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ACUTE EXOGENOUS INTOXICATIONS WITH ORGANOPHOSPHORUS PESTICIDES: DURATION OF THE HOSPITAL TREATMENT AND CLINICAL CRITERIA FOR PROGNOSIS

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ABSTRACT

Purpose: Several criteria have been suggested to estimate the intoxication severity, yet so far no system of clinical criteria has been developed to determine the duration of hospitalisation. The forecast is linked to the influence of the extended corrected QT interval and GCS (Glasgow Coma Scale) on the frequency of the developing acute pulmonary insufficiency and lethality. The average duration of hospital treatment is also crucial. First of all, it is determined by the intoxication severity and lasts from 3 to 26 days. The aim of this study is to develop an individual forecast about the duration of hospitalisation for patients suffering from acute exogenous intoxication with organophosphorus pesticides (OPP).

Materials/Methods: The subjects are 160 patients. We use statistical regression analysis to study the significance of 5 of the most typical clinical indicators of organophosphorus intoxication on the duration of hospitalisation: type of conscience, presence of spasms, pulmonary oedema, shock and multi-organ insufficiency syndrome (MOIS). To forecast the treatment length, we obtain simplified mathematical expressions in the form of score estimates.

Results: The significance of the clinical indicators "MOIS", "conscience" and "spasm" has been confirmed. A forecast matrix that gives the opportunity to forecast the personal duration of hospital treatment for each patient has been built.

Keywords: organophosphates, acute poisoning, duration of hospital treatment, prognosis

INTRODUCTION

Pesticide poisoning is an important public health problem worldwide [1]. The organophosphorus pesticides are biologically active substances featuring more or less pronounced toxic qualities. The large share of severe forms of this type of acute poisonings as well as the substantial omissions when rendering first aid in pre-hospital conditions is the basic premise for the high lethality [2-14]. Several criteria have been suggested to estimate the severity of the poisoning with organophosphorus pesticides [15], yet so far no system of clinical criteria has been developed to determine the forecast and the duration of the hospital treatment in the case of this type of acute poisonings. The average number of hospital days was 11.22 [16]. Patients with low acetylcholinesterase values face bad forecasts [17]. It has been proven that patients with an extended QT interval and low GCS are more frequent to develop acute pulmonary insufficiency, requiring intubation and feature worse forecasts [18, 19]. Obese patients who were poisoned by high lipophilicity organophosphate compounds had a need for the longer use of mechanical ventilation, intensive unit care and the total length of admission [20].

The average duration of hospital treatment is also crucial. Above all, it is determined by the intoxication severity and lasts between 3 and 26 days. The objective of this study is to develop individual forecasts about the duration of hospital treatment for patients suffering from acute exogenous intoxications (AEI) with OPP.

MATERIAL AND METHODS

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

We use statistical regression analysis to obtain the

significance of 5 of the most typical clinical AEI indicators on the duration of hospital treatment: type of conscience, presence of spasms, pulmonary oedema, shock and multi-organ insufficiency syndrome (MOIS). The patients are divided into two groups: basic group – 140 patients, and control group – 20 patients.

RESULTS AND DISCUSSION

To forecast the duration of hospital treatment for patients suffering from AEI with OPP, we obtain simplified mathematical expressions in the form of score estimates. The aim is to determine as fast and straight – forward as possible, while the patient is still being admitted, the approximate duration of hospital treatment based on fundamental clinical indicators.

The evaluation of the respective assumptions, the requirements posed by the mathematical statistics and the size of the data set (160 clinical cases) lead to the conclusion that the desired models must contain maximum five indicators (at least 30 patients per indicator). On the other hand, many of them are directly interdependent and should not be simultaneously present in the mathematical functional relations. Given this and with the help of preliminary analysis we isolate the most important clinical criteria, as mentioned above.

By the observed disorders of patients suffering from AEI with OPP, we use the method of regression analysis to estimate the necessary number of days of hospitalisation. The purpose is to identify the minimum possible number of most significant criteria that would reliably determine the duration of hospital treatment. For that we use the Cox regression method characterised by the following features:

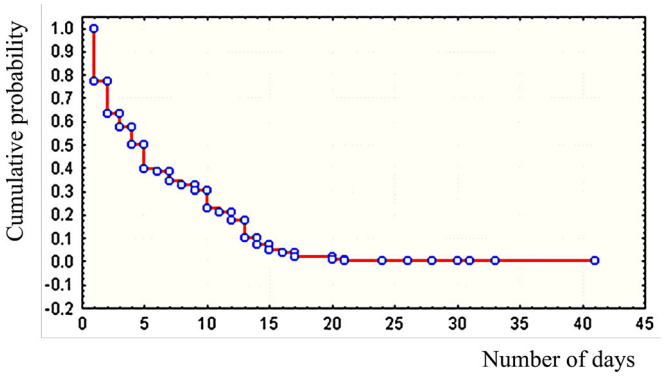
1. It does not require the data to follow the normal (Gaussian) distribution; thus we may start the analysis without first using variational and correlational analysis for which the normal distribution is a must.

2. It statistically analyses the dynamics of the change of the proportion of patients remaining in the clinic to their total number. This proportion depends on time (days) and most often can be represented by a declining exponential function. The function constitutes the cumulative probability that a specific number of patients will be hospitalised for more than some previously fixed number of days. We are looking for an appropriate regression equation for this very time-dependent function. The equation coefficients are dependent on the observed indicators and are supposed to "explain" the steep change in the curve with the passage of time.

3. Each time the Cox regression is applied, the patients that are no longer among the hospitalised are treated according to the specific case - either as deceased (non-survivors) or checked-out (recovered). In the current study, we apply the latter approach – after the indicated number of days of hospitalisation the patient is considered to have checked out as recovered.

At the beginning of the study, we use the data about the basic group and the tools offered by the "STATISTICA" software to construct the form of the desired regression function for the average cumulative probabilities referring to the hospitalisation in days. We obtain the expected exponential relation as illustrated in Fig. 1.

Fig. 1. Probable duration of inpatient treatment with OPP poisonings (n = 140)



Following the Kaplan-Meier methodology, it has been proven the high significance of the observed criteria ("pulmonary oedema", "MOIS" and "spasm") about the modification in the dynamic represented by this curve. The results can be seen in Fig. 2, Fig.3, and Fig. 4.

Fig. 2. Comparison between intoxicated patients with and without spasm by the Kaplan-Meier method (n = 140)

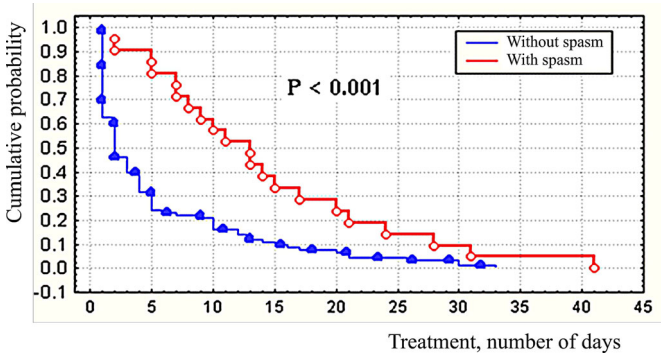


Fig. 3. Comparison between intoxicated patients with or without pulmonary oedema (PE) by the Kaplan-Meier method

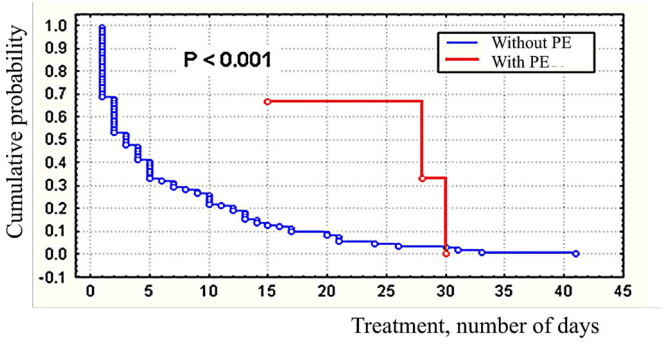
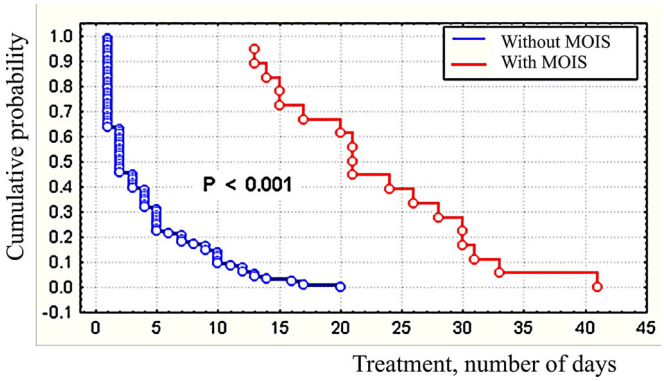


Fig. 4. Comparison between intoxicated patients with and without MOIS by the Kaplan-Maier method (n = 140)



The maximal significance of the indicators mentioned above to determine the necessary duration of hospital treatment is apparent. We evaluate these indicators as most serious candidates to obtain the desired regression relation.

Although the selection of the best group of indicators is automatic, the regression relationship is determined following a procedure with one of three possible strategies: Forward Stepwise, Backward Stepwise, and Standard (the user manages the model optimisation). Each strategy has its advantages and disadvantages, yet with sufficiently robust relations all three must lead to identical final results. In our study, we get the same final result using all three strategies, and we form a subgroup of three of the most significant criteria: "pulmonary oedema", "MOIS" and "spasms".

To check the reliability of the obtained results, we create a separate and sufficiently representative group of 20 patients (the control series) that are not part of the basic group. The set of control data, according to the requirements of the statistical methodology, is destined only as a check and does not take part in the main analysis.

We determine the following Cox-regressional relation:

$$\frac{H(t)}{H(t_o)} = exp(-1.84 * MOIS - 0.205 * Consience - 0.079 * Spasm)$$

The left-hand side constitutes the cumulative probability determined in relative units. The right-hand side contains the regression coefficients to the selected criteria that are used as the exponents in the exponential function.

To make this equation easier to use in practice it is necessary to perform certain transformations related to logarithms and probability normalisation (to link them to the desired estimate of the number of days of hospitalisation). The final result is illustrated in a table of forecasting the necessary duration of hospital treatment (in days) for patients suffering from AEI with OPP.

The expected number of days needed for hospital treatment can be determined by the score sum according to the individual disease diagram shown in Tabl. 1 and Tabl. 2.

Tabl. 1. Weight of the indicators determining the treatment duration of patients with organophosphorus pesticides (OPP)

Indicator	Score
MOIS:	
None	0
Yes	9
Consience	
No change	0
Obnibulation	0
Somnolence	2
Stupor	2
Coma	3.5
Spasm	
None	0
Myofibrillar	1
Clonic-tonic	2

Tabl. 2. Identifying the expected duration of inpatient treatment of specific patients

Score	Expected duration of inpatient treatment
up to 2 points	up to 5 days
between 3-5.5 points	up to 10 days
between 9-10 points	up to 15 days
between 11-14 points	up to 20 days
14.5 points	more than 20 days

CONCLUSIONS

We confirm the significance of the clinical criteria "MOIS", "Conscience" and "spasms" for the duration of hospital treatment. The constructed forecast table allows us to determine in advance the duration of the hospital treatment for each patient individually.

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