ORIGINAL RESEARCH PAPER

Volume-8 | Issue-8 | August - 2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

HIGH DOSAGE OF ATROPINE ADJUSTED WITH THE SEVERITY OF OP COMPOUND POISONING AND EARLY INTIATION OF INJECTION PRALIDOXIME AND INJECTION MAGNESIUM SULPHATE WITHIN 2 HOURS OF POISONING - REDUCTION OF MORTALITY NEAR TO MINIMUM IN OUR STUDY OF 250 PATIENTS WITH OP COMPOUND POISONING IN TERTIARY HOSPITAL IN PESIMSR KUPPAM

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ABSTRACT

Background: Organophosphorus compounds are poor man choice as suicidal poison because of the unrestricted availability and being cheaper. We have studied 250 cases of OP compound poisoning, different parameters like age, sex, rural/urban, mode of poisoning, factors associated with mortality and morbidity have been studied in our patients in ICU, PESIMSR kuppam.

Material and Methods: This series of Organophosphorus poisoning cases were conducted in the department of General Medicine and ICU care, PESIMSR, Kuppam, Chittoor district, Andhra Pradesh. This is a retrospective study of 250 OP compound poisoning patients admitted between April 2012 to June 2019. Diagnosis of OP compound poisoning is based on clinical features, history of exposure to OP poison and low pseudocholinesterase activity. A standard treatment of atropine, PAM and Magnesium sulphate was used.

Results: Of the 250 cases studied 55% cases (136) were male and 45% cases(114) were female,98% cases(245) were suicidal and 2% cases(5) were accidental,81%cases(203) were from rural and 19% (47)cases were from urban population, 29 patients developed intermediate syndrome and 16 died.

Conclusion: The benefit of pralidoxime is significant if it is used as earlier as possible in the treatment of Organophosphorus compound poisoning. The dose of Atropine may go in increasing trends if OP poisoning is severe and the ingestion of poison is too much. Reduction of the dose of atropine in the case of OP compound poisoning is detrimental to patient and it lead to intermediate syndrome. The timely initiation of Atropine, PAM, Magnesium sulphate have prevented acute complications like pulmonary edema, heartblock ,severe bradycardia.

KEYWORDS

Atropine, organophosphorus poisoning, pralidoxime, Magnesium sulphate, Intermediate syndrome pseudocholinesterase, Peradeniya score.

INTRODUCTION:

The first Organophosphorus compound Tetraethyl pyrophosphate was synthesized by French chemist Philippe de Clermont in 1854 and subsequently by German chemist Gerhard Schrader in 1930s with the intension to use it as insecticide for agricultural purpose[1]. The Irony is the Organophosphates have been used as chemical warfare agent by Nazi government in the World war II as nerve gas and still more pathetic is these compounds are being continuously used as poor man's poison which resulted in 2.5 Lakh deaths every year according to WHO [2,3] and also 1 million accidental, 2 million suicidal poisoning worldwide[4].

According to National Crime Bureau of India, suicide by pesticide poison constitutes about 19.4% of all suicidal poisoning in a single year of 2006 [5]. Because of the low cost and easy availability these OP insecticide poisoning are estimated to cause 60-75% of 5 lakh fatalities occurring every year due to suicidal poisoning in india.[6] It is a poison of suicide in the developing countries, so it can be called as social calamity.

MATERIAL AND METHODS:

This series of Organophosphorus poisoning cases were conducted in the department of General Medicine and ICU care, PESIMSR, Kuppam, Chittoor district, Andhra Pradesh. This is a retrospective study of 250 OP compound poisoning patents admitted between April 2012 to June 2019. We excluded the doubtful cases of OP Compound poisoning from the study.

Diagnosis of OP compound poisoning is based on clinical features like bronchorrhea, miosis, salivation, defecation, urination, hypotension, history of exposure to OP poison and low pseudocholinesterase activity. Normal pseudocholinesterase is between 4,000 to 11,000 IU/ml and pseudocholinesterase less than 500 was taken as severe poisoning. All the patients were followed by our team up to recovery or death. Baseline investigation like pseudocholinesterase, blood urea nitrogen, serum creatinine, serum electrolytes, amylase, glucose were done. Various variables studied include age, gender, mode of poisoning, time between consumption and start of treatment, duration of hospital stay, acute complications.

The following findings were not observed in our study like ventricular tachycardia, SVT, OPC induced delayed polyneuropathy, neuropsychiatry disorder, extrapyramidal symptoms like dystonia, chorea, tremors and cog wheel rigidity, Gullain barre syndrome, Optic atrophy, Retinal degeneration, ophthalmoplegia, recurrent laryngeal nerve palsy, ototoxicity, acute pancreatitis.

METHOD OF TREATMENT:

TIME OF START OF TREATMENT	INTERMEDIATE SYNDROME		TOTAL	SIGNIFICANCE	
	NO n(%)	YES n(%)		χ^2	P VALUE
>30 MINUTES	47 (21.27%)	1 (3.45%)	48 (19.20%)	35.3707	0.000
30 MINUTES TO 1 HOUR	75 (33.94%)	3 (10.34%)	78 (31.20%)		
1HOUR TO 2HOURS	57 (25.79%)	5 (17.24%)	62 (24.80%)		
>2 HOURS	42 (19.00%)	20 (68.97%)	62 (24.80%)		

TOTAL	221 (100%)	29 (100%)	250 (100%)		

This is the standard protocol of injection Magnesium sulphate 2 grams iv stat, Pralidoxime 30mg/kg iv over 15-30min (max-2gm) followed by 8mg/hr infusion (max-500mg/hr) for 48hrs or until atropine required(2-5days) [7], atropine 1 ampule(each ampule contains 0.6 mg) bolus followed by 10mg/ hour infusion and then incremental dose of atropine until atropinisation. The highest dose of atropine used in our study is 7500mg and the lowest dose is 10mg. This protocol worked excellently as it reduced mortality to 6.2 %.

RESULTS:

Of the 250 cases studied 55% cases(136) were male and 45% cases(114) were female, 98% cases(245) were suicidal and 2% cases(5) were accidental, 81%cases(203) were from rural and 19% (47)cases were from urban population, 29 patients developed intermediate syndrome and 16 died.

OUTCOME OF THE STUDY:

The benefit of pralidoxime is significant if it is used as earlier as possible in the treatment of Organophosphorus compound poisoning. The dose of Atropine may go in increasing trends if OP poisoning is severe and the ingestion of poison is too much.

In our study, 2 patients received total dose of 7000 mg of atropine and the patient was revived and discharged after 29 and 21 days of hospital stay respectively.

Reduction of the dose of atropine in the case of OP compound poisoning is detrimental to patient and it lead to intermediate syndrome in 29 patients in our study.

The timely initiation of Atropine, PAM, Magnesium sulphate have prevented acute complications like pulmonary edema ,heartblock ,severe bradycardia. Use of magnesium prevents prolongation of QT interval and its complication- Torsades de pointes type of VT

Patient coming to casualty with unknown compound poisoning presence of 4 features 1. Miosis, 2. Pungent smell of Organopho sphorus compound, 3. Pulmonary complications, 4 Bradycardia lead to rapid diagnosis and immediate effective treatment with Atropine, PAM and MgSO4.

Even if the side effects of atropine like Atrial tachycardia, Ventricular tachycardia, Ventricular fibrillation occurs, the complications need to be treated and the dose of Atropine should not be reduced.

Though so many controversies regarding therapeutic benefits of PAM exist throughout the universe, our therapeutic protocol including MgSO4, PAM, Atropine we achieved a therapeutic success as evident by only 16 deaths out of 250 patients.

MORTALITY	TREATMENT REGIMEN		TOTAL n(%)	SIGNIFICANCE	
	ATROPINE ALONE n (%)	ATROPINE,PRALIDOXIME, MAGNESIUM SULPHATE n (%)		$\chi 2$	P VALUE
NO	53 (80.30%)	181 (98.37 %)	234 (93.60 %)	26.4677	0.000
YES	13 (19.70%)	3 (1.63%)	16 (6.40%)		
TOTAL	66 (100.00%)	184 (100.00%)	250 (100.00%)		

TIME OF START OF TREATMENT	MORTALITY		TOTAL	SIGNIFICANCE	
	NO n(%)	YES n(%)		$\chi 2$	P VALUE
>30 MINUTES	48 (20.51%)	0 (0.00%)	48 (19.20%)	29.6999	0.000
30 MINUTES TO 1 HOUR	77 (32.91%)	1 (6.25%)	78 (31.20%)		
1HOUR TO 2HOURS	60 (25.64%)	2 (12.50%)	62 (24.80%)		
>2 HOURS	49 (20.94%)	13 (81.25%)	62 (24.80%)		

TOTAL	234 (100%)	16 (100%)	250 (100%)		

In our study of 250 patients, atropine and PAM and Magnesium sulphate used in most of the cases, they have averted death than using atropine alone in few cases

Our PES hospital situated in the rural area is a tertiary care hospital with well-equipped ICU setup and good supportive care from staff nurses , rapid initiation of all 3 drugs prevented convulsion ,severe bradycardia, renal failure, intermediate syndrome and critical care polyneuropathy.

In our study the sample size of people was from low income group. 98% of cases used it for suicidal purpose, 2 %cases accidental and no homicidal poisoning. We have followed very strict criteria for OPC case definition. It is a retrospective study and also prospective study by following them,with increased accuracy of findings.

INTERMEDIATE SYNDROME	TREATMENT REGIMEN		TOTAL n(%)	SIGNIFICANCE	
	ATROPINE ALONE n (%)	ATROPINE,PRALIDOXIME, MAGNESIUM SULPHATE n (%)		$\chi 2$	P VALUE
NO	48 (72.73%)	173 (94.02 %)	221 (88.40%)	21.4805	0.000
YES	18 (27.27%)	11 (5.98%)	29 (11.60%)		
TOTAL	66 (100.00%)	184 (100.00%)	250 (100.00%)		

In our study OP poisoning more male than female. We have not come across any late complication like critical care polyneuropathy.63.20 % of the patients were between 21 to 40 years of age group

Age group	No. of patients	Percentage
< 20 years	48	19.20 %
21 to 40 years	158	63.20 %
41 to 60 years	41	16.40 %
>61 years	3	1.20 %
Total patients	250	100.00 %

In our study regarding the cardiac toxicity of OP compound only bradycardia, first degree AV block was witnessed and no VT, VF was witnessed.

Most of the study done all over the world do not support the PAM in the treatment of OP poisoning but in our study with combined use of Atropine and PAM, mortality is very low..

We are following only serum Pseudocholinesterase as a measurement of toxicity . In our study if serum Pseudocholinestarase was below 500, it lead to more complications. Patients were monitored safely, serially until serum Pseudocholinesterase reach above 1000.We are assessing severity by Peradeniya organophosphorus poisoning scale.

In a study conducted in Vietnam article published in Asia Pacific journal of medical toxicology September 2014 by Pham Due, Hanoi Medical university, Vietnam supported our study of the new protocol of injection PAM and Atropine with MgSO4 will prevent the death of the patient. So our treatment protocol has been standardised with flexible doses of PAM, Atropine and MgSO4.[8]

In a study conducted by Sanjay A. Mundhe, et.al., Swamy Ramanand Tirth Rural Government Medical College, Ambajogai, India early initiation of decontamination, injection PAM, Atropine with good ICU care with intensivist, good support care will definitely prevent adverse outcome to patient.[9]

Our conclusion remarks:

1. Don't be chicken hearted and start very low dose of Atropine as it lead to intermediate syndrome and other neurological complications.
2. The dose of Atropine should correlate with dose of ingested poisoning. In our study maximum dose reached is 7 grams.
3. Even after using the high dose of atropine, if the patient dies it is

not because of high dose of Atropine but due to other systemic complications like renal failure, MODS.

4. Even if Tachyarrhythmias occurs because of high doses of Atropine the tachyarrhythmias are to treated and the dose of Atropine should not be tapered
5. In our study of OP compound poisoning serum amylase is not increased even in with high dose of OPC poisoning.
6. Hyperglycemia is found in most of the cases.
7. Neurological complications like seizures found only in 9 cases out of 250 cases constitutes 3.6 % .

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