ORGANOPHOSPHATE POISONING: A MALAYSIAN INTENSIVE CARE EXPERIENCE OF ONE HUNDRED CASES

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SUMMARY

From 1970 to 1984, 100 patients suffering from organophosphate poisoning were treated in the Intensive Care Unit at the University Hospital. These patients developed signs and symptoms of cholinergic over-activity and were treated with continuous intravenous atropine.[1] *Many of the patients also developed Acute Respiratory Failure, which necessitated ventilatory support in the form of intermittent positive pressure ventilation.*[2] *Other measures included the use of inotropes and nutritional support.*[3] *Daily estimation of serum cholinesterase levels*[2] *were useful in assessing degree of recovery of the patients from the effects of the organophosphates.*

INTRODUCTION

The toxic properties of organophosphate compounds were identified in the early 1930's. Their initial use was as chemical warfare agents by the Germans. In the early 1950's, further study of the toxicology of organophosphates led to their wide use as pesticides. In Malaysia, organophosphate insecticides are freely available, and are widely used in plantations and in the homes. As a result, these highly toxic compounds are often ingested in suicidal attempts.

From 1970 to October 1982, there were 152 cases of all types of poisoning in the Intensive Care Unit, University Hospital, Kuala Lumpur. 100 of these cases (65.7%) were due to organophosphate poisoning (Table I). This paper is a retrospective study of these cases of organophosphate poisoning.

PATIENTS

The average age of the patients was 19.2 years, with an age range of three – 54 years. 88 were female. The racial distribution amongst the three main ethnic groups of West Malaysia showed a startling preponderance amongst the Indians (Table I). 98 patients attempted suicide by oral ingestion of insecticides. The other two patients developed organophosphate poisoning accidentally.[4] Seven patients succumbed, giving a case fatality rate of 7.0%.

From 1970 to 1974, there were 11 cases, of which four died, whilst from 1975 to October 1982, there were 89 cases with three deaths, giving case fatality rates of 36.4% and 3.4% respectively. Pralidoxime iodide (P-2-AM) was excluded in the treatment from 1975.[5-8]

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TABLE I
RACIAL AND SEX DISTRIBUTION OF 100 CASES OF ORGANOPHOSPHATE POISONING*

	Males	Females	Total
Indians	8	88	96
Chinese	3	0	3
Malays	0	0	0
Others	1	0	1
Total	12	88	100

* The cases were treated at the Intensive Care Unit, University Hospital between 1970 – October 1984; average age 19.2 years; range three – 54 years.

MANAGEMENT

Organophosphate insecticides emit a characteristic foul odour which can be detected on the patients, their clothings and vomitus. The symptoms are basically due to an accumulation of acetylcholine, resulting from inactivation of cholinesterases by the organophosphates. There is muscarinic overactivity with constriction of pupils, increased vagal tone leading to bradycardia and excessive sweating, stimulation of lacrimal, salivary, nasopharyngeal, bronchial and gastrointestinal secretion, bronchial spasm, increased gastrointestinal tract motility, and urinary bladder sphincter relaxation with detrussor contraction. There is nicotinic overactivity with initial muscle fasciculation followed by paralysis, and initial stimulation of sympathetic ganglia and adrenal glands followed by paralysis. The muscarinic symptoms are present in almost every case whilst both nicotinic and muscarinic overactivity are seen in the more severe cases of organophosphate poisoning.[9]

A stomach washout, preceded by endotracheal intubation when protective reflexes were depressed, was commenced as soon as possible. This was followed by an insertion of a Salem sump (Sherwood Medical Industries Inc., St. Louis, MO 63103) tube (a naso-gastric tube) and a continuous irrigation with Ringer's lactate solution commenced through the Salem sump, at a rate of 250 mls/hr to 100 mls/hr till the gastric effluent was clear and free of odour.

Atropinization was commenced with an initial bolus dose of 2 to 4 mg intravenously.[9] The 2mg dose was repeated when there was unsatisfactory clinical response with persistent bradycardia, sweatiness, constricted pupils and rales in the chest. A continuous infusion of atropine[1] was commenced to maintain pulse rates between 100 to 120 per minute, pupillary size of over 3 mm in diameter, and a warm dry skin. The infusion consisted of a solution of 20 – 50 mgs of atropine in 100 mls of Dextrose 5% in a 100 ml burette chamber. The drip rate was adjusted till the above criteria were reached, and then maintained at a steady rate. Progressive reduction of the drip rate was titrated with signs of clinical improvement and serum cholinesterase levels.

During atropinization, restlessnsss and hallucination in the patients were signs of atropine toxicity from over-atropinization. Reduction of atropine dosage within limits of its beneficial (anti-muscarinic) effects together with administration of regular intravenous diazepam were found to be helpful in these cases.

Sedation

Diazepam was the sedative of choice for all the patients,[9] many of whom were restless. It was also effective in those who were hallucinating from over-atropinization. All patients who were being ventilated were routinely given diazepam too, to help maintain artificial ventilation. The dosage was 0.1 mg/kg to 0.2 mg/kg given at four to six hourly intervals regularly. It was effective in most cases, except in one violently suicidal patient who had to be sedated with chlorpromazine.

TREATMENT OF ACUTE RESPIRATORY FAILURE, PREVENTION AND AMELIORATION OF THE ADULT RESPIRATORY DISTRESS SYNDROME (ARDS)

In severe cases of poisoning, when there were both nicotinic and muscarinic overactivity, there was severe respiratory distress[10] which is fatal if untreated. Early treatment with respiratory support

by artificial ventilation was mandatory and effective. The patients were ventilated using a volume-cycled ventilator, with tidal volumes calculated at 10 mls/kg at respiratory rates of 10 to 14 breaths a minute.[11] A positive end-expiratory pressure (PEEP) of 5 to 10 cm H_2O was used to maintain PaO_2 between 80 to 150 mm Hg; using inspired oxygen concentration gas profile improved. To help in the initial adjustment of the patient to the respirator, a non-depolarizing muscle relaxant was initially used, followed with diazepam sedation.

Several patients had developed the clinical picture of the Adult Respiratory Distress Syndrome (ARDS).[12,13] Subsequently, early use of positive end-expiratory pressure (PEEP) in the artificial ventlation of these patients was instituted.[14] Early cardiotonic support with dopamine (5 to 20 μg/kg/min) was also instituted to help maintain cardiovascular and renal functions.[15] Nutritional requirements[16] (25 to 50 cals/kg/24 hours) were met with intravenous hyperalimentation followed as soon as feasible by enteral hyperalimentation, with the return of normal bowel activity. Prophylactic antibiotics and glucocorticoid therapy[17,18] were administered in these patients. These multi-system supports were considered important modalities in the management of the ARDS.[3]

Daily serum cholinesterase estimation

Monitoring the trend in the enzyme levels was a useful prognostic guide (the red blood cell cholinesterase level was most significant). The usual trend in our patients showed a progressive fall initially (often to 0%) which steadied within 48–72 hours and then showed a rising trend.

From bitter, earlier experience we had seen that a relapse of life-threatening symptoms (respiratory inadequacy, for instance) could occur within 48–72 hours following improvement after the first 24 hours. The possible reason[1] is that initial mild poisoning can develop into severe, lethal poisoning as some of the compounds undergo conversion within the body into more potent inhibitors of cholinesterases during the first 72 hours (Parathion to Paraoxon and Malathion to Malaoxon).

Pralidoxime Iodide (2-formyl-methyl pyridinium iodide oxime or P-2-AM)

P-2-AM is commonly used in the management of organosphosphate poisoning. It is supposed to be of benefit by reactivating the phosphorylated cholinesterases, and by inactivating any free organophosphate compounds in the blood.[5] Since 1975 we had stopped using P-2-AM because studies in the department[6] had confirmed our clinical impression that P-2-AM therapy made no significant improvement in the outcome of the picture.

Under experimental conditions it had been shown[7] that whole blood acetylcholinesterase (ACHE) inhibited 100% by Parathion, Paraoxon, Methyl Parathion, Terracur and Sumioxon after two hours of incubation, could be reactivated by a pharmacological concentration of P-2-AM incubated for upto three hours. In this study however ACHE inhibited by Malathion and Tamaron was not reactivated at all by P-2-AM. What was more startling was that, with Tamaron, increasing the P-2-AM concentration produced increased inhibition of ACHE, possibly indicating that the phosphorylated oxime of Tamaron is a more potent inhibitor.

From the above, it could be said that although P-2-AM could inactivate some types of organophosphates, there was always the danger of producing and releasing more potent phosphorylated oximes with other organophosphates such as Tamaron and Surin.[8] Tamaron, Bidrin, Malathion with Malaoxon are commonly used organophosphate compounds in Malaysia. It had also been shown[6] that P-2-AM given early (within three to six hours of severe poisoning) led to no clinically apparent reactivation of cholinesterase which was supported by similar results in experimental conditions stimulating an *in vivo* biological system.

We have not used P-2-AM in the management of our cases since 1975. The nicotinic effects (eventually producing muscle paralysis) could be managed by respiratory supportive therapy until the effects wore off simultaneously taking measures to prevent the onset of ARDS.

PSYCHIATRIC MANAGEMENT

As almost all of our cases of organophosphate poisoning resulted from attempted suicide (98 out of 100), the psychiatrist was brought in to interview the patient as soon as the latter was communicable. The psychiatrist also advised us as to which ward the patient should be sent on discharge from the intensive care unit (ICU) – to the general medical ward or to the psychiatric ward, depending on the psychiatric assessment of any persisting suicidal tendency. Follow-up psychiatric care was also arranged.

DISCUSSION

Research work and interest in organophosphate poisoning carried out in our department has perhaps contributed to the high percentage of such cases sent to our intensive therapy ward for management (100 cases of organophosphate poisoning out of 152 cases of all poisonings – 65.79% during 1970 – October 1982).

The high incidence among young Indian females (88 out of 100 or 88%) is an interesting revelation. The easy availability of insecticides in the rubber estates among rubber tappers is presumed to be an important factor.

The low incidence of mortality (3.37%) during 1975 – October 1984 can be attributed to better organised facilities in our intensive therapy ward, more nursing personnel and more experience with such cases. We feel that aggressive supportive therapy with vigilant, alert ICU staff, particularly over the initial 48–72 hours is the key to successful management of patients with organophosphate poisoning.

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