31. AGGRESSIVE ATROPINIZATION AND PROLONGED ADMINISTRATION OF OXIMES IN THE TREATMENT OF SEVERE POISONING WITH ORGANOPHOSPHOROUS COMPOUNDS

Tonci Vuinac, Ingrid Bosan-Kilibarda and Vlasta Jasprica-Hrelec
Zagreb Emergency Medical Centre, Djordjiceva 26, HR-10000 Zagreb, Croatia,
Tel. + 385 1 3025 917, e-mail: tonci.vuinac@usa.net

INTRODUCTION

Organophosphorus compounds (OP) are among the most toxic agents known today. As insecticides, they are indispensable in the production and storage of food, but as warfare agents they present a constant threat and danger. They cause more than 20.000 deaths and more than 3 million poisonings per year, mostly in underdeveloped countries. The most serious poisonings are usually intentional or accidental, and without adequate and specific treatment always have lethal outcome.

Essential point of specific treatment of OP poisoning is rapid atropinization with high doses of atropine, adequate continuation of atropine administration and gradual withdrawal, because of potentially threatening rebound effect. Early and adequate administration of oximes is an integral part of therapy, necessary for faster recovery and it also prevents so-called "intermediate syndrome" i.e. sudden respiratory arrest during the third or fourth day of poisoning.

RESULTS

During the 15-year period (1978-1992) the Emergency Medical Centre in Zagreb treated a total of 216.093 patients in a population of about one million inhabitants of Zagreb. There were 14.752 cases of poisoning, and 664 (4,5 of all poisonings) were pesticide poisonings. Among them 254 (38,2%) were caused by OP insecticides and 126 (49,6%) were suicide attempts. All severe poisonings were due to ingestion, and 83% of ingestions were suicidal. The highest dose ingested was 350 ml of concentrated insecticide (quinalphos and phosalon) in two cases. In 28% of cases there was a concomitant ingestion of alcohol (Brandy). In 72% of cases the victims were women and family or marital problems resulted with poisoning attempt. The most common cause of accidental OP poisoning was a mix-up with alcohol and usually occurred when the victim was already drunk. Poisoning in children younger than 14 years are not included because they were treated at the paediatrics clinic. In all cases we performed gastric lavage with activated charcoal administration, suction of bronchial secretion and the majority of patients needed intubations and artificial respiration for 30 minutes to as long as 24 hours, because of respiratory depression or arrest. In several cases excessive atropinization required decreasing dosage of atropine and diazepam and it usually occurred during a first few days of therapy. There were no cases of late respiratory arrest i.e. the so-called "intermediate syndrome", and we believe that this is the result of prolonged administration of oximes. There was one case of respiratory depression that started the first day of poisoning and lasted for 30 days, but with assisted ventilation the patient recovered without sequelae. It is well known that, contrary to OP insecticides, the OP warfare agents have an extremely quick onset of action and the survival depends on momentarily application of antidotes by auto-injectors. Because of the rapid metabolism of all OP warfare agents the treatment usually does not require massive doses of atropine (usually 4-25 mg) but because of fast "ageing" syndrome the reactivation of cholinesterase is very controversial.

Since 1980, in all serious poisonings we have used the method of aggressive atropinization initially 10-mg i.v. followed by 50-100 mg of atropine in the first hour of

treatment to maximally 130 mg during the first 24 hours. Average total doses of atropine were 50-650 mg, and the highest total dose of 780 mg in 10 days was administered during successful treatment of a 62-year female following a suicidal ingestion of 350 ml of concentrated quinalphos. We also know that in case of serious OP poisoning treated in city of Split a total dose of 3100 mg of atropine was used and the patient needed artificial ventilation for 40 days. Before 1981 we had three lethal outcomes. Two women, 89 and 90 years old died 8 days after ingestion of chlorpiryphos and phosalon, but post mortem toxicological findings were not available. A 48-year old men with a history of cardiac disease and severe arrhythmia's and VES after ingestion of phosalon, died soon after he was transferred to cardiology clinics probably because of abrupt cessation of atropine administration. None of those three cases was especially severe from the toxicological point of view. After 1981 we had no further deaths caused by OP poisoning. Since summer of 1993 the Toxicology Unit of Emergency Medical Center in Zagreb was closed, probably for financial reasons, and since then all adult poisonings are treated in 5 internal medicine departments in the city hospitals and clinics.

CONCLUSION

Serious OP poisoning is always directly life threatening. Prompt and accurate diagnosis, emergency resuscitation procedures and aggressive therapy reduce lethality to minimal. Priorities are cleaning and suction of airways, intubation, assisted ventilation and oxygenation, which should prevent cyanosis and diminish the risk of bronchospasm. Basic condition of survival is high initial dose of atropine and in cardiac arrest atropine should be introduced into circulation by means of persistent cardiac massage. Early and adequate administration of cholinesterase reactivators, oximes, contributes to faster recovery and helps avoiding the danger of late respiratory paralysis i.e. the so-called "intermediate syndrome".

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TABLES

Table 1 Pesticides and organophosphorous insecticide poisonings

Table 2 A case of suicidal poisoning with 100 mg quinalphos, treated with pralidoxime (male, 23years)

Table 3 A case of suicidal poisoning with 120 mg quinalphos, treated with hi-6 (male, 31 years) End of Example.

Table 1: Pesticides and organophosphorous insecticide poisonings (1978 - 1992) Toxicology unit/EMC Zagreb

Year	*Poisonings*	*Pesticides*	*%*	*Pest./ Suicides*	*%*	*OFI*	*OFI/Pest.[%]*	*OFI/Suicides*	*%*
1978	737	23	3,1	10	43,5	11	47,8	6	54,5
1979	786	28	3,6	10	35.7	11	39,3	5	45.5
1980	684	37	5,4	14	37,8	13	35,1	6	46.2
1981	902	44	4,9	16	36,4	20	45,5	6	30.0
1982	1009	50	5,0	19	38,0	24	48.0	8	33,3
1983	984	48	4,9	19	39,6	19	39,6	9	47,4
1984	1052	51	4,8	19	37,3	18	35,3	9	50,0
1985	988	46	4,7	18	39,1	19	41,3	9	47,4
1986	1131	51	4,5	19	37,3	19	37,3	9	47,4
1987	1116	46	4,1	19	41,3	15	32,6	8	53,3
1988	1110	51	4,6	20	39,2	19	37,3	8	42,1
1989	1108	70	6,3	38	54,3	24	34,3	16	66,7
1990	1025	48	4,7	22	45,8	14	29,2	10	71,4
1991	1042	35	3,4	13	37,1	16	45,7	10	62,5
1992	1078	36	3,3	14	38,9	12	33,3	7	58,3
Total:	**14752**	**664**	**4,5**	**270**	**40,7**	**254**	**38,3**	**126**	**49,6**

Table 2: A case of suicidal poisoning with 120 mg Quinalphos, treated with HI-6 (male, 31 years)

Time	*Atropine [mg]*	*Pralidoxime [g]*	*Diazepam [mg]*	*A-ChE*	*%*	*S-ChE*	*%*
1st hour	38	2,0	20	561	4,3	238	4,8
1st day	116	2,5	40	564	4,3		
2nd day	34	2,5		361	2.8	413	8,3
3rd day	21	2,0		513	3.9	352	7.0
4th day	17	2,0		631	4,9	344	6.9
5th day	15	2,0		2168	16,7	430	8,6
6th day	12	4 x 0,5 or.		988	7.6	438	8.8
7th day	12	-"-		1422	10.9	477	9,5
8th day	10	-"-		2750	21,2	626	12,5
9th day	8	-"-					
10th day	6	-"-					
14th day	4	-"-					
16th day	1	2 x 0.5 or.		3758	28.9	1110	22.2
Total:	**256**	**25**	**40**	**3758**		**1110**	

Table 3: A case of suicidal poisoning with 100 mg Quinalphos, treated with Pralidoxime (male, 23years)

Time	*Atropine [mg]*	*HI-6 [g]*	*Diazepam [mg]*	*A-ChE*	*%*	*C-ChE*	*%*
1st hour	30	0,5 im.	20	430	3,3		
12th hour	100	1 im.	20	930	7,2		
1st day	130	2 im.	50	4000	30,8	450	9,0
2nd day	23	2 im.		6500	50,0		
3rd day	20	2 im.					
4th day	18			9000	69,2		
5th day	10						
6th day	6						
10th day	1			11800	88,0	2200	44,0
Total:	**216**	**6**	**50**				