CONTINUOUS ATROPINE INFUSION IN THE MANAGEMENT OF ORGANOPHOSPHORUS INSECTICIDE POISONING

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INTRODUCTION

The availability of insecticides containing organophosphorus for use in the home and the garden, makes them an easy source for poisoning in suicide attempts. The annual returns of Medical Unit III, shows the increase of such suicide attempts by the ingestion of this product (Table I).

There is no specific antidote to organophosphorus compounds, which act as a cholinesterase inhibitor through its phosphorylation of the enzyme active centre. This results in an accumulation of acetyl-choline, which causes the clinical picture due to organophosphorus poisoning. The antidote to the effects of excess acetyl-choline is atropine which has been given intermittently in varying doses as the need arises (Barr, 1964). This requires close supervision of patients and early recognition of the effects of acetyl-choline excess. In the treatment of this series of patients, a continuous infusion of atropine was used. This method of treatment we felt, would require less supervision and free the ward personnel to continue with the care of other patients.

TABLE I

Shows the sex distribution, results of treatment and the total admissions of organophosphorus insecticide poisoning to the unit for the years 1968, 1969 before and after commencement of treatment of this series with intravenous atropine, and up to May 1970.

Year		Sex		Result		Total Admission
		Male	Female	Alive	Died	
1968		—	1	—	1	1
1969	Before	1	1	—	2	—
	After	—	4	4	—	—
1970 (May)		—	5	4	1	5

MATERIAL AND METHOD

After the unsuccessful management of the first two admissions of organophosphorus insecticide poisoning in the Unit in 1969, it was decided to review the method of management of this problem. The method devised, we felt, had to be simple and had basically to ensure that the patient was adequately "atropinized". This was necessitated by the fact that, the care of such patients was in an open ward. The staff was that employed in the routine management of in-patients.

It was decided to use continuous intravenous atropine infusion diluted into dextrose or saline as a basis of management and the level of adequate "atropinization" was to be essentially one of "over-atropinization" or near atropine toxicity. This level was clinically arrived at if it was seen that (1) the skin of the patient was warm and flushed; (2) the pulse rate was maintained at a steady 120 per minute; (3) the pupils were widely dilated; (4) there was absence of muscle weakness and (5) the patient was conscious and alert. In addition all patients were to have a tracheostomy.

On admission, the first essential was to clear the patient's airway with a simple aspiration of all secretions and vomitus from the mouth and pharynx. Endotracheal intubation was necessary if there was cyanosis. Early tracheostomy was a routine to ensure adequate oxygenation and also to envisage the necessity of the use of assisted respiration.

The routine adopted was that all atropine was given intravenously. In the mild cases atropine was to be given immediately, however, in the more severely poisoned patients, it was necessary to correct the anoxaemia, before atropine was administered. The first dose of atropine was 3·6 mgm. i.e. 6 cc. of a gr. 1/100 solution and was repeated at 5 to 10 minute intervals till it was observed that the patient was mildly "atropinized". Continuation of "atropinization" was then proceeded with dilutions of 12 mgm. or 18 mgm. of atropine in a pint. Supplements of atropine were given in doses of 1·2 mgm. to 3·6 mgm. intra-

venously or the quantity of atropine in the drip increased and administered till a level of clinical "over-atropinization" was achieved. Intravenous fluids were limited to four pints in the first day to avoid over-hydration and aggravation of pulmonary oedema.

The first dose of 1 gramme of 2 P.A.M. (2 pyridine aldoxamine methiodide) administered intravenously was given as soon as possible, and a second dose of ½ gramme was repeated half an hour later.

Stomach washout with small volumes of 2% sodium bicarbonate (not exceeding 300 cc.) was proceeded with after the establishment of the airway and adequate "atropinization". All clothing was removed, and the patient bathed. Blood levels of cholinesterase were estimated. Antibiotics, penicillin and streptomycin, were given as a routine to prevent chest infection.

Milk feeds were given via a ryles tube only when a stable state of control of the toxicity was achieved. Strict intake-output fluid measures were adopted. Intravenous fluids were raised to 6 pints after the first 24 hours and the dosage of atropine added to each pint was titrated to the needs of the individual patient. The quantity of atropine was reduced according to the clinical response of the patient and when the level of serum cholinesterase showed a rising trend.

RESULTS

The present study consists of nine patients seen from the period of 10.7.69 to 16.6.70 (Table II). Most of the patients presented early after the ingestion of the organophosphorus insecticide. The clinical effects attributable to the acetyl-choline excess of the organophosphorus toxicity were mild and only four patients presented with drowsiness and none with pulmonary oedema (Table III). However, the cholinesterase level at the time of admission i.e. on the first morning showed that 4 were below 20 units and 1 below 30 units against a normal of 95-177 Biggs units (Tan, 1965) (Table II).

TABLE II

Shows the common symptoms on admission of the series.

Presenting Symptoms	Total
Drowsiness - - -	4
Restlessness - - -	2
Muscle weakness - -	2
Giddiness - - -	1
Headache - - -	1

The regime of "atropinization" was as stated previously. It was carefully titrated to the individual patient to attain the satisfactory level of "atropinization". This necessitated the atropine dosages to be increased or supplemented with bolus of 1·2 mgm. to 3·6 mgm. of atropine to be given intravenously at 5 to 10 minute intervals initially. The dose of atropine given per day, therefore varied according to the requirements of the individual patient, and a high dose of 368 mgm. per day was given in patient A (Table IV). It can

TABLE III

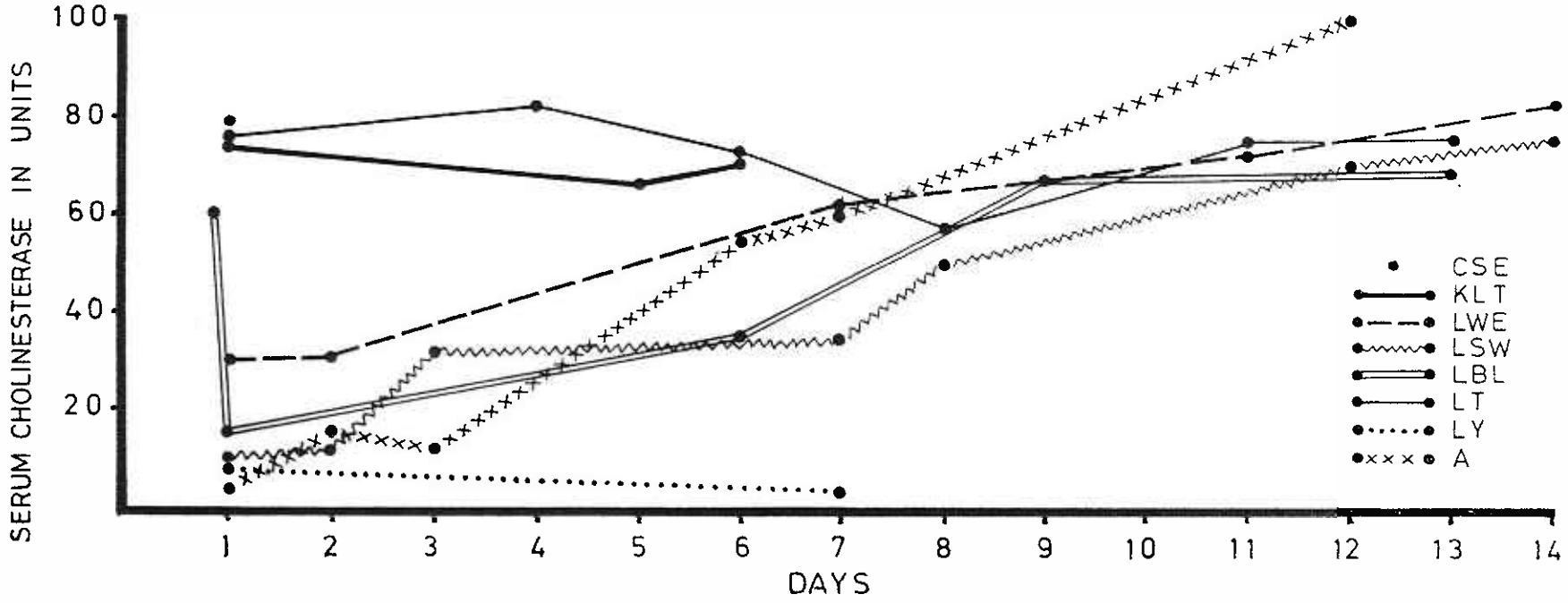
Shows the age, sex, date of admission, duration of treatment, cholinesterase level on the morning of admission, type of organophosphorus, and the results of treatment.

Name	Age	Sex	Date of Admission	Cholinesterase Level	Duration of Treatment in Days	Type of Organophosphorus	Result
1. Y.S.N.	18	F	10.7.69	11 units	14	Dimethyl Dichloro-phenyl phosphate	Alive
2. A.	18	F	10.9.69	5 units	8	Dimethyl Dichloro-phenyl phosphate	Alive
3. C.S.E.	31	F	16.12.69	80 units	4	Diazinon	Alive
4. K.L.T.	18	F	18.12.69	74 units	4	Malathion	Alive
5. L.Y.	71	F	10.2.70	10 units	7	Diazinon	Died
6. L.B.L.	18	F	19.2.70	15 units	14	Diazinon	Alive
7. L.T.	22	F	8.5.70	77 units	14	Malathion	Alive
8. N.S.K.	36	F	10.5.70	144 units	Nil	Malathion	Alive
9. L.W.E.	15	F	16.6.70	20 units	12	? Diazinon	Alive

TABLE IV

Shows the total atrophine (in mgms.) required per day for the individual patients. the duration of treatment and the corresponding level of serum cholinesterase.

	TOTAL ATROPINE REQUIRED PER DAY													
DAY	0	1	2	3	4	5	6	7	8	9	10	11	12	13
LYS	40	60	50	48	110	102	72	72	72	72	54	54	54	54
A		103	368	173	188	240	156	96	120	7				
CSE	35	48	36	36										
KLT		16	36	66	36	24								
L Y		30	216	150	312	300	300	300						
L BL		74	90	36	8	13	12	13	20	30	45	45	9	
LT		24	24	24	26	24	24	24	30	30				
LWE		24	44	44	44	44	44	44	44	44	28	24	4	



be seen from Table IV, that there was a tendency to probably use larger total daily atropine doses in the treatment of the earlier patients e.g. L.Y.S. A., L.Y. than the later patients. This may be attributed to the increased confidence and familairity of the staff with the use of this regime in the management and treatment of organophosphorus poisoning. 2 P.A.M. was used as a routine in all patients and fresh blood transfusion was given in 5 patients.

Tracheostomy was performed in 8 patients and a Portex tracheostomy tube with cuff was used in all cases. Fortunately no assisted respiration was required. This can be attributed to early admission for treatment and also adequate and vigorous "atropinization". Unfortunately, the use of routine tracheostomy was not without its complications even with prophylactic antibiotics for chest infection. Two patients developed pseudomonas pyocyanea septicaemia through infection of the tracheostomy wound. One patient L.B.L. had osteomyletis of the clavicle in addition to the septicaemia which fortunately responded to a course of Trimethoprime—Sulphamethoxazole. The other patient L.Y. was a 72 year old with untreated diabetes mellitus. She unfortunately succumbed to the infection inspite of a host of antibiotics—kanamycin, cephaloridine, and ampicillin. The Portex tracheostomy tubes were in addition found to be a source of irritation to the tracheal mucosa. This resulted in many occasions of inspissation of tracheal secretions in the tube resulting in respiratory obstruction. The danger of anoxaemia had to be prevented as large doses of atropine were being used.

Family disputes, disagreement with boy friends and disappointment with school examination success constituted the major reasons for the suicide attempts. The overall mortality in the series was 11%. This was in a 72 year old woman L.Y. She was the most determined of the suicides, having expressed the desire to die after a family quarrel. She was judged to have consumed the greatest volume of a locally prepared organophosphorus insecticide. In addition, she had untreated diabetes mellitus. She succumbed to a Pseudomonas Pyocyanea septicaemia. At the time of death, the level of her serum cholinesterase was only 3 units inspite of 7 days of continuous treatment.

DISCUSSION

That there is an upward trend in suicidal poisoning by the ingestion of organophosphorus insecticide in Singapore is shown by post-mortem studies of suicides (Chao, 1970). After the initial two deaths due to this cause in the unit in early 1969, it was correctly predicted that poisoning with organophosphorus insecticides would increase with its easy availibility. In 1968, there was only one case of such poisoning, however in 1969 and up to May 1970, there has been a considerable increase in incidence (Table I). Trivial problems, such as disputes within the family or disagreement with boy friends or insufficient success with examinations prompted these suicide attempts. The younger aged patients formed the majority (Table II).

The pharmacology of organophosphorus poisoning has been thoroughly reviewed by Barr (1964). Essentially, it combines with cholinesterase at its esteratic site and this inhibits its physiological action which is to split acetyl-choline into choline and acetic acid. The organophosphorus compounds used in the suicide attempts were readily available and sold for household use as an insecticide spray or as a powder to be reconstituted and used as a spray. The patients were all females and except for one aged 72, were all in the younger aged group. This is in contrast to the figures given for the deaths from organophosphorus insecticide in Singapore from 1960-1969, which showed a predominence of male to females in the ratio of 3:2 (Chao, 1970).

In the treatment of organophosphorus poisoning, atropine has to be given in large doses. We decided that the use of continuous intravenous atropine would ensure that the patients received adequate therapy and would not be neglected in this aspect of the treatment when other emergencies arose in the ward. The quantity of atropine used in each patient was individualized to her needs achieving a level of "over-atropinization" (Redaksie, 1967). It is important to note that restlessness and mental confusion can be the result either of insufficient or excessive atropine. However, as Barr (1964) has pointed out, when insufficient atropine is being administered, restlessness is accompanied by severe weakness of muscles, whereas excessive atropine administered is accompanied by normal muscle power. Supplements of atropine were used when necessary to achieve this level of treatment with additional bolus of atropine of 1·2 mgm., 2·4 mgm. or 3·6 mgm. We felt it was necessary to achieve this clinical level of "over-atropinization" as we could then be certain that the patients were sufficiently treated. It was not possible nor necessary, to continually measure the levels of cholinesterase as there may be little co-relation between the enzyme levels and clinical signs (Barr, 1964). The strength of the atropine was reduced according to the patient's clinical response as the days of therapy progressed.

The duration of therapy in the series varied from 4 days to 16 days. (Table II). Attention is drawn to the patient L.Y. whose level of serum cholinesterase at the 7th day of treatment was only 3 units, and she was alert and conscious with adequate "atropinization" till she unfortunately succumber to a septicaemia.

2 pyridine aldoxamine methiodide (2 P.A.M.) was used routinely in all patients. The benefits of 2 P.A.M. have been described by Barr (1964) and essentially it has three main actions of:—

1. Reactivation of cholinesterase inhibited by phosphorylation.
2. Inactivation of the organophosphorus compound.
3. In excessive dosages, inhibition of cholinesterase.

More recent work has resulted in the discovery of a reactivator of cholinesterase which appears to have certain advantages over 2 P.A.M. and with greater beneficial effects. This new compound has been given the generic name of toxogonin and might be termed another antidote to organophosphorus poisoning, in that it has the ability to pass the blood brain barrier which 2 P.A.M. does not possess or does so to only a small degree (Steyn, 1966; Dean and Coxon, 1967). Unfortunately, this product was not available for use here.

Routine antibiotic cover of Penicillin and Streptomycin was given to all patients to prevent intercurrent chest infection which could lead to anoxaemia predisposing the heart to fatal ventricular fribrillation in the presence of the large doses of atropine used, (Durham and Hayes, 1962). Inspite of this antibiotic therapy, two patients developed pseudomonas pyocyanea septicaemia resulting in one death. The other fortunately responded to a course of Trimethoprine-Sulphamethoxazole in spite of the complication of osteomyelitis from this septicaemia. Tracheostomy was a routine in all the patients except one. This was deemed necessary in all cases to ensure adequate oxygenation and facilitate clearance of bronchial secretions during therapy. A cuffed Portex tracheostomy tube was used as a prophylactic measure in case assisted respiration was required. This tube was unfortunately very prone to be obstructed by inspissated mucus and blood thus endangering the patient, and required to be frequently changed.

Fresh blood transfusion was given in five of the patients. It was hoped that the infusion of fresh blood would increase the level of serum cholinesterase. Only phenobarbitone was used for sedation when it was required and phenothiazine compounds avoided as they tend to aggravate the cholinesterase deficiency. Organophosphorus compounds have been found to be neutralized in alkaline solutions and hence a sodium bicarbonate solution was used in the stomach washout. Small volumes of the solution were used at a time to prevent washing of organophosphorus into the duodenum.

Only one patient in the series of nine died but then of septicaemia (11% mortality). She had an untreated diabetes mellitus and was also judged to have swallowed the largest volume of a common locally manufactured insecticide. There was no deterioration of the clinical state of the patients once treatment was started. This is attributed to conscientious care of the patients and a thorough knowledge of the clinical picture of organophosphorus insecticide poisoning. Notwithstanding, all the bed-side care, we feel that it is the continuous "atropinization" of our patients that prevented any deterioration of the clinical state of the patients from occuring. We would, without hesitation, recommend this regime of treatment in the management of organophosphorus poisoning.

SUMMARY

The increasing incidence of organophosphorus insecticide poisoning and its treatment with large doses of atropine given continuously via drip infusion are emphasised. This method of treatment is essentially simple to manage and basically it satisfies the aim of ensuring that the patient is continuously receiving an adequate dose of atropine. Only one patient in the series died (11% mortality) of a complication of pseudomonas pyocyanea septicaemia.

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