SERUM PSEUDOCHOLINESTERASE ESTIMATION IN THE MANAGEMENT OF ORGANOPHOSPHATE POISONING CASES AND THE EFFECT OF PAM ON REGENERATING IT

T Saravanapavananthan

Department of Pharmacology
Faculty of Medicine
University of Jaffna
Jaffna, Sri Lanka

T Saravanapavananthan, MBBS (Ceylon), FFARCS (Lond), FFARCS (I), DA (Lond)
Senior Lecturer and Honorary Anaesthetist
General Hospital, Jaffna
Sri Lanka

SYNOPSIS

The serum pseudocholinesterase was estimated in organophosphate poisoning cases and found to be of value in the diagnosis and management of severe cases. In these patients the value was markedly below the low normal range and it took a long time to return to normal levels. It was also significantly reduced in the mild to moderately severe cases but less than in the severe cases. A normal value can be used as a test to exclude organophosphate poisoning.

It was also observed that the antidote Pralidoxime (PAM) had only slight or no effect in raising the serum pseudocholinesterase when estimations are done within the first 2 hours after I.V therapy.

INTRODUCTION

It has been observed that the incidence of organophosphate poisoning is still high in the primarily agricultural regions of northern Sri Lanka and some of them end fatally.

The physicians were faced with a problem when some patients who on admission appeared to have mild symptoms later developed serious complications. It was also noticed that some patients who were fit for discharge developed symptoms by about the eighth day. The reason for this is not known. In this study an attempt was also made to determine the effectiveness of PAM in regenerating serum pseudocholinesterase.

Hence a study of the serum pseudocholinesterase levels at various times during the course of the illness was undertaken.

METHOD

Twenty six cases of organophosphate poisoning admitted to the emergency unit of the General Hospital, Jaffna during the period October 1984 to January 1985 were studied.

The age distribution was mainly between 20—40 years, the extremes being 16 years and 67 years. There were 22 males and 5 females. The interval between the ingestion and admission to the nearest hospital was usually short ½—3 hrs. It was difficult to get particulars regarding the amount consumed.

All cases of suspected organophosphate poisoning were admitted to the emergency unit of the General Hospital, Jaffna for immediate treatment.

Treatment included suction of secretion when present, stomach wash in the case of ingestion of the poison, or washing the body with soap and water in the case of sprayers. Atropine (2 mg) and PAM (Pralidoxime) 1 g were administered I.V, when symptoms of poisoning were present. They were then assessed and initially severe cases who were suspected might need ventilation or cardiac monitoring were treated in the intensive care unit. Others were sent to the wards. Further doses of PAM and atropine were given as required. Most of them needed as much as 300 mg of atropine and PAM was repeated on the following days when twitching was present. When respiratory paralysis occurred positive pressure ventilation was instituted.

Blood for pseudocholinesterase estimation was taken from patients on admission and at intervals thereafter. Whenever PAM was given the estimation was done ½ hr, 1 hr, and 2 hrs after the I.V injection. Serum cholinesterase estimation was repeated on the 2nd day, and by the end of Ist week, 2nd week, and 3rd week.

The estimation was done by the De La Huega's method which gives a normal range of 2.2—5.2 KU/L. The value for our population was done on 10 volunteers mainly medical students and Table I shows the results. The dibucaine number to identify patients with atypical pseudocholinesterase was not done in these cases.

TABLE I: SERUM PSEUDOCHOLINESTERASE OF NORMAL SUBJECTS

Serial No.	Values
1	4.2 KU/L
2	3.8 KU/L
3	2.7 KU/L
4	2.8 KU/L
5	2.4 KU/L
6	2.8 KU/L
7	2.9 KU/L
8	2.4 KU/L
9	2.9 KU/L
10	3.5 KU/L

The means of 10 cases is 3.1 KU/L

Patients were grouped into 3 categories, depending on the presence or absence of certain symptoms and an arbitrary score was given for each symptom (Table II).

Table III shows the compounds used by the patients its form and route of poisoning.

TABLE II: GROUPING OF CASES WITH SCORES

Group I	Group II		Group III			
No symptoms	Mild symptoms		Severe symptoms		Complications	
	Giddiness	1	Secretions	3	Respiratory arrest	6
	Vomiting	1	Convulsions	4	Cardiac arrrest	6
	Miosis	2	Diarrhoea	4		
	Twitching	2	Pulm. oedema	4		
			Unconsciousness	4		

TABLE III: COMPOUND USED AND ROUTE OF POISONING

	No. of cases	Form	Route Ingestion	Injection	Spraying
Baytex	4	Liquid	4	—	—
Malathion	4	Powder	4	—	—
Tameron	4	Liquid	3	1	—
Monocrotophos	1	Liquid	1	—	—
Metasystox	1	Liquid	1	—	—
Masprax	1	Liquid	1	—	—
Runbug	5	Liquid	5	—	—
Eka-tox	1	Liuqid	1	—	—
Lebaycid	1	Liquid	1	—	—
Dimethoate	1	Liquid	1	—	—
Ecodex	2	Liquid	1	—	1
Polymax	1	Liquid	1	—	—

RESULTS

Table IV shows the severe cases who on admission had at least one of the severe symptoms or developed them later. All these patients had a pseudocholinesterase below 2 KU/L and most of them were below 1 KU/L. Nos 5, 10, and 7 were exceptions. Nos 5 and 10 although they had values below 1 KU/L had a low score of 8, but it was found that their serum esterase levels rose to the normal values quickly as shown in Table V. Case No 7 although he had a serum pseudocholinesterase level above 1 KU/L subsequently developed a respiratory arrest and died. This patient however on admission was found to be malnourished and an alcoholic, and terminally developed jaundice and a bleeding tendency. It is probable that other factors contributed to his fatal end or that he was a patient with atypical pseudocholinesterase. The mean pseudocholinesterase value for this group was 1.03 KU/L and the "t" value of this group compared with the volunteers was 7.3 which was in the highly significant range.

Table VI shows the mild-moderate group having a mean serum pseudocholinesterase of 2.1 KU/L and a "t" value of 4.9 indicating that the lowering was again significant.

Table VII shows six cases with no symptom but a history of contact with organophosphate with a mean serum pseudocholinesterase of 3.7 KU/L which is almost the same as the mean of the volunteers.

The correlation between the severity of the poisoning and the serum pseudocholinesterase is illustrated more obviously in Fig 1 when a graph is drawn against the score and the serum pseudocholinesterase.

Table VIII shows the effect of PAM on serum pseudocholinesterase. It is seen that there is either a slight increase or no increase in the level within the first 2 hours after the injection.

TABLE IV: SEVERE CASES

Serial No.	Score on admission	Final Score	Pseudo. on admission	Complication	Outcome	Days in Hospital	Substance
1	4	20	0.6 KU/L	R. arrest C. arrrest	Recovered	22	Baytex
2	10	14	0.7	R. arrrest	Recovered	8	Monocrotophos with alcohol
3	10	18	0.6	R. arrest C. arrest	Died	1	Malathion
4	5	14	0.7	R. arrest	Recovered	18	Baytex
5*	5	8	0.8	R. arrrest	Recoverd	7	Ekatox
6	8	8	1.8 (3rd day)	—	Recovered	9	Masprax
7*	10	18	1.6	R. arrest	Died	11	Metasystex
8	9	9	1.5	—	Recovered	10	Runbug
9	8	12	1.6	—	Recovered	12	Baytex
10*	4	8	0.6	—	Recovered	8	Tameron

x = 1.03 KU/L

TABLE V: TIME TAKEN FOR THE SERUM PSEUDOCHOLINESTERASE TO RETURN TO NORMAL LEVELS

Serial No	1st day	3rd day	1 week later	2 weeks	4 weeks
1	0.65 KU/L	—	1.1	2.3	
2	0.7	0.8	1.1	2.1	
3	0.64	0.8	0.85	1.0	2.3
10*	0.6	2.6		3.5	
5*	0.7	2.8			
12*	3.5	5.0			
15	2.0	3.0			

TABLE VI: MILD TO MODERATE CASES

Serial No.	Score on admission	Final Score	Pseudo. on admission	Complication	Outcome	Days in Hospital	Substance
11	2	2	1.2 KU/L	—	Recovered	6	Tameron injection
12	4	4	3.5 3rd day	—	Recovered	12	Baytex
13*	2	2	2.7	—	Recovered	4	Ecodex (Spray)
14	2	2	1.6	—	Recovered	8	Runbug
15	4	4	2.0	—	Recoverd	3	Dimethoate
16	5	5	2.5	—	Recovered	7	Malothion
17	4	4	2.7	—	Recovered	7	Labaycid
18	3	3	1.8	—	Recovered	7	Tameron
19	4	4	1.4	—	Recovered	3	Tameron with alcohol
20	2	2	1.7	—	Recovered	3	Ecodex (Spray)

x = 2.1 KU/L

TABLE VII: NO SYMPTOMS — GROUPS I

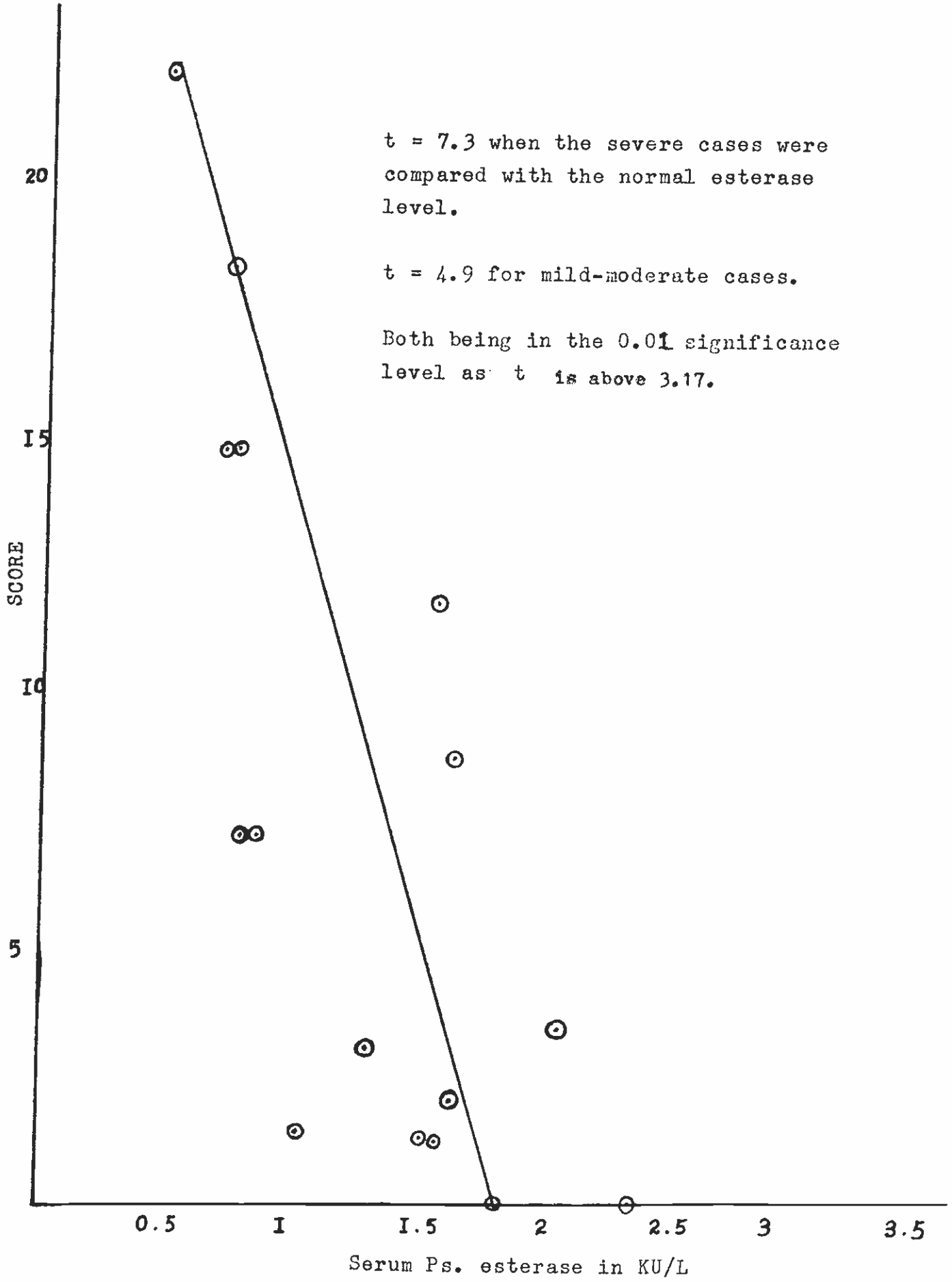
Serial No	Score	Pseudo. level on admission	Stay in hospital	Substance used
21	0	2. KU/L	4 days	Malathion
22	0	3.5	2	Malathion
23	0	5.3	3	Runbug
24	0	3.8	1	Spray
25	0	4.2	1	Runbug
26	0	3.5	1	Polymax

x = 3.1 KU/L

TABLE VIII: LEVELS AFTER PRALIDOXIME (PAM)

No	Before PAM	½ hr later	1 hr later	2nd hr
14	2.5 KU/L	2.7 KU/L	2.7 KU/L	3.1 KU/L
4	2.1	2.2	2.2	—
7	1.6	1.6	1.8	2.3
10	0.6	0.6	0.65	1.3
1	0.6	0.66	0.6	0.6
5	0.6	0.9	0.9	0.6
2	0.7	0.7	—	0.7
19	4.2	4.2	4.2	—

Figure 1: SHOWS A NEGATIVE CO-RELATION BETWEEN THE SEVERITY AND SERUM PSEUDOCHOLINESTERASE LEVEL



DISCUSSION

Pseudocholinesterase is an enzyme present in serum and its normal function is not known. It closely resembles acetylcholinesterase present at the nerve endings which is responsible for the break down of Acetylcholine. It is also found within red cells. Organophosphate compounds are anticholinesterase and initially the combination with cholinesterase is reversible. The cholinesterase at nerve endings cannot however be measured. Fortunately it is known that the serum pseudocholinesterase is also decreased (2) in cases of organophosphate poisoning whether by ingestion or following spraying.

Organophosphate insecticides came into popular use in the 1950's (1). Hazards have been observed by many workers (1,2,3,6,7,9,10) and much research has been done during the period 1950—1960. Pralidoxine (PAM) came into use as an antidote by about 1957 or 58. It acts by regenerating cholinesterase if given during the early stages of poisoning. Prior to this the physiological antidote, atropine was used as it blocks the actions of Acetylcholine (A.C) at the parasympathetic nerve endings. This however does not counteract the effects of A.C at the neuromuscular junction. Many patients were successfully treated but some succumbed to the poisoning (2,4,6). In 1958 Tatusji Namba, (1) reported 5 cases of organophosphate poisoning following spraying; Some of these cases though unconscious at the beginning, fully recovered following treatment with intravenous PAM alone.

In the present study it was noticed that although patients were treated with both PAM and atropine, some of them developed respiratory arrest and even died. These patients had however ingested the poison with a suicidal intent and would have consumed a large amount of the poison unlike sprayers.

The outcome depends largely on the nature and the amount of pesticide absorbed. It has been observed that ingestion of Baytex and Tameron produce a more serious course of illness than ingestion of Malathion. Therefore serum pseudocholinesterase level is useful in determining the severity of the case (1,3,5). In order to identify persons who can get repoisoning by about the 8th day; the serum pseudocholinesterase should be done by about the 6th day and if it is in the normal range patients could be discharged. The pseudocholinesterase rises slowly reaching normal levels by about 3—4 weeks while the acetyl cholinesterase in red cells rises to normal levels by 3 months and therefore reexposure should be avoided during this period (Table V).

Patients having low levels of the enzyme in serum or having the atypical pseudocholinesterase are susceptible to the depolarising muscle relaxant suxamethonium, miotics like physostigmine and ecothiapate and drugs like procaine which are hydrolysed by the serum enzymes (4).

It is interesting to note that the effect of PAM on red cell acetyl cholinesterase is different from that of serum cholinesterase in man and rabbits. In man the two are different and PAM produces a significant rise in red cell cholinesterase with only a transient rise in the serum enzyme (1). While in the rabbit both enzymes rise markedly as they are similar. This is in harmony with findings in the present study where PAM showed a slight increase or no increase in the serum pseudocholinesterase level. In vitro studies on serum pseudocholinesterase regeneration (1,8) also indicate that PAM produces only a slight increase in the enzyme level.

It is therefore important to know at least by animal experiments whether the acetyl cholinesterase at neuromuscular junctions rise, following the administration of PAM in order to evaluate the place of PAM in the therapy of organophosphate poisoning.

ACKNOWLEDGEMENTS

I wish to thank the academic and nursing staff of the emergency unit of the General Hospital, Jaffna, Sri Lanka for their kind co-operation, Mr T. Balasingham of the Pharmacology Department for all the technical assistance and Miss T. Ponnudurai for the secretarial work.

REFERENCES

1. Namba T, Hiraki K: PAM (Pyridine-2-Aldoxime Methiodide) therapy for alkylphosphate poisoning. JAMA 1958; 166: 1834-9.
2. Bidstrup PL: Poisoning by organic phosphorus insecticides. Br Med J 1950; 2: 548-51.
3. Pidetcha P. Laboratory Findings of Parathion Poisoning. Proceeding of the 1st Asian Pacific Conferences on Legal Medicine and Forensic Sciences; 1983; 252-5.
4. Edson EF: Emergencies in General Practice. Agricultural Pesticides. Br Med J 1955; 1: 841-4.
5. Anandadas JA, Nadesalingam K: Bedside estimation of cholinesterase in organophosphate poisoning. Jaffna Med J 1970; 10: 112-4.
6. Vethanayagam AVA: Folidol Poisoning. Ceylon Med J 1962; 7: 209-11.
7. Jayawardena CHS, Saravanapavananthan N: Insecticide poisoning. Ceylon Med J 1966; 11: 143-52.
8. Sentheshanmugnathan S, Rajaratnam M: In vitro studies on human blood cholinesterase and its action towards organophosphate insecticides. J Natn Sci Coun sri Lanka 1975; 3: 51-63.
9. Franklin CA, Fenske RA, Greenhalgh R, et al: Correlation of urinary pesticide metabolite excretion with estimated dermal contact in the course of occupational exposure to Guthion. Toxicol Environ Health 1981; 7: 715-31.