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Observation on a Human Intentional Poisoning Case by the Organophosphorus Insecticide Fenthion.

María del Rosario Brunetto[*], *José Luis Burguera*[*], *Marcela Burguera*[*], *Fanny Villegas*[*], *Carmen Bastidas*[**].

[*]Department of Chemistry, Faculty of Sciences, University of Los Andes, P.O. Box 542, Mérida 5101-A, Venezuela. [**]Toxicological Center, Luis Razetti Hospital, Barinas, Venezuela.

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Abstract. A case of acute poisoning by oral ingestion of fenthion is reported. Plasma cholinesterase activity and fenthion whole blood concentration were throughly evaluated during the therapeutic intervention that consisted in administration of atropine, toxogonine and fresh plasma. Correlation studies between clinical signs, cholinesterase activity and fenthion levels revealed that pChE activity was not as helpful as the patient's clinical status in determining when the atropine infusion could be stopped. Morever pChE was also useless in signaling sudden relapses. It is concluded, based on this case, that supportive care combined with antidotal therapy remains the cornerstone of treatment specially in severe acute poisoning cases.

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INTRODUCTION

Fenthion [0,0-dimethyl-o-(4-methylthio)-m-tolyl] phosphorothioate (12) is an organophosphorus insecticide with physical and chemical properties which makes it suitable for use as residual spray in the field against a wide range of flies and mosquitoes (9). Fenthion is of moderate toxicity to mammals (LD_{50} PO rate = 230 mg/Kg (10), and differs from a number of other well-known phosphorothionates of the same general type in that the signs of poisoning develop rather slowly. The complexity of the metabolism makes it difficult to predict how susceptible man could be to the ingestion of different doses of the insecticide (8).

Atropine has been used successfully to treat poisoning with orga-

nophosphate insecticides for many years (5,7). During an organophosphate poisoning the compound bindswith acetylcholinesterase (ChE), there by rendering it inactive. Atropine acts by blocking the acetylcholine excess from becoming apparent (1). On the other hand, the assay of plasma cholinesterase activity (P-ChE) is considered to be useful, not in the diagnosis of the cholinergic crisis (which is clinically obvious) (11), but in determining the degree of correlation between cholinesterase inhibition in plasma with fenthion levels in blood.

We report here the outcome in a patient who ingested an undefined quantity of fenthion in a suicide attempt and underwent various types of therapeutic measures. The evolution of P-ChE and fenthion in whole blood was evaluated.

CLINICAL OBSERVATION

A 41-year-old man was brought to the hospital twenty hours after intentionally swallowing an undefined quantity of fenthion (Trade name Lebaycid). On admission, the patient was found to be coherent and lucid, was afebrile and the neurologic exam was normal. He had sore throat, dysphagia, distended abdomen, decreased bowel sounds and striking pinpoint pupils. He was hypotensive showing a slow pulse rate. The following tests were performed: full blood count, urea and electrolytes, glucose and liver function tests; all of them were normal. Urianalysis showed protein ++ and routine culture was sterile; chest X ray, blood gases and spirometry were normal. He was treated with gastric lavage and atropine. After 10 doses of 0.5 mg of atropine every ten minutes and two doses of 500 mg of toxogonine every four hours given intravenously, the patient developed a tachycardia of more than 150/min which prevented, at least temporarily, the continuation of atropine theraphy. Thereafter, the dosage of suministered atropine was solely dictated by the clinical situation to complete the maximum dosage of 30 mg/day (4). At that time, the lungs were clear, neither fasciculations nor myosis were observed and the patient was still conscious. However, after the 2nd day, the symptomatology worsened: respiratory distress appeared due to copious mucinous secretions in the trachea and bronchi. He had generalized intense fasciculations and abundant diarrhea which persisted for about 12 hours. Thus, he was intubated and placed on a respirator. Full atropinization was maintained at rate of 3 mg every ten minutes and two ampoules of 500 mg of toxogonine every four hours were supplied which lead to pressure above 100 and a pulse between 130 and 140. Although, at this moment the atropine requirements were high (18 mg/hr), this dose was lower than that reported by LeBlanc et al. (7). During the 4th day severe cholinergic manifestations with convulsive crises appeared, which lead to exchange transfusions twice and the administration of 0.1 mg/min atropine. By the 5th day, acute renal failure (diuresis 20 cc/h) developed and pulmonary function deteriorated. During the 6th day, the patient became delirious and suffered a se-

cond bout of hypotension, bradycardia and hypoxia. The patient died on the 7th day from a refractory cardiovascular collapse associated with an acute respiratory distress syndrome. Post-mortem examination showed acute emphysematous pulmonary edema, pinky froth in the trachea and bronqui and marked and generalized organs congestion, specially in liver and kidneys.

MATERIALS AND METHODS

P-ChE was determined by the method of Kalow and Genest (6) using a Varian 634 UV-spectrophotometer.

The fenthion in whole blood was determined by gas chromatography: the instrumentation used was a Varian 3600 gas chromatograph. A 1/2 O.D." x 2 mm i.d., packed with Chromosorb W/HP, 8/100 mesh and coated with 3% OV 17 glass universal column was used. A flame photometric detector in the phosphorus mode (= 526 nm) was used. Three ml of heparinized blood and 3 ml of benzene were transfered to a 20 ml separatory funnel and shaked vigorously for 10 minutes. After centrifugation at 300 rpm, the organic layer was allowed to separate from the water phase for a minimum of 5 minutes. After collecting the benzene extract in a graduate flask, this was evaporated to a final volume of 0.2 ml with a dried nitrogen flow. The recommended optimized conditions for the gas chromatograph were: column temperature 200 °C; injector and detector temperature 240°C; nitrogen was used as carrier gas at a flow rate of 2.5 ml/min; hydrogen, air inlet 1 and air inlet 2 flow rates to the detector, were of 140, 80 and 170 ml/min, respectively. The atenuation and range of the detector were 8 and 10^{-10} A/mV, respectively. By injecting 1 1 sample volume, the limit of detection was 2 ng fenthion/ml of whole blood and the response was linear from 0.1 to 12 ng/ml. Recovery of fenthion from blood samples was always within the 89 to 92% range. Within-batch coefficient of variation was 1.6% for the determination of 1 ng fenthion/ml.

RESULTS

During the patient's hospitalization blood fenthion concentration and P-ChE were monitored frequently (Fig. 1). On admission, 20 hours after the ingestion, the blood fenthion concentration was 0.27 mg/l and the P-ChE was 0.56 IU/ml. However, on the first day, a worsening of the clinical status was seen together with an important elevation of fenthion blood levels to 0.78 mg/l and a decrease of P-ChE to 0.06 IU/ml. As expected, P-ChE increased to normal values (P-ChE 0.5 IU/ml) (8) after atropine treatment and the first exchange-transfusion (4th day). After the 2nd day the blood levels of the pesticide decreased to values which consistently varied within the 0.16 - 0.30 mg/l levels.

DISCUSSION

Reports on oral intoxication with fenthion are uncommon (4). Fenthion differs from a number of other well-known phosphorothionates of the same type in that the

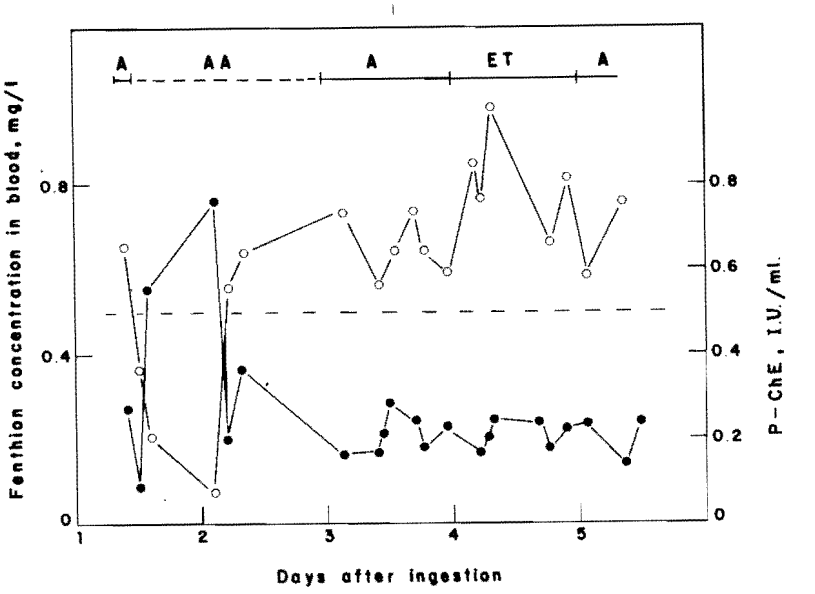

Fig. 1. Time course of (●) fenthion concentration in whole blood and (o) P-ChE. A: indicates times during which full atropinization was maintained. AA: indicates time during which suministred atropine doses were dictated by the clinical situation. ET: indicates time during which exchange transfusions were performed.

signs of poisoning develop rather slowly but persist several days. In our case, the cardio-circulatory effects might have been induced by the preponderance of the adrenergic system at the earliest stage of the intoxication by fenthion (2).

Atropine is the classical antidote of anticholinesterase agents, and in our particular case its dosage was solely dictated by the clinical situation. Excessive administration of atropine was avoided as overdoses of atropine may cause symptoms similar to those of organophosphates poisoning and death byhyperthermia may occur (3,4). In our observation, the dosage of atropine was sufficient to antagonize muscarinic effects like salivation and vomiting. As previously reported by LeBlanc et al. (7) and Mahieu et al (8), we also did not find P-ChE to be as helpful as the patient's clinical status in determining when the atropine infusion could be stopped or re-started.

It has been previously reported by Kimmerle (unpublished result) toxogonine has a marked antidotal effect on fenthion and it is even more active when associated with atropine. In our case after its administration a marked decrease on pesticide levels and an increase on P-ChE activity was observed.

Our patient exhibited a slight improvement of consciousness after the first exchange-transfusion. This temporary clinical improvement was likely due to the exogenous contribu-

tion of fresh red blood cells, but never associated with the slight increase of p-ChE activity observed.

Despite of the therapeutic measures, the progressive worsening of the clinical picture could be due to a progressive release of the pesticide initially stored in the adipose tissue followed by its activation in the liver into a direct cholinesterase inhibitor (1). These facts may explain the duration of the symptomatology.

In conclusion a number of factors may have contributed to the severity of this poisoning. First, the ingestion could have involved a large quantity of concentrated insecticide. Second, attemptsto prevent absorption by gastric lavage were not completely effective, since by the time the patient was admited to the hospital the absorption of the pesticide may have already ocurred.

In this case of organophosphate poisoning, we did not find P- ChE to be as helpful as the patient's clinical status in determining when the atropine infusion could be stopped. More over P-ChE was also useless in signaling sudden relapses. Until more human data become available, supportive care combined with antidotal therapy remains the cornerstone of treatment, specially in severe acute poisoning cases.

RESUMEN

Observaciones sobre un caso humano de envenenamiento intencional por el insecticida organofosforado fention. Brunetto M.R. (Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Apartado 542, Mérida 5101-A, Venezuela), Burguera J.L., Burguera M., Villegas F., Bastidas C. *Invest Clin 33(3) 89-94, 1992.*

Se reporta un caso de envenenamiento por ingestión oral de fention. La actividad de colinesterasa plasmática y de fention en sangre completa fue evaluada durante toda la intervención terapéutica del paciente la cual consistió en administración de atropina, toxogonina y plasma fresco. Los estudios de correlación entre los signos clínicos, actividad de colinesterasa y niveles de fention revelaron que la actividad de colinesterasa no resultó tan útil como el estado clínico del paciente ni para determinar cuándo se debe detener la infusión de atropina ni como señal de recaída. Se concluye que cuidados intensivos combinados con terapia antidotal siguen siendo la piedra fundamental del tratamiento, especialmente en casos de envenenamiento agudo severo.

REFERENCES

1- DAVIES J.E., BARQUET A., FREED V.H., HAQUE R., MORGADE C., SONNERBORN R.E., VACLAVEK C.: Human pesticide poisoning by a fat-soluble,organophosphate insecticide. Arch Environ Health 30:608-613, 1975.

2- DEAN J., COXONN J., BRERETON D.: Poisoning by an organophosphorus compound: A case report. S Afr Med J 41:1017-1019, 1967.

3- DE MONCHY J.G.R., SNOEK W.J., SLUITER H.J., UGES D.R.A., MEYER S., JAGER A.E.J.: Treatment of severe

parathion intoxication. Vet Human Toxicol, Suppl 21:115-117, 1979.

4- GONZALEZ D., TORRENT E., VIVES A., GRAU A., BOFILL D.: Intoxicación por plaguicidas. Med Integral 11:480-486, 1988.

5- HOPMANN G., WANKE H.: Maximum dose atropine treatment in severe organophosphate poisoning. Dtsch Med Wsch 99:2106-2108, 1974.

6- KALOW W., GENEST K.: Detection of atypical forms of human serum cholinesterase: Determination of dibucaine numbers. Can J Biochem Physiol 35:339-346, 1957.

7- LEBLANC F.N., BENSON B.E., GILG A.D.: A severe organophosphate poisoning requiring the use of an atropine drip. Clin Toxicol 24:69-76, 1986.

8- MAHIEU P., HASSOUN A., VAN BINST R., LAUWERYS R., DEHENEFFE Y.: Severe and prolonged poisoning by fenthion. Significance of the determination of the anticholinesterase capacity of plasma. J Toxicol Clin Toxicol 19:425-432, 1982.

9- METCALT R.L., FUKUTO T.R., WINTON M.Y.: Chemical and biological behaviour of fenthion residues. Bull Wld Hlth Org 29:219-226, 1963.

10- SCHRADER G.: Die Entwicklung neuer insektizer Phosphorsaure-Ester. 3rd. ed., Verl Chimie, Weinheim/Berstrasse, 1963.

11- SENANAYAKE N., KAFALLIEDDE L.: Neurotoxic effects of organophosphorus insecticides. N Engl J Med 316:761-763, 1987.

12- WAYLAND J.H. Jr.: Fenthion in: Pesticides Studies in Man. pp. 367-370. William & Wilkins, Baltimore, 1982.