

CLINICO-EPIDEMIOLOGICAL RESEARCHES ON THE USE OF THE ANTIDOTE IN ACUTE ORGANOPHOSPHATE POISONING ON PATIENTS ADMITTED IN THE MEDICAL CLINIC OF "SF. IOAN" EMERGENCY CLINIC HOSPITAL, IASI, DURING 2003-2009

GABRIELA PUHA¹, J. HURJU², CĂTĂLINA ELENA LUPUȘORU³, LAURENȚIU ȘORODOC⁴

^{1,2,3,4} "Gr. T. Popa" University of Medicine and Pharmacy, Iași

Keywords: intoxication with organophosphate substances, antidote therapy

Abstract: In the present study we have analyzed the clinical evolution of the patients intoxicated with organophosphate insecticides, depending on the prescribed treatment, being a well-known fact that the reactivators of cholinesterase are administered only in the first 48-72 hours from the ingestion of the toxin, while after this period there appears a dealkylation of the complex cholinesterase – organophosphate substance (OPs), which triggers the irreversibility of the process of blocking the cholinesterase. Material and method: we have analyzed retrospectively a number of 137 patients hospitalized in the period 2003-2009. Results: all the patients were given supportive treatment and the association of Atropine, Obidoxime (Toxogonin) and plasma was administered only for 25,5% of the intoxications with OPs. There are no statistically significant differences between the evolution of the patients intoxicated with OPs treated only with Atropine and those treated with Atropine and Toxogonin

Cuvinte cheie: intoxicația cu substanțe organo-fosforice, terapie antidot

Rezumat: Am analizat în acest studiu evoluția clinică a pacienților intoxicați cu insecticide organo-fosforice, funcție de tratamentul administrat, fiind știut faptul că reactivatorii de colinesterază se administrează doar în primele 48-72 de ore de la ingestia toxicului, după acest interval survenind o dezalchilare a complexului colinesterază-substanță organo fosforică, ce produce ireversibilitatea blocării colinesterazelor. Am analizat retrospectiv un număr de 137 pacienți spitalizați în perioada 2003-2009. Toți pacienții au primit tratament suportiv, iar asocieră de Atropina, Obidoxinum (Toxogonin) și plasmă s-a administrat doar la 25,5% din intoxicațiile cu SOF. Nu există diferențe semnificative statistic între evoluția pacienților intoxicați cu SOF tratați doar cu Atropina și cei tratați cu Atropina și Toxogonin.

INTRODUCTION

The International Programme on Chemical Safety defines the antidote as a therapeutic substance used in order to annul the toxic action of a xenobiotic. The antidotes must act specifically on a functional cellular complex, must have a high intrinsic activity and must not determine serious side-effects; the antidote must be effective for a long period of time and must not create toxic active compounds through metabolization. The number of substances that meets these conditions is relatively small.

Less than 5% of the intoxications have an antidote treatment (4,15). The classification of the antidotes can be carried out using several criteria, but one of the best criteria is the action mechanism. In the case of intoxications with organophosphate insecticides (OPs), the atropine acts through competitive antagonism at the level of the receptor, the obidoxime, through a mechanism of enzymatic reactivation (1,5,16). The reactivators of cholinesterase are administered only within the first 48-72 hours from the ingestion of the toxin, while after this period there appears a dealkylation of the complex cholinesterase – organophosphoric substance, which triggers the irreversibility of the process of blocking the cholinesterase. (7,15)

MATERIAL AND METHOD

We have analyzed retrospectively a number of 137

patients hospitalized in the Clinic of Internal Medicine and Toxicology of "Sf. Ioan" Clinical Emergency Hospital, in the period 2003-2009. The following parameters have been investigated: age, sex, social background, the time of treatment in the Medical Clinic or Intensive Care Unit after the ingestion of the substance, personal pathologic antecedents, acute or chronic alcoholism, biological investigations centered on the urine toxicological screen and on the dosage of seric cholinesterase, the supportive treatment and antidote administered, complications appeared during the admission, the evolution of the patients under treatment, depending on the moment of administration of the antidote and on the period of time elapsed from the exposure to the toxin and the administration of the antidote.

RESULTS AND DISCUSSIONS

From the total number of intoxications registered in the period of investigation (2850), 7,8% (221) were patients diagnosed with insecticides, among which 62% with organophosphoric substances (OPs) (Fig. 1).

Focusing on the cases of intoxication with insecticides registered between 2003-2009, it is to be noticed that the tendency was decreasing ($y = 36,71 - 2,36 x$), and the intoxication with OPS falls into this trend ($y = 27,71 - 2,04 x$) (fig. 2)

The statistic analysis on sex shows the greatest

¹ Corresponding Author: Gabriela Puha, 63 A. Toma Cozma street, A, Iasi, Romania; e-mail: puhab@yahoo.com; tel +40-0723632434
Article received on 28.02.2011 and accepted for publication on 03.06.2011
ACTA MEDICA TRANSILVANICA September 2011; 2(3)361-363

CLINICAL ASPECTS

frequency for the age group 20-29 years and 40-49 years old for females (10,2%) and for the age group 30-39 years old for males.(10,2%) (fig. 3)

Figure no. 1. Distribution of the cases depending on the presence of the toxin under analysis

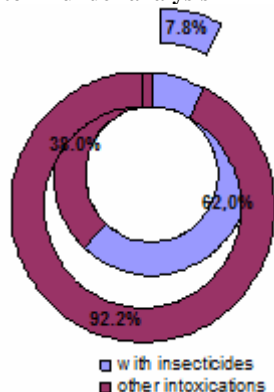


Figure no. 2 Total number of intoxications with insecticides and the tendency between 2003-2009

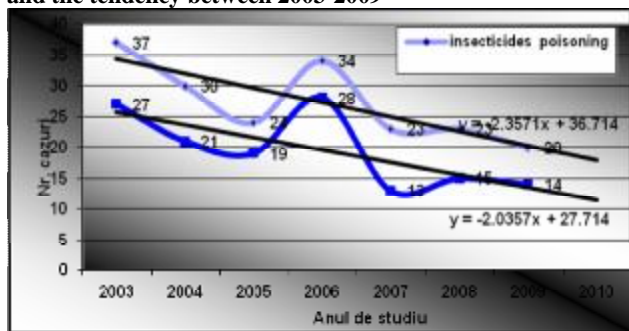
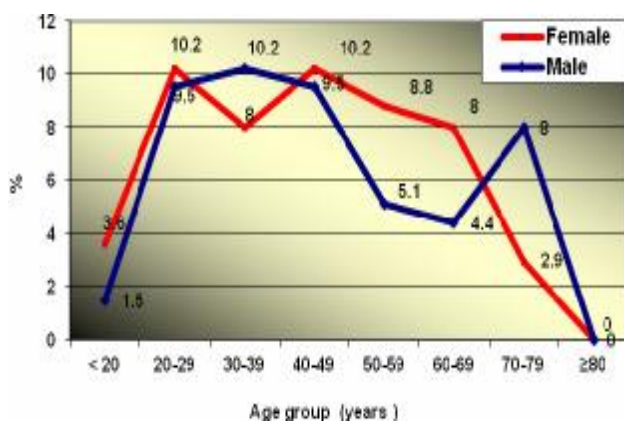


Figure no. 3. Distribution on sex and age groups of the patients from the lot under investigation



As far as the social background is concerned, in rural environment the distribution was bimodal, with the greatest frequency for the age group 30-39 and 40-49 years old (12,4%) ; in urban environment, statistic analysis shows frequency peak for the age group 20-29 years old. (10,2%) (fig. 4).

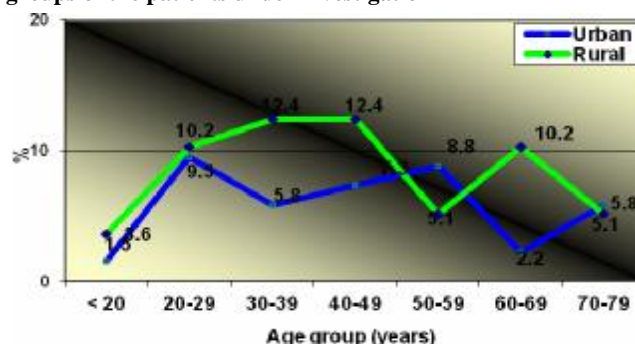
The patients' age varied in the interval 17 -78 years, with an average of $44,68 \pm 17,13$ years.

For the female sex the average age was slightly lower ($43,89 \pm 16,38$ years) as related to the male sex ($45,53 \pm 17,98$ years), but the difference is not statistically significant ($t = 0,56$; $GL = 135$; $p > 0,05$).

The patients from the rural background showed a

slightly lower age average ($44,29 \pm 17,21$ years) as compared to the urban background ($45,27 \pm 17,15$ years), without significant differences however. ($t = 0,33$; $GL = 135$; $p > 0,05$).

Figure no. 4. Distribution on social background and age groups of the patients under investigation

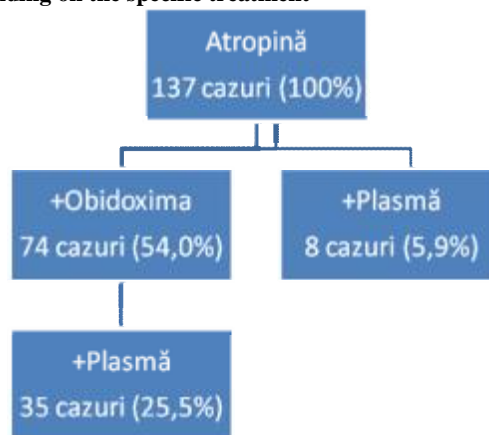


The statistic analysis shows the greatest frequency for females (51,8%) and for the patients from rural area (59,1%).

Supportive treatment was administered to all patients (100%).

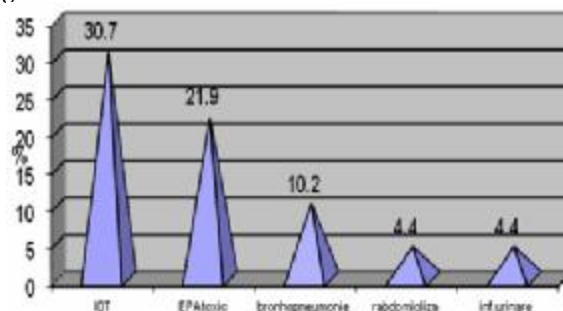
All the patients with acute intoxication with OPS received atropine treatment (100%), associated in proportion of 54% with obidoxime. It is to be noticed that for 31,4% of the patients of the OPS lot plasma was administered, a treatment associated in proportion of 25.5% with atropine and obidoxime, and only in proportion of 5,9% with atropine (fig. 5).

Figure no. 5. Distribution of the cases from the OPS lot depending on the specific treatment



The evolution in the Intensive Care Unit shows a great number of patients who required endotracheal intubation (30,7%), followed by cases of toxic EPA (21,9%) and small frequencies of bronchopneumonia (10,2%), rhabdomyolysis 4,4%), and urinary infections (4,4%).(fig.6)

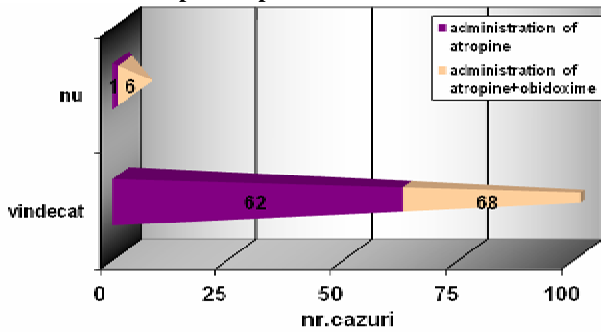
Figure no. 6. Evolution in ICU



CLINICAL ASPECTS

Considering the fact that all the patients from the OPs lot received atropine as an antidote, and comparing the patient's condition when leaving the hospital we can notice that the patients who received and association of atropine and obidoxime but nevertheless died (6/74) failed to show significant differences as compared to those who only received atropine as an antidote (1/63) ($\chi^2=1,79$; GL=1; $p=0.181$) (fig. 7)

Figure no. 7. Distribution of the cases from the OPS lote depending on the administration of the antidote and the health condition upon hospital leave



CONCLUSIONS

The number of intoxications with OPs follows a descending trend in the period under investigation. The statistic analysis shows the greatest frequency for females (51,8%) and for the patients from rural area (59,1%).

The hospitalization period ranged from 2 to 26 days. All patients received supportive treatment and the association of atropine, toxogonin and plasma was administered only for 25.5% of the OPs intoxications. There are no statistically significant differences between the evolution of OPS intoxicated patients treated only with atropine and those treated with atropine and toxogonin.

The evolution in the Intensive Care Unit shows a great number of patients who required endotracheal intubation (30,7%), followed by cases of toxic EPA (21,9%) and small frequencies of bronchopneumonia (10,2%), rabdomiolosis (4,4%), and urinary infections (4,4%).

BIBLIOGRAPHY

1. Bowden C.A., Krenzelok E.P. Clinical application of commonly used contemporary antidotes: aUS perspective. *Drug Safety*, 1997; 16: 9-47.
2. Bălălu Dan, Baconi Daniela-Toxicologie generala-Editura Tehnoplant Company SRL, 2005, 314-322;
3. Barile A. Frank-Clinical Toxicology Principles and Mechanisms-CRC PRESS, 2004
4. Krenzelok E.P., -Clinical applications of commonly used contemporary antidotes.A US perspective-*Drug Saf*, 1997 jan; 16(1): 9-47
5. Cristea Aurelia Nicoleta-Tratat de Farmacologie-Editura Medicala 2005-1151-1187;
6. Cotrău M., Popa L., Stan Th, Preda N., Kincses-Ajtay M-Toxicologie-Editura Didactică și Pedagogică, București 1991;
7. Das Gupta S., Ghosh A.K., Chowdhri B.L., Asthana S.N., Batra B.S. Actions and interactions of cholinolytics and cholinesterase reactivators in the treatment of acute organophosphorus toxicity. *Drug Chem Toxicol* 1991; 14: 283-91
8. Ellenhorn M.J.,-Ellenhorn's Medical Toxicology:Diagnosis and Tratament of Human Poisoning,Williams &Wilkins, 1997, editia a II a;

9. Hanna J., Danel V-Antidotes, antagonises et techniques d.eurpuration en toxicologie;
10. Harrison T.R., -Principiile Medicinei Interne-vol.2-Editura Teora, 2003, a 14-a ediție;
11. Jacobsen D.-The relative efficacy of antidotes,*Journal of Toxicology.Clinical Toxicology*, 1995; 33(6): 705-8.
12. Mogoș Gh., Sitcai N.,-Toxicologie Clinica Intoxicații medicamentoase vol II, Editura Medicala, 1990;
13. Robert J., Flanagan PhD., FRCP ath Alison L Jones MD FRCP(E), *Antidotes*, 2001, Guy's and St Thomas' Hospital Trust, London
14. Sellström Å. Anticonvulsants in anticholinesterase poisoning. In: *Clinical and Experimental Toxicology of Organophosphates and Carbamates*. Ballantyne B, Marrs TC (eds). Oxford: Butterworth-Heinemann, 1992: 578-86.
15. Șorodoc Laurențiu, Lionte Cătălina, Frasin Mihai, Andrei Radu, Simionescu Victorița, Petriș Ovidiu-Toxicologie Clinica de Urgență-vol I, Editura Junimea, 2005;
16. Voicu V. Victor, Macovei R, Miclea L -Ghid de Toxicologie, Editura Almatea, 1999;