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Research Article

EVALUATION OF CLINICAL PROFILE AND PLASMA CHOLINESTERASE ACTIVITY IN ORGANOPHOSPHORUS POISONING

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Abstract: OBJECTIVE: To assess the clinical profile of acute organophosphorus (OP) poisoning and to correlate it with plasma cholinesterase (ChE) activity. MATERIALS AND METHODS: The study was conducted at Civil Hospital Ahmedabad, for the duration of one year on 50 patients of acute OP poisoning. Patients were followed up for 28 days and plasma ChE level was measured at the time of admission and on day 3,7,14 and 21. History and details of management were noted in a modified case record form prescribed by WHO. RESULTS: Loss of consciousness, vomiting, diarrhea, lacrimation, visual abnormalities, areflexia, bradycardia, hypotension, hypothermia, miosis and dyspnoea were common signs and symptoms. At the time of admission all the patients had a lower value of plasma ChE than normal. Atropinization was the main treatment. A baseline plasma ChE value < 2.0Ku/l and quantity of consumed poison > 200ml. were usually associated with death. No deaths were reported when plasma ChE value was > 2.0Ku/l and consumed amount of poison was < 200ml. CONCLUSION: Plasma ChE value may have a prognostic value in cases of acute OP poisoning. Atropine and ventilatory support have a life saving value in the treatment.

Key**words:** Organophosphorus compound, Cholinesterase enzyme level, Acetylcholine, Atropine.

INTRODUCTION

Organophosphorus compounds are the substances most commonly use as an insecticides & pesticides. Important pesticides are used extensively for advanced farming **[4]**. Because these substances are available freely in the market, they are also the most common cause of poisoning.

Cholinesterase is an enzyme which hydrolyses Acetylcholine (Ach), and thus checks the concentration of Ach at the various sites of nervous system. Ach is a neurotransmitter, cholinergic in nature and present at pre-ganglionic autonomic fibers, all postganglionic parasymphatic fibers and few postganglionic sympathetic fibers. In the absence of cholinesterase enzyme the level of Ach increases and leads to increases cholinergic activity.

The organophosphates are cholinesterase (ChE) inhibitors and hence the symptoms of their poisoning are entirely because of increased acetylcholine (Ach) concentration at the synapses that leads to exaggeration of the cholinergic activity**[18]**. In case of Organophosphorus poisoning, the diagnosis and the management is usually based on clinical features and the laboratory help is hardly ever sought. Diagnosis of acute Organophosphorus poisoning should usually be based on history of exposure and concentration of plasma cholinesterase**[16]**. In our study we assess the clinical profile and investigate the pattern of management and the resultant outcome in all Organophosphorus poisoning cases. We also tried to correlate this with serially measured plasma cholinesterase activity.

MATERIALS AND METHOD

We did our study at civil Hospital Ahmadabad. Total numbers of patients were 50, all the patients were adult (>18 years old) and belongs to either sex. We use a specially designed porforma prescribed by WHO. However a standard proforma was slightly modify by us keeping in view the facilities available at our institute. Measurement of plasma cholinerterase was done on RA-50 chemical Analyzer (Bayer India Ltd.) along with a ready-made kit for estimation of acetyl cholinesterase activity (Zydus Pathline ludia).

We took history of the patients at the time of their arrival in casualty department. After taking the history, General and systemic examination were done and several laboratory investigations like hematological, Blood chemistry, routine urine examination and X-ray examination of chest were also done. Details of treatment given to the patients were recorded everyday into the proforma until the time of discharge. Advice given at the time of discharge was also recorded.

Plasma cholinesterase estimation was done in all patients at the time of admission and repeated on day 3,7,14 & 21. It was done by the method based on KINETIC DGKCH technique described by kendel M. and Al.. After collecting 2 ml of venous bld. in heparinised vial it becomes centrifuged at 3000 PPM for five minutes. Supernatant

(Plasma) was collected in a separate glass tube. Then 1 ml of reagent-A from the kit is added to serum and the mixture is incubated at 37^0c for five minutes. Subsequently reagent-B is added to the test tube and absorbance is measured at 405 mm using RA-50 chemistry analyzer. Three readings were taken at an interval of 90 secs. to minimize the variation and validate the procedure.

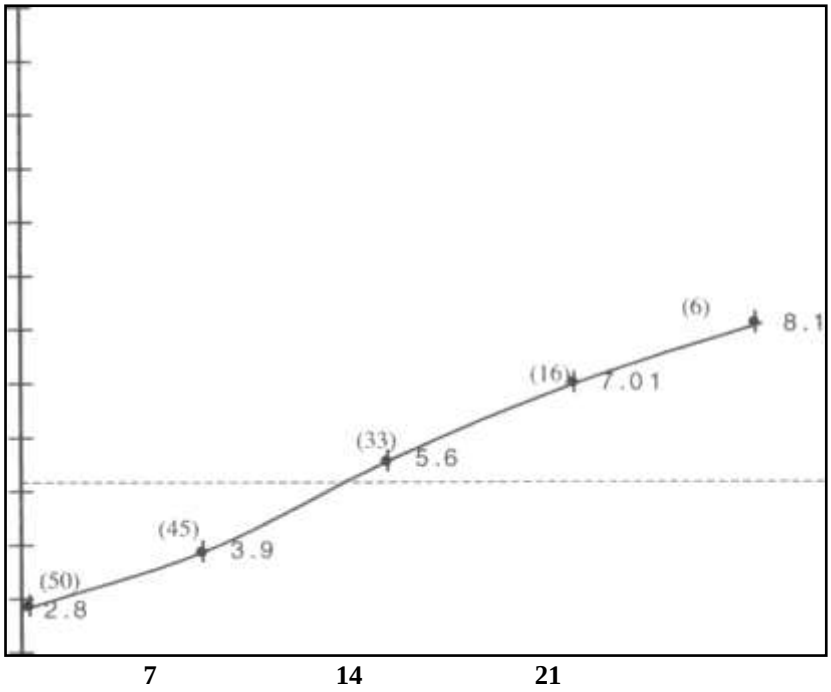
RESULTS

In our laboratory serum cholinesterase conc. 5.1 to 12.1 Ku/l is consider to be normal for adult male and postmenopausal women. While value of 4.1 to 11.9 ku/l is consider normal in adult premenopausal woman.

During our study we found that mean plasma cholinesterase value was 2.83 + or - 0.19 Ku/l at the time of admission (Range 0.5 to 5.0Ku/l in adult male and postmenopausal women and 0.4 to 3.9 Ku/l for premenopausal adult females). So, diagnosis of organophosphorus poisoning was confirmed in all the suspected cases.

This value increases significantly ($p<0.001$) on day 3 to 3.94 +/ - 0.26 ku/l (n=45) and become normal (5.67 + / - 0.36 Ku/l) on day 7 (n=33). The mean plasma cholinesterase continued to be rise in surviving patients and became 7.01 + or - 0.5 Ku/l on day 14(n=16) and 8.11 +/ - 1.06 Ku/l on day 21(n=6).

Rise in serum cholinesterase concentration was statistically significant (as compared to base line value recorded at the time of admission) at all intervals at day 7 ($p<0.001$), day 14 ($p<0.001$) and day 21($p<0.001$).



Graph – 1.: Serum cholinesterase concentration (Mean + SEM) at various time intervals post-exposure. Figures in bracket are the number of patients (n). Vertical bars represent the SEM and the dotted line is the lowest, normal cholinesterase value (5.1Ku/l) for adult males (and post menopausal women) established in our laboratory.
*P<0.001 as compared to the baseline value (Student's 't' test).s

The numbers of deaths were 5 between day 1 & 3, and 6 between day 4 & 7. Six, seventeen and ten patients recovered and were discharged between day 4-7, 8-14 and 15-21 respectively. Of the remaining six patients, four were discharged between days 22-28 and thus only two patients remained in the hospital on day 28 when the follow-up ceased.

During our study 11 pts. were died, and all these 11 pts. had baseline plasma cholinesterase value < 2.0 km/l. No deaths took place in those having baseline plasma cholinesterase concentration > 2.0 km/l. (Table - 1).

Table-1: Baseline plasma cholinesterase value

Baseline value of serum serum cholinesterase (Ku/**1)**	No. of Patients	No. survived (%)	No. expired (%)
2.1 and more	32	32(100)	00(00)
1.1-2	11	03(28)	08(72)
0-1	07	04(57)	03(43)
Total:	50	39(78)	11(22)

DISCUSSION

OP compounds have been used globally for past control over hundreds of years **(10).** The high potency of OP compounds and their peculiar nature of action (irreversible cholinesterase inhibition leading to accumalation of acetylcholine at the receptor site) and easy availability led to an hormonous problem of poisoning. OP poisoning is usually sucidal in nature but accidental or occupational exposures may occur.

The WHO estimated in 1974 that globally about 0.5 million causes of acute pesticide poisoning occur with 9000 or more deaths, and there members are increasing with time**[22]**. According to one study about 60% of the death in case of OP poisoning occurs after self poisoning **[7,9]**. He aria region thousands of peoples are dying from OP poisoning and million of peoples are treated for same. **[7,11]**. In india although the clear picture is not available, isolated series of large number of cases have been reported from various places in past **[1,14,15,20,21]**.. As the number of poisoning cases are increased but the progress in treatment and diagnosis is very slow. **[3]**.

The diagnosis and treatment of OP poisoning has always been conventional and stagnant and in majority of the case it is symptomatic. **[1,12]**. Commonly administrated antidote is atropine and PAM **[20]**. Ach is a neurotransmitter present in ANS. Initial substrate for synthesis of Ach are glucose and choline. The acetylation of choline with acetylcholinesterase leads to formation of Ach with stored in synaptic vehicles of neurone. When the aciton potential arrives at motor nerve terminals there is release of Ach **(13,17)** The released transmitter interact with receptor of effector cell membrane.

There are two type of cholinergic receptors present with are muscarinic and nicotinic. Depending on their location of the receptors, stimulation of receptors leads to physiological changes in the system. which mainly leads to with hydrolyse with the help of enzyme km of Acetylcholinesterase (ACHE), and this leads to teramination of action of Ach. The enzyme cholinesterase are of two types erythrocyte cholineterase and serum cholinesterase. Erythrocyte cholinesterase is specified in the sense that it only hydrolyze choline esters, while serum cholinesterase is non specific and so, depending on this characteristic they are also known as true and Pseudocholinesterase respectively. **(19).**

Organophosphates causes poisoning primarily by phosphorylation of acetylcholinesterase enzyme (AchE) at nerve endings. So, in case of OP poisoning the level of cholinesterase will go down below the minimum normal level. So, the level of Ach will remain uncheck and its level increases at synaptic level and so the signs and symptoms of cholinergic overactivity will found which are related to the SLUDGE syndrome, (increased salivation, lacrimation, urinary incontinence, diarrhea, gastrointestinal cramping and emesis.

In some cases of survival after a high dose of poisoning may result in long term effects on the CNS called 'Organophosphate induced delayed neuropathy' (OPION) due to inhibition of the enzyme neuropathy target esterase. These include neuropathies, confusion and thought disorders. The diagnosis of the acute OP poisoning has usually been based on a suspicion and the recognition of typical signs and symptoms. Atropine is a anticholinergic drug and it blocks the muscranic effect of Ach till the signs of atropinization appears, and PAM as a main antidote **[20,21]**.

Within one to two days of initial organophosphate binding to acetylcholinesterase, some phosphorylated acetylcholinesterase enzyme can be de-phosphorylated and become reactivated by the axime antidote. Pralidoxime (PAM). As the time progresses, the enzyme-phosphoryl bond is strengthered by loss of one alkyl group and so reactivation with PAM is not possible. this process is km as 'aging' of enzyme and so,the efficacy of current antidote is largely unproven**[3,5,6]**.

So, the level of acetyl choline (Ach) rises at cholinergic neuroeffactor junction (Muscarinic effects) at skeletal nerve-muscle junctions, at autonomic ganglia (nicotinic effect) and in the brain. This ultimately leads to muscle twitching. increased secretion from various glands and slasory and behavioural distrubance along with incoordination and depressed motor function. Depression of respiration and palmonary edema finally leads to death. and recovery of patients depend on generation of new enzyme**.**

Additionally, there are many other gray areas in the diagnosis and the treatment of acute OP poisoning. These include intercommunity ethnic differences in the extent, type and the amount of poison consumed, extent of application and utility of the diagnostic measures **[8]**, the role of antidotes**[20,21]** and the correlates of the outcome. So, there is a definite need to boost the research on OP poisoning and to overcome the apathy in this area internationally**[3]**.

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