

CLINICAL MANIFESTATION AND MANAGEMENT OF
PATIENTS WITH ACUTE POISONING BY
ANTICHOLINESTERASE INSECTICIDES
(ANTI-ChEI)

BY

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ABSTRACT

The problem of acute poisoning by insecticides is increasing nowadays due to the widespread use in agriculture and household. Acute poisoning by insecticides accounted for 8.1% of the total patients with acute poisoning admitted to Alexandria Poison Center (A P C) in 1989. The majority of poisoning events were intentional (31.0%). Accidental occupational poisoning or accidental ingestion constituted 19.0%. A sample of patients with acute insecticides poisoning were fully investigated (n = 30). Poisoning by organophosphorus insecticides (OPI) represents 63.3% , while carbamate insecticides (CI) were responsible for 36.7% of poisoning cases. A significant elevation of the level of cholinesterase (ChE) activity was observed after treatment with atropine sulphate and ChE reactivator, e.g. obidoxime chloride (Toxogonin). The study showed that early administration of ChE reactivators in CI poisoning will help in prompt reactivation of the inhibited enzyme. Programs in public awareness about the safe and careful use of anti-ChEI and its health hazards and how to prevent poisoning are mandatory.

INTRODUCTION

Many pesticides are potentially very hazardous not only to human health but also to other organisms in the environment. Damage to an ecosystem may in itself lead to reduced agricultural production, causes unwanted effects on the environment, and other economic losses (1).

OPI and CI are chemicals that inhibit the enzyme acetylcholinesterase (AChE) at various sites within the peripheral and central nervous system. The resultant accumulation of the neurotransmitter acetylcholine (ACh) at cholinergic receptor sites causes stimulation and then suppression of transmission to the various effector organs (2, 3).

Generally, acute poisoning by anti-ChEI are classified according to the inhibition level of serum ChE into mild (50%-20% of normal), moderate (20%-10% of normal), and severe (less than 10% of normal) (4). The clinical manifestations of CI poisoning are similar to that of OPI toxicity, with the exception that spontaneous hydrolysis of the carbamate ChE complex leads to less severe and shorter duration of symptoms (5). Acute poisoning by insecticides was the leading cause of toxic coma (39.2%) in the Intensive Care Unit of APC (6).

The present investigation was designed to study the magnitude of acute poisoning by anti-ChE insecticides in Alexandria City. Also, to diagnose and determine severity of poisoning through clinical manifestations and measuring the level of serum ChE activity in a sample of exposed patients, and finally to assess the efficacy of supportive and specific treatment.

MATERIALS AND METHODS

The study includes all patients with acute poisoning by insecticides admitted to the APC and other hospitals in Alexandria City. A group of thirty patients with acute poisoning by anti-ChE insecticides admitted the APC were investigated. Circumstances of poisoning, clinical manifestations, estimation of serum ChE level (7) and management were recorded. A control group of five healthy adult persons not exposed to anti-ChE insecticides were included in the study. Statistical analysis was done using the arithmetic mean, Standard deviation and T-test at 5% level when indicated.

RESULTS

Acute poisoning by anti-ChEI constituted 305 patients (8.1%) out of the total patients with acute poisoning (n = 3754) admitted to the APC during the year 1989.

Fifty patients with acute insecticides poisoning reported by hospitals related to Ministry of Health were not included in the study as no recorded data about them were available. Most of the hospitals in Alexandria refer their patients to the APC because of the specificity and the availability of good medical care to acutely poisoned patients.

Age of Patients with Acute Poisoning by Anti-ChEI (n=305):

The age of patients with acute poisoning by anti-ChEI ranged from 2 up to 55 years with a mean age of 19.62 ± 11.14 years (Table 1). More than half the patients were in the age group 15-35 years (59.0%) followed by the younger age

Table (1): Patient with acute insecticide poisoning (n=305) admitted to the Alexandria Poison Center during the year 1989 and age.

Age in Years	Number of Patients	
	No.	%
- 5	40	13.1
5 -	15	4.9
10 -	39	12.8
15 -	145	47.5
25 -	35	11.5
35 -	21	6.9
45 - 55	10	3.3
Total	305	100.0

$$\bar{X} \pm S.D = 19.62 \pm 11.14$$

Table (2): Patients with acute insecticide poisoning (n=305) admitted to the Alexandria Poison Center during the year 1989 , by months of the year, and sex.

Months of the Year	Sex				Total	
	Males		Females			
	No.	%	No.	%	No.	%
January	11	7.3	7	4.5	18	5.9
February	9	6.0	14	9.0	23	7.5
March	14	9.3	9	5.8	23	7.5
April	5	3.3	6	3.9	11	3.6
May	10	6.0	19	12.3	29	9.5
June	12	8.0	15	9.7	27	8.9
July	13	8.8	12	7.7	25	8.2
August	18	12.0	21	13.5	39	12.8
September	16	10.7	16	10.3	32	10.5
October	18	12.0	11	7.2	29	9.5
November	12	8.0	13	8.4	25	8.2
December	12	8.0	12	7.7	24	7.9
Total	150	100.0	155	100.0	305	100.0

groups less than 5 years (13.1%) and that of 10-15 years (12.8%).

Months of Admission and Sex:

Table(2) reveals that females slightly outnumbered males (50.8% and 49.2%, respectively). Poisoning by insecticides in males was more likely to occur in the months of August, September and October (12.0%, 10.7% and 12.0%, respectively), while acute poisoning in females was more likely to be met with in May, August and September (12.3%, 13.5% and 10.3%, respectively). In general, irrespective of sex, the months August and September showed the highest incidence of admission (12.8% and 10.5%, respectively).

Months of Admission and Circumstances of

Poisoning:

The majority of acute poisoning by insecticides were intentional (81.0%), while accidental poisoning constituted 19.0% (Table 3). Accidental poisoning was more to be encountered in March (17.2%), followed by October (13.8%), and May (12.0%). On the other hand, intentional poisoning was more or less the same all over the year with its lowest incidence in April, January and March (3.6%, 5.7% and 5.3%, respectively).

A sample of 30 patients with acute poisoning by anti-ChEI who were admitted to the APC were studied in details.

Age, Sex and Residence:

Half the patients were in the age group 15-25 years (50.0%) while more than a quarter (26.7%) were in the age group 25-35 years (Table 4). The mean age of patients was 26.0 ± 8.31 years. Females were slightly younger than males, but the difference was statistically insignificant ($t = 0.657$).

Table (3): Patients with acute insecticide poisoning (n = 305) admitted to the Alexandria Poison Center during the year 1989, by months of the year, and circumstances of poisoning.

Months of the Year	Circumstances of Poisoning					
	Accidental		Self Poisoning		Total	
	No.	%	No.	%	No.	%
January	4	6.9	14	5.7	18	5.9
February	3	5.2	20	8.1	23	7.5
March	10	17.2	13	5.3	23	7.5
April	2	3.5	9	3.6	11	3.6
May	7	12.0	22	8.9	29	9.5
June	2	3.5	25	10.1	27	8.9
July	3	5.2	22	8.9	25	8.2
August	6	10.3	33	13.4	39	12.8
September	5	8.6	27	10.9	32	10.5
October	8	13.8	21	8.5	29	9.5
November	3	5.2	22	8.9	25	8.2
December	5	8.6	19	7.7	24	7.9
Total	58	100.0	247	100.0	305	100.0

Table (4): Patients with acute insecticide poisoning (n=30) and different parameters.

Different Parameters	Sex				Total	
	Males		Females			
	No.	%	No.	%	No.	%
Age:						
10 -	2	12.5	-	-	2	6.7
15 -	5	31.3	10	71.4	15	50.0
25 -	5	31.3	3	21.4	8	26.7
35 - 45	4	25.0	1	7.2	5	16.6
Total	16	100.0	14	100.0	30	100.0
X $\pm$ S.D	26.9 $\pm$ 9.63		25.0 $\pm$ 6.0		26.0 $\pm$ 8.3	
t = 0.657						
Circumstances of Poisoning:						
Accidental	6	37.5	-	-	6	20.0
Intentional	10	62.5	14	100.0	24	80.0
Total	16	100.0	14	100.0	30	100.0
Type of Insecticides:						
Organophosphates	8	50.0	11	78.6	19	63.3
Carbamates	8	50.0	3	21.4	11	36.7
Total	16	100.0	14	100.0	30	100.0
Severity of Poisoning:						
Mild	8	50.0	4	28.6	12	40.0
Moderate	2	12.5	-	-	2	6.7
Severe	6	37.5	10	71.4	16	53.3
Total	16	100.0	14	100.0	30	100.0

Table (5): Clinical manifestations encountered in patients with acute poisoning by organophosphorus and carbamate insecticides (n=30).

Degree of Poisoning	Muscarinic Manifestations	Nicotinic Manifestations	CNS Manifestations
Mild (n = 12)	* Sludge in all patients in a mild form * Constricted pupils, normal reaction to light * Tightness in chest	Negative	* Conscious * Restlessness
Moderate (n = 2)	* Sludge in all patients * Restlessness with varying degree of severity * Miosis with slow reaction to light * Tightness in chest * Some difficulty in breathing * Wheezes * Slow pulse	* Muscle fasciculation (limited to the eyelids) * Unable to walk	* Confusion * Drowsiness * Irritability
Severe (n = 16)	* Sludge in all patients and repeated especially diarrhea * No reaction to light * Dyspnea, cyanosis pulmonary oedema (n=8) * Slow pulse**	* Muscle fasciculation (in the eyelids, whole face & neck) * Tremors especially in the extremities	* Varying grades of coma

* Sludge (Salivation, lacrimation, urination, diarrhea, gastrointestinal cramp, emesis).

** Tachycardia 130/minute encountered in two patients.

Elramel, Moharem Bey and Karmouz referred most of the patients (23.3% , 20.0% and 20.0% , respectively). Outside Alexandria (Kafr El-Dawar, Beheira Governorate) referred 16.7% of patients. Mina El-Basal and El-Attaren referred 10% each.

Circumstances of Poisoning:

The majority of patients with acute poisoning by anti-ChEI were intentional (80.0%), only 20.0% were due to either accidental ingestion or exposure during spraying. All female patients (n = 14) were self-poisoned.

Types of Anti-ChEI:

Poisoning by OPI constituted 63.3% of the total sample , e.g. Diazinon , Methamidophos , Dimethoate. While poisoning by CI was responsible for 36.7% of patients. The commonly involved CI was Aldicarb. Only one case with methomyl poisoning was recorded.

Severity of Acute Poisoning:

Patients were divided into mild, moderate and severe poisoning according to the severity of clinical manifestations and the ChE level in the serum. In the present study, more than half the patients suffered severe poisoning (53.3%). Mild poisoning constituted 40.0%, only two patients (6.7%) had moderate degree of poisoning. The same Table (4) showed that mild poisoning was more likely to be among males (50.0% compared to 28.6%, among females), while severe poisoning was more to be among females (71.4% compared to 37.5% among males).

Clinical Presentation of Patients:

The clinical manifestations in patients with OPI poisoning (n = 19) were listed in Table (5) according to the degree of severity of poisoning whether mild, moderate or severe.

Table (6) : Patients with acute insecticide poisoning (n = 30) by degree of poisoning and serum cholinesterase level before and after treatment.

Grades of Poisoning	Serum Cholinesterase Level (UI)	
	Organophosphates X $\pm$ S.D	Carbamates X $\pm$ S.D
Mild:	(n = 3)	(n = 9)
Before treatment	999.3 $\pm$ 83.64	1255.11 $\pm$ 276.6
Mean %	42.0 %	52.6 %
Activity after treatment	2408.3 $\pm$ 377.17 t = 6.31	2848.8 $\pm$ 659.5 t = 6.68
Moderate:	(n = 2)	
Before treatment	882.33 $\pm$ 173.78	
Mean %	37.0 %	
Activity after treatment	1914.50 $\pm$ 219.9 t = 5.20	
Severe:	(n = 14)	(n = 2)
Before treatment	161.79 $\pm$ 50.74	222.5 $\pm$ 17.68
Mean %	6.8%	7.6%
Activity after treatment	1621.2 $\pm$ 443.03 t = 8.68	2929.5 $\pm$ 833.68 t = 4.59

Cholinesterase level of the control group (n = 5)

X $\pm$ S.D = 2384.6 $\pm$ 653.52 UI

Table (7): Lines of treatment followed in patients with acute poisoning by Organophosphorus and Carbamate insecticides (n = 30) and degree of poisoning.

Lines of Treatment	Degree of Poisoning		
	Mild	Moderate	Severe
Respiratory Care	No need	Oxygen inhalation suction of secretion	Done , O ₂ inhalation suction of secretions, ventilator (n = 4)
Prevention of Absorption	- Emesis by syrup of Ipecac - Activated charcoal	- Gastric lavage by sod.bicarb. (5%) - Activated charcoal	- Gastric lavage by sod.bicarb. (5%) - Activated charcoal
IV Fluids (saline 0.9% +Dextrose 5%)	Given in some when indicated	Given to all	Given to all
Atropine Sulphate	18.8 $\pm$ 9.6 Amp.	21.5 $\pm$ 4.9 Amp.	30.4 $\pm$ 14.8 Amp.
Obidoxime* (Toxogonin)	Not indicated	1 - 2 ampoules	1 - 3 ampoules
Treatment of Pulmonary Oedema	—	—	Drugs given** when indicated

* Given to both Organophosphorus and Carbamate Insecticides.

** Dexamethazone , Frusemide , Aminophline & Aqueous penicillin.

In patients with CI poisoning (n = 11), the clinical manifestations were similar to OPI poisoning, where mild degree (n = 9) showed the same manifestations. No moderate degree of poisoning was encountered. Severe degree of poisoning (n = 2) showed both muscarinic and nicotinic manifestations and in one of them tremors all over the body were observed. All patients were conscious or confused.

Serum ChE Level on Admission and their Treatment:

OPI poisoning (Table 6)

In mild degree of poisoning the mean level of serum ChE on admission was 999.3 ± 83.64 UI, while after treatment the level significantly increased to 2408.3 ± 377.17 UI ($t=6.31$). The mean degree of activity of ChE in patients with mild degree of poisoning was 42.0% of the normal activity. On the other hand, the mean activity of ChE in moderate degree of poisoning was 37.0%, while in severe cases the activity was 6.8%. In general, there was a significant elevation of ChE activity after treatment in mild, moderate and severe degrees of poisoning ($t = 6.31, 5.20$ and 8.68 , respectively).

CI poisoning (Table 6)

In mild degree of poisoning the mean percent activity of ChE was 52.6% of the normal, while in severe degree of poisoning it was 7.6% of the normal. No moderate degree of poisoning was encountered. A significant increase in the level of serum ChE was observed after treatment in both mild and severe poisoning ($t = 6.68$ and 4.59 , respectively).

Lines of treatment

The lines of treatment adopted in OPI and CI were the same according to the degree of severity of poisoning (Table 7). The general lines of treatment as respiratory care, prevention of

absorption by emesis or gastric lavage, IV fluids (saline 0.9% and dextrose 5.0%) and atropine sulphate were given to all patients when indicated. The dose of atropine sulphate ranged from 8-17 ampoules with a mean of 18.8 ± 9.6 ampoules in mild degree of poisoning and 30.4 ± 14.8 ampoules in severe cases of poisoning. ChE reactivators as obidoxime chloride (Toxogonin) in ampoules of 250 mg was administered to moderate and severe degree of poisoning with OPI and are given also to severe degree of CI poisoning (within 3 hours after intake of the CI). Patients with pulmonary oedema and bronchospasm were treated with dexamethasone, aminophylline and antibiotics when indicated.

DISCUSSION

The incidence of acute human poisoning by insecticides is increasing. During the year 1989, acute poisoning by insecticides constituted 8.1% of the total patients with acute poisoning admitted to APC. In a previous study (8) done during the year 1985 in APC, acute poisoning by insecticides constituted 3.9% of the total patients with acute poisoning.

Out of the total 305 patients with acute insecticides poisoning, fifty patients who were admitted to the different hospitals belonging to Ministry of Health in Alexandria City were excluded from the study as no data were recorded in their medical sheets as age, sex, residence, circumstances of poisoning, lines of treatment adopted ... etc. These data are important as all cases of acute poisoning are of medicolegal implication (9).

The study showed that more patients were encountered in the age group 15-35 years (59.0%). This is the age of attempted suicide by

self poisoning (10) and accidental occupational exposure in agriculture during spraying or accidental poisoning through drinking water from a container previously used for insecticides storage (11). The second age group to be affected was children less than 5 years (13.1%). This is the age of accidental ingestion of these insecticides as they are widely present in the Egyptian homes to control pests and insects (12). Insecticides are usually present in unsafe sites which can be reached easily by young wildering children (13).

The majority of acute poisoning by insecticides were intentional (81.0%) which could be attributed to the easy availability of insecticides. Moreover, these insecticides are sheep.

A sample of thirty patients with OPI (n=19) and CI (n = 11) poisoning were studied. The mean age was 26 ± 8.31 years. As regards the type of insecticide responsible for acute poisoning still OPI were the commonly encountered (63.3%), especially diazinon, dimethoate and methamedophos. On the other hand, CI were responsible for 36.7% of acute poisoning especially aldicarb.

Poisoning by insecticides was classified into mild, moderate and severe degrees of poisoning according to the clinical manifestations and level of serum ChE (4). Severe degree of poisoning was more likely to be among females than males (71.4% compared to 37.5%). This could be attributed to the fact that all females in the present study were intentionally self poisoned. They took the insecticide in large amounts, the act is committed in secret, so most of these patients presented late after the discovery of the act.

The clinical presentation of patients with mild degree of poisoning was the same in OPI and CI poisoning. In moderate degree of poisoning

muscarinic effects still present added to its nicotinic manifestations in the form of muscle fasciculations in the eyelids with generalized muscle weakness and inability to walk. Severe muscle weakness and inability to walk. Severe degree of poisoning was reported in 16 patients, 14 with OPI and 2 with CI. Two patients presented with tachycardia (pulse 130/minute) and hypertension instead of bradycardia and hypotension. This could be due to stimulation of the sympathetic ganglion by the abundant ACh (14).

Serum ChE Activity and Severity of Poisoning:

In mild degree of poisoning by OPI, the mean serum ChE enzyme activity was significantly elevated after treatment than on admission ($t = 6.30$), although the level still does not reach the normal value. On the other hand, a significant elevation of serum ChE had occurred after treatment of CI poisoning ($t = 6.88$) and reach above the normal level. This marked increase in the ChE activity was described by Hayes (1982) (15) to be due to a rebound phenomenon. The mean serum ChE activity in mild poisoning by OPI was significantly more depressed than that in CI on admission and before treatment ($t = 2.45$). This finding indicates the more marked and rapid effect of OPI compared to the CI.

In severe degree of poisoning, serum ChE activity was significantly depressed in OPI than CI on admission ($t=3.29$). After treatment a significant elevation in serum ChE level occurred in OPI and CI ($t=8.68$ and 4.59 , respectively). It was reported that normalization of ChE enzyme take place within 4-6 weeks (16).

The study showed that in severe degree of poisoning by CI, the ChE activity after treatment rises beyond the normal level. This could be attributed to the spontaneous reactivation of the enzyme combined with the reactivation caused

by early administration of ChE reactivator, i.e. obidoxime (Toxogonin).

Lines of Treatment:

Treatment of patients with acute OPI and CI toxicity consists of general supportive care with particular emphasis on maintaining a clear patent air way and supporting respiration, removal of secretions and oxygen administration whenever cyanosis is present. Prevention of absorption through either emesis by syrup of ipecac in mild degree of poisoning or gastric lavage by sodium bicarbonate (5%) in moderate and severe grades of poisoning. Powdered activated charcoal was left in the stomach after emesis or gastric lavage. IV fluids (saline 0.9% and dextrose 5.0%) were administered to support circulation.

The specific treatment by atropine sulphate was the main stay of therapy in both OPI and CI poisoning. It antagonizes the cholinergic effects by blocking muscarinic receptors (17, 18). The mean dose of atropine sulphate given in the present study varies from 18.8 ± 9.6 ampoules in mild poisoning and up to 30.4 ± 14.8 ampoules in severe poisoning.

In the present study, atropine sulphate was given to all patients (n=30) and even to those suffering tachycardia but with caution (the dose is less with long interval in between doses).

The study showed that the clinical manifestations in moderate and severe grades of OPI and CI poisoning were more or less similar. It is difficult to differentiate clinically between them especially if the insecticide responsible is unknown and if no available laboratory facilities for determination of serum ChE level. In this situation, ChE reactivator as obidoxime chloride (Toxogonin) is administered and no

complications are observed. This line of treatment is also recommended by Haddad and Winchester (1990) (19) , although ChE reactivators were contraindicated by others (17 , 18) in CI poisoning.

RECOMMENDATIONS:

1. Early administration of ChE reactivators in CI poisoning will help in prompt reactivation of the inhibited enzyme , and amelioration of patient's clinical state.
2. Increasing public awareness about the safe and careful use of insecticides is highly recommended.
3. Programs in prevention of poisoning by insecticides are to be encouraged for personnel handling these insecticides and in homes for parents having young children.
4. All noxious and potentially toxic substances like insecticides that are kept in home must be stored in child proof containers and in locked cabinets to be out of reach of children.
5. Special attention should be paid to the medical records of acutely poisoning patients as acute poisoning in such events is of medicolegal importance.

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الملخص العربى

الأعراض الاكلينيكية للتسمم الحاد بالمبيدات الحشرية المشكلة لعمل الكولين استريز

أ.د. ليلي عبد المجيد ، أ.د. السيد محمود سالم

أجريت هذه الدراسة لمعرفة مشكلة التسمم الحاد بالمبيدات الحشرية في مدينة الاسكندرية خلال عام ١٩٨٩. كذلك تم أخذ عينة من هؤلاء المرضى (العدد = ٣٠) الذين أدخلوا مركز الاسكندرية للسموم وتم دراستهم من حيث السن - الجنس - ظروف التسمم - مدة أعراض التسمم - مستوى انزيم الكولين استريز في مصل الدم عند الدخول وبعد استكمال العلاج ، كذلك طرق العلاج.

ولقد أظهر البحث الآتى:

- كوت حالات المبيدات الحشرية ٣٠٥ حالة (٨١%) من مجموع حالات التسمم الحاد التي أدخلت مركز الاسكندرية للسموم خلال عام ١٩٨٩. وكان عدد هذه الحالات أكثر في شهور أغسطس - سبتمبر - أكتوبر ومايو. معظم الحالات حاولوا الانتحار بالمبيدات الحشرية (٨١%) أما التسمم العرضى بالمبيدات سواء عن طريق الأخذ بالفم أو الرش فكان ١٩% من مجموع الحالات.
 - بدراسة الثلاثون مريضا وجد أن المبيدات الحشرية العضوية الفسفورية كوت ١٩ حالة (٦٣.٣%) أما التسمم بالمبيدات الكرباماتية فكانت ١١ حالة (٣٦.٧%).
 - كون التسمم الحاد البسيط ٤٠% والمتوسط ٦.٧% أما التسمم الحاد الشديد فكان ٥٣.٣%.
 - أظهر مستوى الكولين استريز في مصل الدم ارتفاعا ذودلالة احصائية معنوية بعد العلاج في جميع الحالات البسيطة والمتوسطة والشديدة.
 - اتبع نظام ثابت في علاج الحالات سواء كانت بالمبيدات العضوية الفسفورية أو الكرباماتية وقد أعطى المضاد الفسيولوجى (التوكسوجونين) في الحالات المحسوسة والشديدة في المبيدات الفسفورية بينما أعطى في الحالات الشديدة فقط في المركبات الكرباماتية خلال ثلاث ساعات من حدوث التسمم وحدث تحسن ملحوظ في هذه الحالات ولم ينتج أى أضرار.
 - وقد أوصى الباحثان بالآتى:
- ١- ضرورة عمل دراسة على المستوى القومى لمعرفة حجم مشكلة التسمم الحاد بالمبيدات الحشرية واتخاذ الخطوات الايجابية لمجابهتها.
 - ٢- تعريف المواطنين باخطار الاستعمال السيئ للمبيدات الحشرية حتى لاتقع حوادث عرضية للتسمم بها مع امكانية منع حدوثها.
 - ٣- استعمال منقطات الكولين استريز في حالات التسمم الشديد بالمركبات الكرباماتية حيث أظهر تحسنا سريعا في الحالة الاكلينيكية مع عدم ظهور أى أعراض جانبية.