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PREDICTIVE ANALYSIS OF NEUROMUSCULAR WEAKNESS IN ACUTE ORGANOPHOSPHATE COMPOUND POISONING: A STUDY FROM CENTRAL INDIA

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ABSTRACT

Background: Organophosphate (OP) based pesticides are widely used and have emerged as the Major contributor to ill health associated with pesticides worldwide.Though accidental Poisoning can occur following exposure or inhalation, serious poisoning often follows Suicidal ingestion

Aims and Objectives: The present study was undertaken to identify the factors, which help in predicting the neuromuscular weakness in acute organophosphate poisoning, to identify the clinical parameters which help in early identification of patients who may develop respiratory failure due to neuromuscular weakness.

Material and Methods: The diagnosis of organophosphate was made on the basis of definite history of OP poisoning by patients or attendants. For each patient enrolled in the study a detailed clinical history was taken. A detailed clinical examination was carried out in each patient as per Proforma. The patients were divided into two groups. The first group had patients who developed neuromuscular weakness.. The second group had patients who did not develop neuromuscular weakness. The various factors were studied which help in early prediction of respiratory failure

Results: 100 patients of OP poisoning were studied. The patients were divided into two groups the first group with neuromuscular weakness and the second without neuromuscular weakness. Thesymptoms in the present study was vomiting(95%), increased secretions (79%), diarrhea (24%), abdominal pain (23%), diminished vision (12%) and convulsions (8%).The frequently observed signs were miosis(82%), secretions (79%), fasciculations (76%) bradycardia(52%), typical odor(50%), hypotension(22%).The youngest patient was 14 years and oldest was 70 years. The maximum number of patients belonged to age group of 21 to 30. On multivariate analysis the identified predictors included Time lag in receiving treatment (p = 0.012), Presence of convulsions (p=0.000); Grade of poisoning (p=0.000); Presence of fasciculation (p=0.000); G.C.S. score on admission (p=0.000); Pupillary size on admission (p=0.010)

Conclusions: The predictors of neuromuscular weakness in acute organophosphate poisoning are severe clinical grade of poisoning on admission; increased duration of time elapsed prior to treatment; level of sensorium on admission; presence of fasciculations on admission; pupil's size on admission and presence of convulsions on admission.

Keywords: diarrhea, abdominal pain, diminished vision, bradycardia, typical odor, fasciculations

Introduction

Organophosphate (OP) based pesticides are widely used and have emerged as the Major contributor to ill health associated with pesticides worldwide.Though accidental Poisoning can occur following exposure or inhalation, serious poisoning often follows Suicidal ingestion.[1] Worldwide, an estimated 3,000,000 people are exposed to organophosphate or carbamates agents each year, with up to 300,000 fatalities [2-4] The leading cause of death in OP poisoning is respiratory failure which results from a combination of respiratory muscle weakness, central respiratory depression, increased

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bronchial secretions, bronchospasm and pulmonary edema.[4] The present study was undertaken to identify the factors, which help in predicting the neuromuscular weakness in acute organophosphate poisoning.This study also aims to identify the clinical parameters which help in early identification of patients who may develop respiratory failure due to neuromuscular weakness. Since respiratory failure is the most common cause of death in OP poisoning, early identification and effective management will help in reducing overall mortality in OP poisoning.

Material and Methods

This prospective observational study was conducted from December 2015 to November 2017 in the department of Neurology of Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha, Maharashtra, India, which is a tertiary care hospital, serving patients from central India. The study was approved by Institutional Ethics Committee of the above institute. Informed written consent was obtained from patients or their relatives prior to enrolment in the study. All Provisions of declaration of Helsinki were followed during the study. We studied 468 patients with organophosphate compound poisoning who were admitted to the intensive care unit of our institution.

Inclusion criteria

The patients admitted to hospital with a diagnosis of OP compound poisoning. A diagnosis of organophosphate was made on the basis of definite history of OP poisoning by patients or attendants. This was substantiated by examination of the container. Only those patients who gave definite history and in whom the poison could be identified by the container were included in the study. The diagnosis was further substantiated by typical clinical features (hypersalivation, miosis and fasciculation) and characteristic or of stomach wash or vomitus. The diagnosis was confirmed by using the Serum cholinesterase levels.

Exclusion criteria

1. Patient with pre-existing pathology that is likely to worsen the respiratory failure due to OP poisoning
2. Patient with chronic lung diseases e.g. COPD, Pulmonary TB, interstitial lung diseases.
3. Patient with chronic cardiac diseases.
4. Patient with known neuromuscular diseases like myasthenia gravis or muscular dystrophy.
5. Patients with poisoning with two different agents such as opioids, benzodiazepine or barbiturates.

For each patient enrolled in the study a detailed clinical history was taken. The history was recorded in the Proforma. A detailed clinical examination was carried out in each patient as per Proforma which included examination for presence of respiratory failure, detailed assessment of central nervous system, respiratory system and cardiovascular system. Special reference was given to severity of fasciculations, severity of coma by Glasgow coma scale and pupillary size.

All patients on admission were given a stomach wash and body and eye wash in case of external exposure.[5] Thereafter Atropine was administered to the patient till signs of atropinization; dryness of mucosa, dilated pupils > 7 mm and heart rate > 120/ min appeared. Atropine was continued thereafter in gradually tapering doses with strict monitoring for signs of over atropinization.[4,6,]An initial dose of 30 mg/kg pralidoxime IV followed by an IV infusion of 8 mg/kg/hr. Alternatively, if a continuous infusion was not possible, 30 mg/kg pralidoxime was administered IM or IV every 4 hours. The doses of PAM was continued for 2 to 4 days depending upon the clinical improvement seen in patients.[7-9]

The patients were divided into two groups. The first group had patients who developed neuromuscular weakness.. The second group had patients who did not develop neuromuscular weakness. The various factors were studied which help in early prediction of respiratory failure

Statistical analysis

We used t-test for continuous normally distributed variables. For categorical data chi-square statistics was used and Fischer-exact test was used for small numbers. The variables

which were not normally distributed Wilcoxon's Mann-Whitney U-test was used. P value of 0.05 or less was considered statistically significant.All data analysis was performed by using Microsoft Excel 2007 and SPSS version 17.

Results

We studied 437 patients with organophosphate poisoning during the above study period. There here were 312 (71.4%) males and 125 (28.6%) females. The male: female ratio was 2.49:1. Out of the 437 patients, 399 (91.3%) patients were rural and 38 (8.7%) patients were urban. Mean [standard deviation (SD)] age of the patients was 32.5 (13.8) years [range 14 – 70 years]. Occupations of the patients were as follows: Farmers [230 (52.6%)], housewives [99 (22.7%)], labourers [38 (8.7%)], students [36 (8.2%)], business owners [5 (1.1%)], private employees [6 (1.4%)], government employees [5 (1.1%)], unemployed [11 (2.5%)] and others [7 (1.6%)]. Among the study patients, 267 (61.1%) were married and 170 (38.9%) were unmarried. Most commonly consumed poison wasmonocrotophos [187 (42.8%)], methyl parathion [15 (3.4%)], chlorpyriphos [97 (22.2%)], dimethonate [68 (15.6%)], phorate [15 (3.4%)], quinolphos [55 (12.6%)].Of the total of 437 patients, 418 (95.6%) patients had suicidal intentions and 19 (4.3%) had accidental exposure to organophosphate compounds. Route of exposure was oral in 424 (97%) and parenteral (cutaneous/ inhalational) in 13 (3%) patients. Mean (SD) amount of poison consumed was 14.9 (11.2) ml. Among 418 patients who consumed organophosphates with suicidal intention, various reasons for such a step were financial problems [202 (48.3%)], domestic problems [120 (28.7%)], examination failure [21 (5%)] , failure in love [14 (3.3%)], chronic illness [17(4.1%)], mental disorders [8 (1.9%)] and ; whereas the reason was uncertain in 36 (8.6%) patients. Clinical features, laboratory features and complications are shown in table 1.

Table 1: Clinical features, laboratory features and complications of Neuromuscular weakness due to organophosphate poisoning

Parameter	Patients with Neuromuscular Weakness	Patients without Neuromuscular weakness	Total	P Value
Sex				
Male	20(31.24%)	44(68.76%)	64(64%)	p=0.83
Female	12(33.33%)	24(66.66%)	36(36%)	
Age group				
10 to 20	08 (32%)	17 (68%)	25(25%)	p=0.645
21 to 30	10 (23.25%)	33 (76.75%)	43(43%)	
31 to 40	07 (46.66%)	08(53.34%)	15(15%)	
41 to 50	04(66.67%)	02(33.34%)	6(6%)	
51 and above	03(27.28%)	08(72.22%)	11(11%)	
Total	32	68	100	
Mean age (In years)	30.7+/- 13.06	29.98+/- 14.22	30.22+/13.82	
Time Lag				p=0.012
≤2 hours	3 (17.64%)	14(82.36%)	17	
3 to 4	12(24.00%)	38(76%)	50	
≥5hours	17(51.51%)	16(48.49%)	33	
	32	68	100	

Compound Consumed				
Monochrotophos	14(31.81%)	30(68.19%)	44	p=.9953
Chlorpyriphos	6(27.27%)	16(72.78%)	22	
Dimethonate	5(31.25%)	11(68.75%)	16	
Quilnolphos	4(33.33%)	8(66.67%)	12	
Phorate	1(33.33%)	2(66.67%)	3	
Methyl parathion	2(66.66%)	1(33.34%)	3	

There were total of 100 patients who were included into the study out of them 32 (32%) patients developed respiratory failure. There were 27 patients who developed respiratory failure within 24 hours of admission. However here were five patients (5%) patients who developed late onset respiratory failure (more than 24 hours after admission) or intermediate syndrome.

Of the patients who developed respiratory failure all patients were given ventilatory support. The mean duration of ventilator support required in all patients was 112.32+/- 64 hours. There was a mortality of total 14 patients in respiratory failure group. However there were no deaths in patients who did not develop respiratory failure.

Intermediate syndrome developed in only 5% of our patients. All patients required ventilatory support. The average duration of ventilatory support required was 139.2 +/- 31.2 hours. Out of the 5 patients 3 patients died.The early onset Respiratory Failure (Type I) developed in 27% patients. The mean ventilator requirement was 107.55±72 hours.Table 2shows comparison of various parameters between patients with and without neuromuscular weakness.

Table 2: Comparison of various parameters between patients with and without Neuromuscular weakness in organophosphate poisoning.

Parameter	Number with Neuromuscular Weakness	Number without Neuromuscular Weakness	Total number	P value
GCS				
11 to 15	5(14.28%)	30(85.72%)	35	
7 to 10	12(28.57%)	30(71.43%)	42	**p= 0.000**
3 to 6	15(65.21%)	8(34.79%)	23	
Severity				
Mild	01(05.12%)	18(94.88%)	19	**p= 0.000**
Moderate	4(11.11%)	32(88.89%)	36	
Severe	27(60%)	18(40%)	45	
Fasciculation Score				
0	0(0%)	24(100%)	24	**p=0.000**
1-3	5(14.28%)	30(85.72%)	35	
4-6	11(47.82%)	12(42.18%)	23	
≥7	16(88.89%)	02(11.11%)	18	
Size of Pupil				
1 mm or less	24(57.14%)	18(42.86%)	42	**p=0.01**
2-3 mm	08(20%)	32(80%)	40	
≥ 4 mm	00(00%)	18(100%)	18	
Outcome				
Deaths	14	00	14	**P=0.000**
Survivors	18	68	86	

Table 3 shows the multivariate analysis of predictors of neuromuscular weakness in organophosphate poisoning

Table 3: Predictors of Neuromuscular Weakness in organophosphate poisoning as per multivariate logistic regression:

SR. NO.	Variable	P Value
1	Time lag in receiving treatment	p = 0.012
2	Presence of convulsions	p=0.000
3	Grade of poisoning	p=0.000
4	Presence of fasciculation	p=0.000
5	G.C.S. score on admission	p=0.000
6	Pupillary size on admission	p=0.010

Discussion

One hundred patients of OP poisoning were studied from December 2007 to November 2009. The patients were divided into two groups the first group with respiratory failure and the second without respiratory failure. Of the total of 100 patients 98 %(98) patients had suicidal intention only 2 %(2) patients had accidental poisoning. There were no cases of homicidal poisoning.Goel et al (1998)[3] reported that there was an incidence of 99% patients with suicidal intent. Yurumez et al (2007)[10] reported that most common reason for poisoning was suicide (75.9%). Therefore it is clear from the above study that suicide is the main reason for poisoning in developing countries. This is due to easy availability and the high lethality of the poisons in farming communities. As a consequence of suicidal intention and oral poisoning the poisoning tend to be more severe.

The most common symptom in the present study was vomiting which was present in about 95% patients. The next common symptom was increased secretions which was present in 79% patients. The other symptoms present in the patients were diarrhea (24%), abdominal pain (23%), diminished vision (12%) and convulsions (8%).S.B. Agrawal et al (1993)[11] carried a study of 190 patients of OP poisoning. The most common clinical features were muscarinic such as vomiting (96.8%), miosis (62.2%), excessive salivation (61.1. %), blurred vision (54.71). Seizures were present in 8% of the patients in this study while Wadia et al (1974)[12]reported in 3.33%.

The frequently observed signs were miosis(82%), secretions (79%), fasciculations (76%) bradycardia(52%), typical odor(50%), hypotension(22%).The most common clinical features in a study carried out by Sungur et al (2001)[13] were muscarinic such as vomiting (96.8%), miosis (62.2%), excessive salivation (61.1. %), blurred vision (54.71) and CNS manifestation.

In the present study, 64 patients were males and 36 patients were females. The male to female ratio was around 1.7:1. Hence there was a male preponderance. The percentage of respiratory failure among males was 31.25% compared to females who had a respiratory failure rate of 33.33%. When analyzed statistically by Chi square test, the p value was not significant. (p value 0.83)(p>0.05)

Majority of patients reported within 3 to 4 ours after consumption (50%). The mean duration of the time of reporting to hospital was 3.79± 1.5 hours. Of the patients who received treatment after 5 hours or more 51.51% required ventilator support. In comparison to the patients who presented within 1 hour or less only 17.64% required ventilatory support. The requirement of ventilator was directly proportional to the time elapsed after consumption and prior to start of treatment and the results were statistically significant.In a study carried out by Karki et al (2007)[14]

majority of patients (90%) presented within first two hours of poisoning. The delay in treatment was a common factor in development of respiratory failure.

The op poisoning patients were classified according to the POP scale devised by N Senanayake et al[15]in 1993. Common clinical manifestations of OP poisoning are selected as parameters and each is assessed on a three-point scale varying from 0 to 2(as described on table no 4). The patients were classified into three groups i.e. mild, moderate and severe. Out of the 100 patients, 19 patients belonged to mild severity with 1 (5.12%) patient developing respiratory failure and no mortality. There were 36 patients in moderate poisoning group with 4 (11.11%) patients developing respiratory failure and a mortality of 1 patient.

There were 24 patients who did not have any fasciculations at the time of admission there was no respiratory failure in this group. In patients with fasciculations up to 3 sites there was respiratory failure in 5 (14.28%) patients. In patients with fasciculation at sites between 4 to 6 there were 11cases (47.82%) of respiratory failure. In the last group with 18 patients who had extensive fasciculations 16(88.89%) patients developed respiratory failure. Thus the patients with extensive fasciculations had a higher incidence of respiratory failure as compared to those with localized or absent fasciculations.The similar observations were seen in studies carried out by Goel et al (1998)[3] and Goswamy et al (1994)[16]

Miosis was a common sign on admission in OP poisoning. The degree of miosis correlated well with the severity of OP poisoning. Hence the pupil size can be used to predict the onset of respiratory failure.Similar studies were carried on the pupilary size by Davies et al (2008)[17]the size of the pupils' on admission did not correlate with the severity of OP poisoning.

The mean serum cholinesterase value in the patients in respiratory failure group was 637.03±147.41 whereas the mean serum cholinesterase values in non respiratory failure group were 672.47±138.59. The results were analyzed statistically. The results were found to be statistically insignificant. ($p > 0.05$).

A similar study was carried out by Nouira et al (1994)[18]; the study found out that the mean cholinesterase levels did not correlate with respiratory failure. Rehiman et al (2007)[19] carried out a study in which they showed that the serum cholinesterase values did not correlate with the development of respiratory failure.

A total number of 14 (14%) deaths occurred in our study. All deaths occurred in respiratory failure group, there were no deaths in patients who did not develop respiratory failure. The most common cause of death in our patients was Aspiration pneumonia and respiratory failure (7 patients), followed by sudden cardiac death in 4 patients. There was mortality of 8.74% in study carried out by Goel et al (1998)[3]. In other studies the mortality was found to be Exner CJ 2009 (6%)[20], Tsai JR et al 2007(8%) [21], Saadeh AM et al 1996(4%)[22].

Conclusions:

Our study concludes that the predictors of neuromuscular weakness in acute organophosphate poisoning are severe clinical grade of poisoning on admission; increased duration of time elapsed prior to treatment; level of sensorium on admission; presence of fasciculations on admission; pupil's size on admission and presence of convulsions on admission.

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