CASE REPORT

Review of severe organophosphate poisonings over a period of 11 years (1996-2006)

JUAN CARLOS BARCO[1], CATALINA OMAR[1], JORDI PUIGURIGUER[1,2], INMACULADA COLL[2], BERNARDI BARCELÓ[2], TOMEU CASTANYER[2]

[1]Emergency Department. Clinical Toxicolgy Emergency Unit. [2]Clinical Documentation Department. Hospital Son Dureta, Palma de Mallorca, Spain.

CORRESPONDENCE:
J. Puiguriguer
Coord. Urgencias
Hospital Son Dureta
C/ Andrea Dòria, 55, planta baja
07014 Palma de Mallorca
Illes Balears, Spain
E-mail: jpuiguri@hsd.es

RECEIVED:
16-7-2007

ACCEPTED:
16-4-2008

CONFLICT OF INTEREST:
None

Objective: To review all the organophosphate poisonings (OP) over a 11-year period which required at least seven days of admission at our hospital.
Methods: Descriptive retrospective study of patients with OP attended at the hospital from 1996 to 2006. The variables age, sex, type of poisonous compound, destination at admission, length of stay, environment (rural or urban), cause of poisoning, clinical symptoms, therapeutic measures, acetylcholinesterase measurement, and history of psychiatric disorders were assessed.
Results: Eight patients were included, mean age 49 years (range: 26-65), 50% female. Poisonous compound were pure OP (50%), OP plus herbicide (25%) and OP plus carbamate (25%). Mean hospital stay was 40,5 days. Mean stay in the ICU in 6 patients who required intensive care was 23 days. Five (63.5%) patients were from rural origin and 3 (27.5%) were urban cases. Five cases (62.5%) were suicide attempts, 2 (25%) were accidents and the reason was not clear in one case. 100% presented with cholinergic syndrome, 2 cases (25%) mild muscarinic syndrome and 6 cases (75%) muscarinic, nicotinic and central symptoms. Four cases (50%) presented intermediate syndrome and 4 cases relapse of cholinergic symptoms. Severe hypothermia was present in 2 cases. Respiratory insufficiency was seen in 6 patients, which required orotracheal intubation. Gastrointestinal decontamination was performed in 6 cases. Two patients received activated charcoal without lavage. Atropine was used in 5 cases (62.5%) and pralidoxime in 4. Hemoperfusion with activated carbon and hemofiltration was used in one case. Serum cholinesterase activity was measured in 6 cases.
Conclusion: Severe organophosphate poisonings has multiple symptoms. If general measures adopted are not enough and/or treatment is withdrawn early they can increase significantly. [Emergencias 2008;20:00-00]

Key words: Organophosphates. Poisoning. Suicide, attempted.

Introduction

Poisoning by organophosphate (OP) insecticides represents one of the potentially most severe entities within the setting of poisoning. Its incidence in Spain is relatively frequent in the agricultural areas of Almería, Levante, and the Canary and Balearic Islands[1-3]. Entry routes include digestive (suicide attempts or accidental exposure), cutaneous and/or inhalation (accidental exposure at the worksite), with parenteral poisoning being rare[4].

After receiving a case of severe OP poisoning, similar cases attended in our hospital over the last 11 years were reviewed. All were initially attended in the Emergency Department with a posterior hospital stay of more than 7 days.

Methods

A retrospective review of all the cases coded as poisoning by insecticides (CIE 989) from January 1, 1996 to December 31, 2006 was made through the Clinical Documentation Department of the Son Dureta Hospital in Palma de Mallorca, Spain. A group of 34 cases was obtained of which 18 corresponded to PB and carbamates (CIE 989.3). Of these, the adults attended in our emergency department (16 cases) with a hospital stay of more

than 7 days were selected with the aim of reviewing possible serial laboratory determinations (cholinesterases) and on considering that this hospital stay was representative of the patients with greater clinical repercussion and, consequently, with more data available in their clinical history. The final sample was of 8 cases.

The following variables were studied: sociodemographic, psychiatric history, product causing the poisoning, the cause of poisoning, clinical manifestations presented and complications, therapeutic approach and laboratory determinations as well as the need or not for admission in an intensive care unit (ICU).

The erythrocyte cholinesterase determinations were performed using the butirylthiocholin method. This technique has been adapted to a Hitachi 717 (Roche) analyser. The measurement interval is from 35 to 16,000 U/L and the reference values are: from 6,400 to 15,500 U/L for children, men and women under 40 years of age; from 5,100 to 13,500 U/L for women from 16 to 36 years old; and from 4,400 to 10,900 U/L for women who are pregnant or receiving contraceptives.

Results

The study sample included 8 adults: 4 cases (50%) corresponded to women and the other 4 (50%) men with a mean age of 49 years (range: 26-65 years). The product used was pure OP insecticide on 4 occasions, a mixture of PR and herbicide on 2 (25%) and OP and carbamate the remaining 2 (25%). The mean hospital stay was 40 days with a mean of 23 days in the ICU in the 6 cases requiring admission to this unit (75%). All the patients were discharged following resolution of the clinical picture.

The site of poisoning was a rural setting on 5 occasions (62.5%) and an urban setting in 3 (37.5%). With respect to the causes, 5 were diagnosed as a suicide attempt (62.5%), two as accidents (25%) and one undetermined (12.5%). Six of the 8 patients (75%) presented a psychiatric history.

With respect to the clinical manifestations, the 8 cases (100%) presented a cholinergic syndrome, two as a mild muscarinic syndrome (25%) (sialorrhoea in one and vomiting in another) and 6 with muscarinic, nicotininc and central symptomatology (75%) (Table 1). In addition, 4 patients presented an intermediate syndrome (50%) consisting in respiratory musculature involvement, the neck and the extremities, with severe respiratory insufficiency which appeared from 24-96 hours post-exposure and after having surpassed the cholinergic phase which did not respond to the use of antidotes (atropine and oximes)[5-7]. In 4 cases recurrence of the cholinergic syndrome occurred (50%) (Table 2). Another clinical manifestation observed was severe hypothermia of 32% in 2 cases (25%), myocardial lesions with ST alterations in 3 cases (37.5%), and hyperglycaemia without previous known diabetes on 2 occasions (25%) (Table 2).

Table 1. Most frequent neurological syndromes found in this review

Muscarinic syndrome	8 (100%)
Vomiting	
Myosis	
Sialorrhoea	
Diarrhoea	
Bronchial hypersecretion	
Arterial hypotension	
Bradycardia	
Hypothermia	
Paleness	
Sweating	
Somnolence	
Fever	
Nicotinic syndrome	6 (75%)
Fasciculations	
Electrocadiographic alterations	
Tachycardia	
Hyperglycaemia	
Central syndrome	6 (75%)
Coma	
Confusion	
Convulsion	
Toxic encephalopathy	
Intermediate neuromuscular syndrome	4 (50%)
Tetraparesis	
Tetraplegia	
Respiratory depression	

The most frequent complications observed were respiratory insufficiency in 6 patients (75%), pneumonia due to methicillin-resistant *Staphylococcus aureus, Escherichia coli, Serratia marlescens* and *Pseudomonas aeruginosa* in 5 cases (62.5%) and metabolic acidosis in 4 cases (50%). Plasma anticholinesterase activity was determined in 6 cases (75%).

In regard to therapeutic actions, gastric decontamination was performed with the administration of activated charcoal in 6 cases (75%). In 2, activated charcoal was administered without previous gastric lavage (25%). Atropine was used in 5 cases (62.5%), one intramuscularly[5] (12.5%) in the healthcare centre prior to transfer to the hospital. In 4 cases (50%) oximes were used (pralidoxime). In one case haemoperfusion was performed with activated charcoal and haemofiltration (12.5%). Six patients required orotracheal intubation (75%).

Table 2. Individual clinical, analytical and epidemiologic data of the cases in this series

	1st case	2nd case	3rd case	4th case	5th case	6th case	7th case	8th case
Activity SC	Not deter.	144	Undetectable	590	250	Not deter.	Not deter.	173
Days of admission	8	29	43	135	25	12	35	33
Days of ICU stay	0 18	29 0	30 No consta	30 16				
Clinical manifestations	Musc. syn.	Musc. syn. Nicotinic Interm. Central	Musc. syn. Nicotinic Interm. Central	Musc. syn. Nicotinic Interm. Central	Musc. syn. Nicotinic Interm. Central	Musc. syn.	Musc. syn. Central	Musc. syn. Nicotinic Central
Antidotes	None	None	Atropine Pralidoxime	Atropine Pralidoxime	Atropine	None	Atropine Pralidoxime	Atropine Pralidoxime
Product	Diacinon	Unknown	Chloripyrif	Unknown		Paraquat	Chloripyrif	Dimetoate + Cyclohexanone

CSC: serum cholinesterase; UCI: intensive care unit; Not deter: Not determined; syn: syndrome; musc: muscarininc.

Discussion

A higher incidence of cases of poisoning of this type was observed in the rural setting in accordance with the literature reviewed[3,6]. Three out of the 5 rural cases belonged to the same town (Pollença). It is of note that this population is not particularly known for its agricultural character but rather for being an important tourist centre with a high level of life. The habitual use of these products as pesticides in private gardens, and thus, their easy accessibility may justify this local increase.

All the suicide attempts coincided with psychiatric histories with previous attempts already having been made, similar to the study by Suárez[3]. In one of the cases it could not be determined whether the cause was a suicide attempt or was due to previous cognitive deterioration of the patient (on neurological study).

With regard to the clinical manifestations, it was found that the cases with mild symptomatology (only muscarinic) coincided with accidental ingestion (fumigated parsley and oral contact by ingestion of a product in an inadequate container). In the cases presenting with more persistent symptomatology, which was generally with a severe cholinergic picture, this was produced after the implementation of initially slightly aggressive measures: mildly aggressive or no digestive decontamination, non adequate use of antidotes whether because they were not used or due to early withdrawal (< 48 hours). Greater severity of the episode was also observed with early withdrawal of respiratory support measures and this persistence may be related to redistribution of the toxin in fat tissue because of its high liposolubility[5,7]. Interestingly, the only case in which gastric decontamination was performed with repeated doses of activated charcoal corresponded to accidental poisoning with mild clinical manifestations. Activated charcoal was administered in all the cases without having carried out previous gastric lavage (or aspiration).

The variability in the treatment of the more severe patients requires critical reflection. In one case, despite the presentation of severe, obvious clinical manifestations (in whom plasma anticholinesterase activity was not determined) pralidoxime was not administered but haemoperfusion with activate charcoal and haemofiltration were implemented on admission to the ICU. Another case, with the longest hospital stay and clear, recurrent symptomatology received basic support measures and symptomatic treatment with minimum doses of antidotes in the beginning. Finally, another patient with muscarininc manifestations and an intermediate syndrome requiring several reintubations (for extubations performed too early) underwent up to 12 seried determinations of serum cholinesterase activity (with an initial result of 144 U/L and a last value of 4,814 U/L) with no antidotes having been administered at any time. It therefore seems necessary to perform an update of this syndrome among the personnel working in emergency care services and emergency departments with the aim of unifying and optimising the treatment for this type of patient.

Reintubation was required in all the cases of severe poisoning in whom orotracheal intubation was withdrawn at 24-48 hours, mainly due to recurrence of the muscarinic syndrome or the appearance of an intermediate syndrome with severe deterioration in respiratory function.

The controversy on the use or not of oximes in this type of poisoning is of note. Nogué[5] recommended their use in medium or high severity poisonings before 36 hours and always after the initial use of atropine, although no controlled studies have demonstrated their efficacy. Ferrer[7] reported a si-

milar opinion in an in vitro study recommending the rapid application of oximes which may be effective even 24 hours post-poisoning. Suárez[3] is of note with respect to the contraindication of the use of oximes for poisoning with carbamates because of the possible production of a carbamylate oxime inhibidor of acetylchoinesterase which is potentially more toxic than carbamate itself.

The most frequent complication observed in these patients was respiratory insufficiency followed by pneumonia[10].

Lastly, the difficulties encountered to carry out the present study are worthy of mention mainly due to the deficiencies in the registry systems of clinical histories. The absence of a specific follow up of these patients makes it impossible to determine whether they have presented any type of late sequelae related to the poisoning episode as has been described in the studies by Nogué, Ferrer and Serviá. Likewise, it was not possible to perform a follow up of the evolution of the analytical determinations of plasma anticholinesterase activity in these patients.

As in other poisonings, the importance of obtaining the maximum information possible from the families and/or accompanying persons as well as from the first care givers or assistants at the site should be emphasised to thereby facilitate rapid diagnostic work up and, subsequently, apply the most appropriate and aggressive therapeutic measures early.

References

1 Martínez J. Intoxicación por insecticidas anticolinesterásicos. Rev Toxicol 1990;7:135-49.

2 Yelamos F, Martín JC, Laynez F. Intoxicaciones agudas por organofosforados. Investig Clín 1999;2:134-6.

3 Suárez ML, González-Delgado F, Rubio C, Hardisson A. Estudio de seis suicidios consumados por ingestión de carbamatos en el partido judicial de la Laguna (Tenerife) durante el periodo 1998-2002. Rev Toxicol 2004;21:108-12.

4 Boluda JF, Nogué S, Martínez-Pérez J, Muñoz E. Intoxicación por administración parenteral de insecticidas organoclorados e hidrocarburos aromáticos. Rev Toxicol 2003;20:46-7.

5 Nogué S. Intoxicación por productos agrícolas. Medicina Interna. En Farreras-Rozman, Edición en CD-ROM. AVT Consultores. Ed Doyma S.A. y Mosby-Doyma libros S.A. 2006:2606-10. [consultado13 de diciembre de 2006] Disponible en: http://www.sepeap.es/libros/farreras13/INDICE/indice.pdf.

6 Serviá L, Rodríguez A, Balsera B, Laguardia P. Intoxicación aguda por organofosforados tras ingestión de fruta fresca: ¿síndrome intermedio? Med Clin (Barc) 2001;117:316 [consultado 13 de diciembre de 2006]. Disponible en: http://db.doyma.es/cgi-bin/wdbcgi.exe/doyma/mrevista.fulltext?pident=13018680.

7 Ferrer A. Intoxicación por plaguicidas. Anales Sis San Navarra 2003;26:155-71. [consultado10 de noviembre de 2006]. Disponible en: http://wwwscielo.isciii.es/scielo.php?script=sci_arttext&pid=S1137.

8 Sogorb MA, Vilanova E, Carrera V. Nuevas perspectivas en los tratamientos de intoxicaciones por insecticidas orgonofosforados y agentes nerviosos de guerra. Rev Neurol 2004;39:739-47, 62 R.

9 Ríos JC, Repetto G, Ros A, Del Peso A, Rodríguez-Vicente MC, Repetto M. Efectividad de la pralidoxima en la reactivación de la acetilcolinesterasa eritrocitaria in vitro. Rev Toxicol 2002;19:97-144 Sesión IV.

10 Martín JC, Yélamos F, Laynez F, Córdoba J. Intoxicaciones por insecticidas organofosforados. Estudio de 506 casos. Rev Clín Esp 1996;196:145-9, 28 R.

Revisión de las intoxicaciones graves por insecticidas organofosforados atendidas en un período de 11 años (1996-2006)

Barco JC, Omar C, Puiguriguer J, Coll I, Barceló B, Castanyer T

Objetivo: Revisar las intoxicaciones por organofosforados (OF) en un período de 11 años atendidas en nuestro hospital que requirieron ingreso de 7 días o más.
Método: Estudio retrospectivo descriptivo de pacientes intoxicados por insecticidas OF atendidos entre 1996 y 2006 con una estancia hospitalaria igual o mayor de 7 días. Se analizan las siguientes variables: la edad, el sexo, el tipo de producto, el destino del ingreso y la duración de las estancias hospitalarias que generaron, el hábitat de residencia (rural o urbano), la causa de la intoxicación, la sintomatología clínica, las medidas terapéuticas aplicadas, la presencia de antecedentes psiquiátricos y las determinaciones seriadas de colinesterasas sérica.
Resultados: Se han incluido 8 pacientes, el 50% de los cuales eran hombres, con una edad media de 49 años. El producto un OF puro (50%), un OF más herbicida (25%) y un OF más carbamato (25%). La estancia media hospitalaria fue de 40 días y en los 6 pacientes que requirieron unidad de cuidados intensivos (UCI) su estancia en ella fue de 23 días. Cinco casos procedían del medio rural (62,5%) y 3 del urbano (37,5%), y en 5 casos (62,5%) exitió intención suicida. Todos los pacientes presentaron síndrome colinérgico, el 25% síndrome muscarínico leve el 75% sintomatología muscarínica, nicotínica y central. En el 50% de casos se produjo un síndrome intermedio y en el 50% hubo recidiva colinérgica. Hubo hipotermia severa en 2 casos e insuficiencia respiratoria en 6 pacientes, los cuales requirieron intubación orotraqueal. Se realizó descontaminación gástrica en 6 casos, en 2 se administró el carbón sin lavado previo, en 5 la atropina, en 4 la pralidoxima y en 1 el carbón activado y la hemofiltración. La colinesterasa sérica fue determinada en 6 casos.

Conclusión: Las intoxicaciones graves por OF presentan una gran riqueza sintomática, la cual es mayor cuando las medidas iniciales adoptadas no son enérgicas y/o si se produce una retirada precoz del tratamiento. [Emergencias 2008;20:207-211]

Palabras clave: Organofosforados. Intoxicación. Tentativa suicida.