in the sense of the best group of indicators) is automatic in this case, it is possible to choose one of the three popular strategies: *Forward stepwise*, *Backward stepwise*, and *Standard* (manual input or output). There is a trade-off for each strategy yet with sufficiently robust relations they should lead to identical final results. With the data of our study the end results coincides following all three strategies, i.e. we get a subgroup of the two most significant indicators: "pulmonary edema" and "MOIS" (Tabl. 2).

Tabl. 2. Classification function coefficients to determine the lethality of OPP (n = 140)

Indicator	Healed	Exitus letalis	Confidence level
Pulmonary edema	17.1	30.8	p< 0.001
MOIS	6.41	10.47	p< 0.001
Constant	-12.7	-39.9	p< 0.001

Fischer criterion for the overall model: F (2, 137 d.f.) = 157.1. Confidence level for the overall model: $p < 0.001$. Mahalanobis distance between the two classes: 14.3. The respective classification functions are as follows:

- "healed" class – 17.1 (pulmonary edema) + 6.41 (MOIS) – 12.7

- "exitus letalis" class – 30.8 (pulmonary edema) + 10.47 (MOIS) – 39.9

According to the discriminatory analysis method the patient is added to that class for which the calculated function is bigger. For this the indicators for "pulmonary edema" and "MOIS" are replaced with their weight coefficients. When the value for the "exitus letalis" is almost equal that of the "healed" class (a difference of less than six), the patient is added to the "exitus letalis" class only when the conscience type has a weight coefficient equal to at least 2.7, i.e. the conscience must be at least of the "somnolence" type.

We use the obtained coefficients to check the quality of identification with respect to the basic and the control data set (Tabl. 3, Tabl. 4).

Tabl. 3. Classification matrix for the identification quality of the basic data set (n = 140)

Classes	Correct answers (%)	Healed	Exitus	Total
HEALED	97.3	110	2	112
EXITUS	89.3	3	25	28
TOTAL	95.7	113	27	140

Tabl. 4. Classification matrix for the identification quality of the control data set (n = 20)

Classes	Correct answers (%)	Healed	Exitus	Total
HEALED	87.5	12	2	14
EXITUS	100.0	0	6	6
TOTAL	90.0	12	8	20

With the obtained coefficients we can build a forecast matrix that will contain the score estimates destined for practical work (Tabl. 5).

Tabl. 5. Classification matrix "healed" - "deceased" with AEI from OPP

Indicator	"Healed" class, score estimate	"Exitus" class, score estimate
1. Pulmonary edema		
- Absent	17	31
- Present	34	62
2. MOIS		
- No	6.5	10.5
- Yes	13	21
3. Constant	27	0

From the table we see that the presence of a pulmonary edema almost unambiguously determines the lethal outcome, which we confirm with the direct data check.

In a similar manner, using the method of discriminatory analysis we get a classification matrix also for the cases when artificial pulmonary ventilation is needed (Tabl. 6).

Tabl. 6. Classification matrix to determine the need of artificial pulmonary ventilation for AEI from OPP

Indicator	**Artificial pulmonary ventilation**	
	Score for the"No need" class	**Score for the"It is needed" class**
1. CONSCIENCE		
- no change	2	7
- obnibulation	2	7
- somnolence	5.5	18
- stupor	6	19
- coma	9	28
2. Spasm		
- none	2	3
- myofibrillar	5	8.5
- clonic-tonic	8	13.5
3. Constant	14	0

We can observe that the column "no need of artificial pulmonary ventilation" contains a constant equal to 14, in opposition to a constant of zero in the right column. The straight-forward analysis demonstrates that the artificial pulmonary ventilation will be necessary when this constant will "melt" from the difference in the respective score estimates. This may take place in the following two cases:

1. Conscience impairment from the "stupor" or "coma" type, independent of the presence or absence of spasms, since the difference in the score estimates for "stupor" [4] may not "disappear".

2. Conscience impairment from the "somnolence" type, accompanied by the presence of myofibrillations or spasms.

In all remaining cases, independent of the "type of conscience" and "spasm" indicators, there is no need of artificial pulmonary ventilation.

CONCLUSIONS

The conducted study allows us to determine the basic clinical indicators that are related to the outcome forecast for acute exogenous intoxications with organophosphorus pesticides: type of conscience, pulmonary edema, shock, spasm and multiorgan insufficiency syndrom

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