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Comparison of Efficacy and Safety of Atropine Sulphate and Glycopyrrolate in the Treatment of Organophosphorus Poisoning at St. Martha's Hospital, Bangalore.

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Abstract

Organophosphorus poisoning (OP) is the most common poisoning in India because of their easy availability. Atropine is considered the drug of choice in the management of OP poisoning and continues to be the standard treatment .Glycopyrrolate is a synthetic quaternary amine, a medication of the muscarinic anticholinergic group, with peripheral effects similar to those of atropine. The objective of this study was to compare the efficacy and safety of Atropine and Glycopyrrolate on OP poisoning patients. A total of 33 patients were enrolled in the study. All patients were recruited into two groups and accordingly received either Atropine or Glycopyrrolate as per the recognized dosing schedule as practiced in the hospital. The details of each OP poisoning case was observed and collected in the data collection form and assessed. All 33 patients were admitted to the ICU and the duration of hospital stay ranged from 2 to 21 days the mean ICU stay in Group-A was 5.43±2.50, in Group-B was 6.42±5.13 (P=0.511). In Group-A, 40 patients required ventilation, whereas 40% did not and in Group-B, 36.85% required ventilation, and 63.15% did not (P=0.304). Among the ADRs documented the most prominent one was Altered Sensorium seen in 64.28% cases in Group-A (P<0.001) whereas in Group-B none had Altered sensorium. The total cost for the anticholinergic treatment in Group-A ranged from 43 rupees to 1503 rupees and in Group-B it was 639 rupees to 4032 rupees (P<0.001) . 3 patients expired, two out of which 2 were from Group-A. The study revealed that both the groups had the same efficacy, but Atropine showed a very distinct CNS toxicity and Glycopyrrolate being a relatively expensive drug.

Key words: *Organophosphorus poisoning; Atropine; Glycopyrrolate; safety; efficacy; expensive; toxicity.*

INTRODUCTION

India is a predominantly agrarian country with about 60-80% rural population. Pesticides are routinely used for advanced farming. These are readily available over the counter. Therefore, a pesticide is an easy access source for suicidal purpose. Poisoning is seldom included as a priority for health research in India, though every year, hundreds of people are loosing their lives prematurely from pesticide poisoning.[1]

Organophosphates were first discovered more than 100 years ago, at present the predominant group of insecticides employed globally for pest control. The compounds are toxic to humans and represent an important source of poisoning domestically, in some occupations, or when ingested as a suicidal agent. Today organophosphates are used worldwide in agriculture as well as in most household gardens. This easy availability of the compounds has resulted in a gradual increase in accidental and suicidal poisoning mainly in developed countries.[2]

Deliberate self-harm has often been thought as a problem particularly to the industrialized world. 75% of the world-wide total of deaths from self-harm. Pesticide poisoning from occupational, accidental and intentional exposure is a major developing world public health problem. However, it is deliberate self-poisoning that causes majority of deaths and the immense strain that pesticides put on hospital services, particularly in Asia. Many studies have shown that deliberate self-poisoning has a far higher mortality than accidental poisoning. Reducing deaths from self-harm will require interventions to both reduce the incidence of harmful behaviour and to improve medical management of acute poisoning.[3]

Main stray for the treatment of organophosphorus poisoning is anticholinergic treatment. Conventional

Indian Journal of Pharmacy Practice
Received on 20/03/2010
Accepted on 23/03/2010

treatment being atropine administration to antagonise the excessive cholinergic effects. (bradin) *Glycopyrrolate is a synthetic quaternary amine, a medication of the muscarinic anticholinergic group, with peripheral effects similar to those of atropine. It is longer acting drug and does not cross the blood brain barrier. Thus glycopyrrolate, unlike atropine is less apt to cause altered consciousness in patients being treated for organophosphorus poisoning.*[4]

The aim of this study was to compare the efficacy of glycopyrrolate with that of atropine in patients admitted due to OP poisoning by comparing the number of days of hospital stay and ventilator requirements and to compare the safety by monitoring the side effects.

STUDY DESIGN

A comparative study on 33 patients where the efficacy and safety of the two anticholinergic drugs (Atropine and Glycopyrrolate) was studied on organophosphorus poisoning patients.

PATIENTS AND METHODS

33 patients admitted to the intensive care unit (ICU) due to organophosphorus poisoning from June 2009- Feb 2010, at St Martha's hospital, Bangalore were included in the study. Patients who consumed organophosphorus compounds were admitted to the ICU after treatment at the emergency ward by atropine along with stomach wash. After obtaining the consent from the patients attendants, they were recruited into two groups, Group-A (received atropine) and Group-B (received glyco-pyrrolate) as per the recognized dosing schedule as practiced in the hospital after the emergency ward treatment. The details of each OP poisoning case was observed and collected in the data collection form which included the demographic details of the patients, suspected OP compound consumed, duration of time taken to bring the patients to the hospital, patients taken to other hospital before admission, ICU stay, ventilation requirement, total hospital stay, ADRs, Pseudo-cholinesterase levels, total cumulative dose of anticholinergic treatment, duration of drug given, other clinical manifestations, complications and death.

The patients in both the groups were assessed based on the date collected.

Descriptive statistical analysis was carried out Significance was assessed at 5 % level of significance, Student t test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

33 patients were recruited to receive the treatment in two groups. Among the total patients 22(66.7%) patients were male and 11(33.3%) patients were females. Age group ranged from 18 years to 39 years and above, where majority of the patients were from 18-28 years of age. The mean age being 28.76±12.14 years. 14(42.4%) patients were recruited in Group-A and received atropine and 19(57.6%) patients were recruited in Group-B and received glycopyrrolate. suspected poison consumed was Chlopyrifos (9.1%), Diazone (3.1%), Dichlovos (3.1%) and parathion seen in most of the patients (48.5%).unidentified compound accounted up to 36.4% in both the groups (Group-A-41.7% and Group-B-58.3%).

The baseline characteristics of the patients are shown in Table-1. The treatment groups were comparable in all respects. Clinical outcomes are shown in Table-2. No significant difference could be detected in the efficacy of the two drugs. All parameters in the clinical outcome was statistically significant. Incidence of Altered sensorium was significantly more in Group A when compared to Group B with $P<0.00$ and total cost of drug was significantly more in Group B with $P<0.001$.Among the three patients who died,one was geriatric patient and expired due to cardiac arrest. The second patient was a male of 34 years and died due to respiratory paralysis. The third patient was from Group-B and expired due to delay in admission to the hospital after the consumption of OP compound.

DISCUSSION

The study conducted on 33 OP poisoning patients has shown that the efficacy of the two drugs is similar. All patients were admitted to the Intensive Care Unit and the duration of stay ranged from 2 to 21 days, out of which 9(64.3%) patients from Group-A were in ICU for lesser than 5 days and 2 (14.3%) above 10 days. In Group-B 12 (63.2%) patients stayed for lesser than 5 days and 3(15.7%) above 10 days. The mean ICU stay in Group-A was 5.43±2.50, which is slightly higher than a retrospective study conducted at Hyderabad for a period of two years,[5] where as in Group-B the mean ICU stay was 6.42±5.13; however it is statistically similar between the two groups with $P=0.511$.

Table.1: Baseline Characteristics

	Group-A (Atropine) N=14	Group-B (Glycopyrrolate) N=19
Time duration to admission (hours)	22*	9*
Taken to other hospital before admission (p=0.719)	10 (71.4%)	12 (63.2%)
Treatment prior hospitalisation (p=1.000)	6(42.9%)	7(36.8%)

* *Mean±SD*

Table.2: Clinical Outcomes

	Group-A (Atropine) N=14	Group-B (Glycopyrrolate) N=19
ICU stay (days) P=0.511	5.43±2.50*	6.42±5.13*
Ventilation requirement P=0.304	7 (50%)	8 (36.8%)
Total hospital stay (days) P=0.594	7.21±3.59*	8.16±5.78*
Altered sensorium P<0.001	9(64.3%)	0
Hyperpyrexia	1(7.1%)	0
Tachycardia	14(100%)	16(84.2%)
Cost (rupees) P<0.001	35.92±22.13*	412.58±73.74*
Other clinical manifestations		
Intermediate syndrome	1(7.1%)	2 (10.6%)
Delayed onset encephalopathy and coma P=0.620	0	2(10.6%)
Respiratory infections	1(7.1%)	0
Death	2(14.3%)	1(5.3)

* *Mean±SD*

In Group-A, 7(40%) patients required ventilation whereas 7 (50.0%) did not and in Group-B 8 (36.8%) required ventilation, and 13(63.2%) did not. The ventilation requirement is slightly greater for group-A when compared to group-B with P=0.304, but no statistical significance was seen.

Some of the previous studies revealed that Atropine treatment is effective but carries the risk of toxicity such as CNS effects and tachycardia. [6,7,8] Out of all the patients included in the study altered sensorium was seen in 9 (64.3%) cases and all the 10 cases were from Group-A, none of the patients in Group-B exhibited this. Incidence of Altered sensorium is significantly more Group A when compared to group B with P<0.001.

Among these patients, altered sensorium was seen in 2(14.3%) patients, during admission and in 7(50.0%), 48-72 hours later. Patients where altered sensorium was seen late were admitted in a time duration ranging from 20 minutes to 1 day. The type of poisoning seen in them is majorly parathion and the main neurotoxicity seen was restlessness and hallucinations.

On the other side Group-B consisted of 2(10.5%) patients with altered sensorium during admission which eventually disappeared after 48 hours. Among the ADRs

documented the most prominent one was Altered Sensorium seen in 9 (64.3%) cases in Group-A, followed by Hyperpyrexia in 1(7.1%) and Tachycardia in all patients. 2 patients (10.5%) in Group-B experienced nausea and 3(15.8%) patients did not have tachycardia. Nausea is not applicable in the comparison between the groups as patients treated with atropine were kept NPO (nil per oral).

In Group-A the dosage of anticholinergic treatment ranged from a minimum of 49mg to a maximum of 1g 792mg, total minimum cost of 43 rupees to a total maximum cost of 1503 rupees. In Group-B it ranged from a minimum of 14.5mg to maximum of 89.27mg, minimum cost of 639 rupees to a maximum of 4032 rupees. The cost of Glycopyrrolate is relatively higher than Atropine. Total cost of drug is significantly more in Group B with $P<0.001$.

Other clinical manifestations seen were intermediate syndrome in 1(7.1%) case in Group-A and 2(10.5%) cases in Group-B. Along with this delayed onset encephalopathy and coma were seen in 2(10.5%) patients in Group-B. Among the two patients who developed delayed encephalopathy and coma one patient was admitted 6 hours after the consumption of OP compound, however such small sample size does cannot allow us to conclude if atropine does not manifest this clinical feature, however statistically other clinical manifestations are similar in both the groups with $P=0.620$. A study carried out in south India reported a few cases of patients developing delayed encephalopathy and coma 4-5 days after the consumption of OP compound but this study did not suggest any other specific drug treatment for this.[9]

Respiratory infection was seen in 1(7.1%) case from Group-A. Out of 33 cases 31 patients recovered and three patients expired, out of which two were from Group-A. Incidence of mortality is also statistically similar in both groups with $P=0.561$.

The mortality rate seen was 14.3% in Group-A and 5.3% in Group-B.

CONCLUSION

This study revealed that atropine and glycopyrrolate showed similar efficacy; however CNS toxicity was greater in the group receiving atropine. Glycopyrrolate was found to be a relatively more expensive drug than atropine.

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