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EFFECT OF ATROPINE AND GLYCOPYRROLATE IN PATIENTS WITH ORGANOPHOSPHATE POISONING

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Abstract:

Objective: *To determine the drug therapy effects of atropine alone and the combined therapy of atropine and glycopyrrolate in patients with organophosphate poisoning.*

Patients and methods: *Total one hundred patients with history of organophosphorus poisoning were included in the study. These patients were divided in to two groups with 50 patients each. One group was treated with atropine alone while the other group was treated with atropine in combination with glycopyrrolate. The results of treatment of both groups were compared after 48 hours of the treatment and data was analyzed on SPSS version 18.0 and statically evaluated by using paired student T-test.*

Results: *During one year study period total one hundred patients with OP poisoning were evaluate as far as management is concerned. The mean ± for age (years) for overall population was 23.74±4.72. The group-A consisted of 50 patients out of which 28 were males and 22 were females. All belonged to the mean age of 22.82 ± 1.166% mostly from rural areas (62%). The group–B also consisted of 50 patients with 29 males and 21 females having mean age of 22.88 ± 1.1. Majority of patients in this group i-e 88% belonged to rural areas with 56% of them were from low economic status. The mortality rate among patients treated with atropine alone was 20% (10 patients), whereas the mortality rate recorded with a combined therapy of on atropine and glycopyrrolate therapy was only 8% (P> 0.05).*

Conclusion: *Since, glycopyrrolate doesn't cross the blood brain barrier thus; it has no effects on Central Nervous System. Therefore, the combined therapy of atropine with glycopyrrolate showed more positive results as compared to therapy with atropine alone, in the management of mild to moderate cases of organophosphate poisoning.*

Key words: *Organophosphorus poisoning, atropine, glycopyrrolate, blood brain barrier.*

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INTRODUCTION:

Organic phosphates (OPs) are the most commonly used chemicals as the pesticides. More deaths are caused in Asia and in developing countries like Pakistan due to pesticide poisoning as compared to infectious diseases [1, 2). The data in African countries show 40 to 60% in accidental inhalation of pesticides [3]. In Sri Lanka alone 10,000 to 20,000 people are admitted to hospitals due to OP poisoning every year out of which 10% die [4]. In Central America the mortality rate due to OP is 20% where the most deaths are due to intentional intake as compared to accidental poisoning [5]. The mechanism of OP poisoning in the pesticide poisoning, is its multiple action on many enzymes in the body specially acetyl cholinesterase (AchE) which is also component of red blood cells. Reaction with this enzyme is of enormous significance as it inhibits this enzyme from its normal action [6]. Atropine, glycopyrrolate and oximes which are generally used as antidotes to OP poisoning, generally have deficiency in treating respiratory insufficiency completely. But if used and managed properly all these antidotes are very effective therapy and can treat the patient to a great extent. The syndromes which are seen on OP poisoning are dry mouth, dry skin, tachycardia and visual disturbances [27]. Glycopyrrolate shows the similar outcome in preventing death of OP poisoned patients as compared to atropine. It is an anticholinergic (antimuscarinic) agent, which act by inhibiting the action of acetylcholine on structures which have postganglionic cholinergic nerve endings and on smooth muscles also. It does not pass through BBB and therefore, it has lesser effect on CNS and hence, combination of atropine and glycopyrrolate may show positive results in controlling mild to moderate OP poisoned patients.

PATIENTS AND METHODS:

The one year comparative study was conducted at tertiary care teaching hospital on the subjects with organophosphate poisoning. The subjects were divided in group A (on atropine (n=50) alone and group B combined atropine + glycopyrrolate (n=50) while the exclusion criteria of the study were the patients with other kind of poisoning (as Methanol, carbon monoxide, and salicylate poisoning etc). The results of treatment of both groups were compared after 48 hours of the treatment while the detailed proforma was filled in for the purpose of recording history, data, and detail of treatment given to organo-phosphorus poisoning whereas along with the immediate emergency management the detail history was taken and appropriate investigations were advised. The cases and statistical data were analyzed on SPSS version 18 and the frequencies, mean ±SD and percentages was calculated.

RESULTS:

During one year study period total one hundred patients with OP poisoning were evaluate as far as management is concerned. The mean ± for age (years) for overall population was 23.74±4.72.

The group-A consisted of 50 patients out of which 28 were males and 22 were females. All belonged to the mean age of 22.82 ± 1.166% mostly from rural areas (62%).

The group–B also consisted of 50 patients with 29 males and 21 females having mean age of 22.88 ± 1.1. Majority of patients in this group i-e 88% belonged to rural areas with 56% of them were from low economic status. The mortality rate among patients treated with atropine alone was 20% (10 patients), whereas the mortality rate recorded with a combined therapy of on atropine and glycopyrrolate therapy was only 8% (P> 0.05). The results of the study are presented in following figures (1-5).

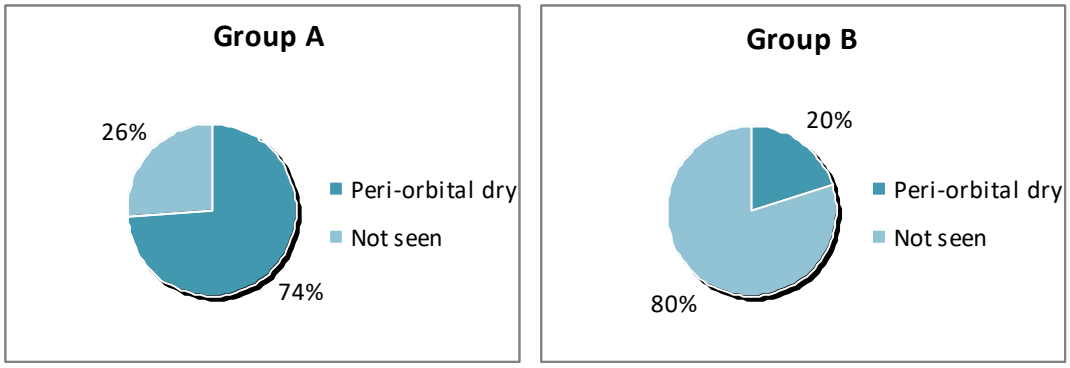

Fig. 1: The figure shows effect of peri-orbital dryness in group A and B of the patients on admission to the hospital.

Both drugs produce marked depression of salivary secretion though the effects of glycopyrrolate are clearly more intense and prolonged. 74% were found peri-orbital dry in group A whereas only 20% in group B (Fig. 1).

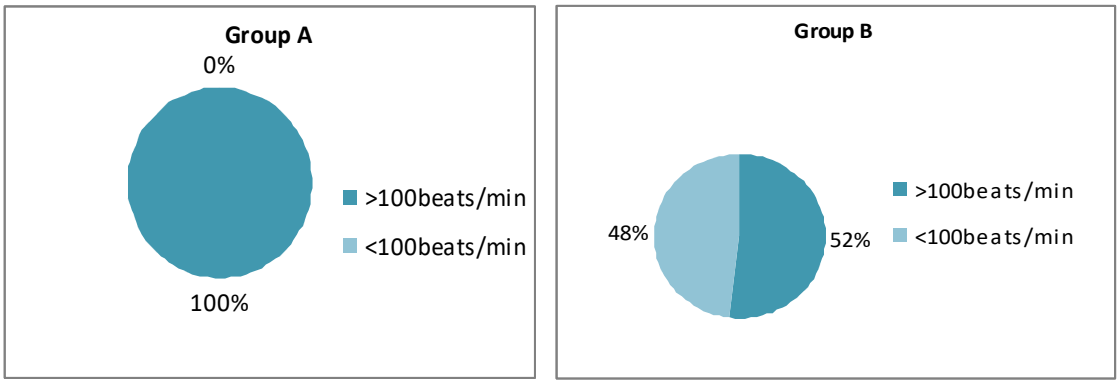

Fig. 2: the figure shows effect on heart beats on the treatment in group a and B

The heart rate of group A patients have more than 100 beats per minute as compared to 52% of patients in group B shows heart rate more than 100 beats per minute.

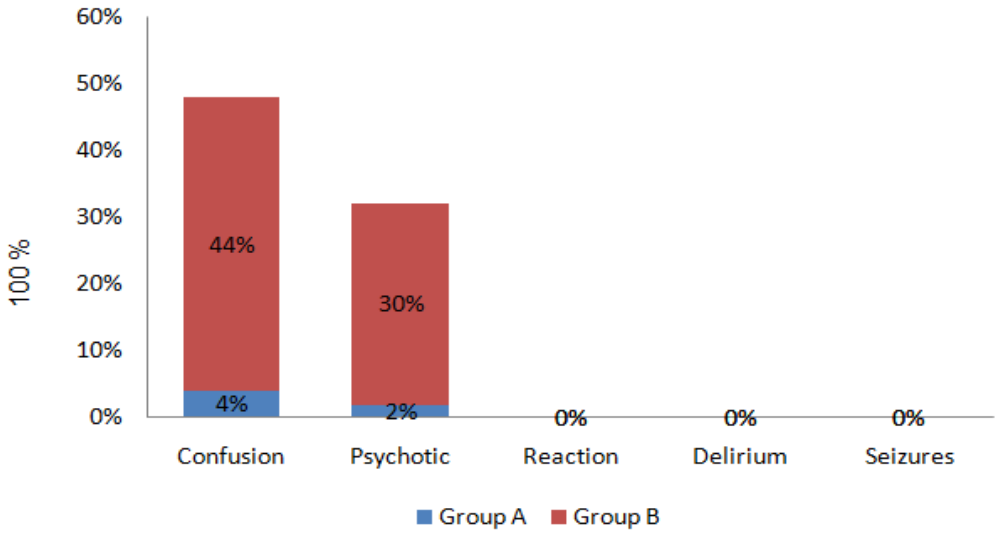

Fig. 3: The Figure shows effects of state of mind of patients on the treatment

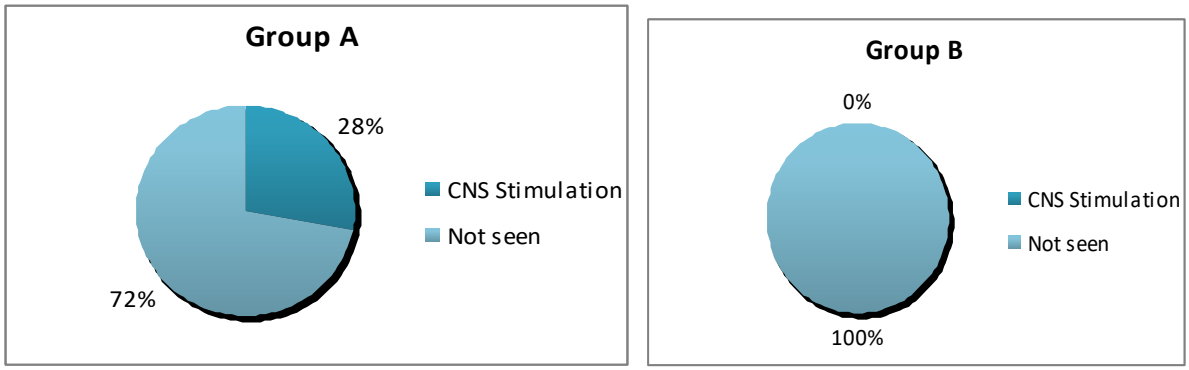

Fig. 4 The figure shows effect of CNS stimulation on the treatment in group A and B

CNS stimulation is seen in 28% of Group A whereas none of the patients show any CNS stimulation of Group B (Fig. 4)

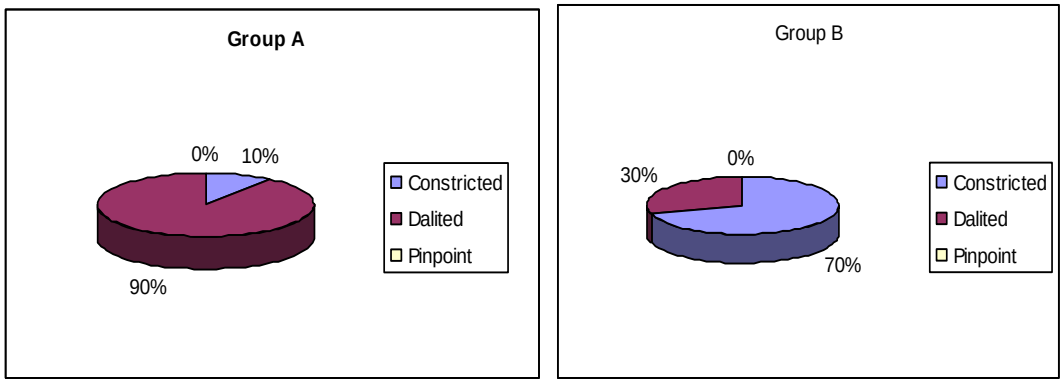

Fig. 5 the figure shows effect pupil size on the treatment in group A and B

DISCUSSION:

To understand the health manifestations associated with pesticide exposures it is essential to have knowledge of different scientific fields like toxicology, physiology, pharmacology, epidemiology, and sociological studies. There are four clinical syndromes that affect the patient with OP poisoning for example the cholinergic crisis, intermediate syndrome, delayed neuropathy and chronic organophosphate inducted neuropsychiatric disorder [8]. Nicotinic effects such as fasciculation's, muscle weakness, tachycardia and hypertension are motor and sympathetic manifestations. One recent retrospective study on OP poisoning revealed that muscarinic sign and symptoms were the most frequent (84%) followed by the affecting CNS (78%) and nicotinic effects (17%) [9]. The patho physiology of OP poisoning is not completely understood however many reports indicate that OP interfere with the control of acetylcholine-regulated homeostatic mechanisms such as temperature regulation. Broad range of symptoms appear affecting the functioning of nerves and initial symptoms similar to the flu, vomiting, abdominal pain, dizziness, and headache, skin and eyes allergies appear [10]. Various studies have shown that OP poisoning is also associated with chronic symptoms like respiratory depression, memory disorders, dermatologic conditions, cancer, depression, neurologic deficits, miscarriages, and birth defects [11-13]. Recent review by Van Maele-Febry [14] has put light on the association between pesticide exposure and cancer. The Non-Hodgkin lymphoma (NHL) has a clears association with OP poisoning [15]. Another review has reported that broad range of nonspecific symptoms, including headache, dizziness, fatigue, weakness, nausea, chest tightness, difficulty in breathing and Insomnia occurs in pesticide poisoning [16]. Though, the Atropine is universally accepted antidote most frequently used for the patients of OP poisoning [17] but the exact recommended dose of atropine is still unknown. The results give wide variations in requirements of atropine in clinical manifestation while countering the muscarinic effects of OP especially the cardiovascular effects and bronchial secretions. Some studies have shown that higher doses were mostly associated with hypothermia, while hyperthermia was only seen with lower doses of atropine [18, 19]. Atropine treatment is also a cause of agitation, confusion, urinary retention, hyperthermia, bowel ileus and tachycardia whereas; the use of mixed therapy of atropine and glycopyrrolate improves tachycardia with no changes in body temperature and CNS stimulation. It could be assumed that in Group A, Atropine shows this effect in 2 days of observation as it passes through blood-brain barrier. In developing countries like Pakistan, it is very difficult to accomplish to treat the OP poisoning patient with poor initial resuscitation and non availability of antidotes. Toxic reaction is the most common side effects which results from the use of anti-muscarinic drugs which may appear at the normal therapeutic doses. The allergic reactions include local manifestations and systemic reaction in the form of anaphylaxis.Other anti-muscarinic drugs recommended for OP poisoning includes glycopyrrolate and scopolamine. Glycopyrrolate is a peripheral anti-muscarinic drug while, scopolamine is an anti-muscarinic drug with both peripheral and central effects [20]. Glycopyrrolate (glycopyrronium bromide) is a quaternary ammonium anti-cholinergic agent with anti-muscarinic activity and peripheral actions like to that of atropine. Because of the marked differences in the chemical structure of atropine and glycopyrrolate, patients allergic to atropine will most probably not be allergic to glycopyrrolate. Indications for the use of glycopyrrolate include to reduce the gastric secretion volume and acidity in patients undergoing surgical procedures. Glycopyrrolate is frequently used for peptic ulcer so it helps in reducing secretion during anesthesia and reverses the effects of muscle

relaxants [21]. Glycopyrrolate is twice as potent as atropine for peripheral effects, so half dose can be given for comparable response. It can be safely use during pregnancy as it doesn't cross the placental barrier [22]. It does not have any detectable central anti-cholinergic effects at doses capable of blocking peripheral cholinergic receptor sites because glycopyrrolate has less penetration across the blood-brain barrier [23].

CONCLUSION:

Therefore, the combined therapy of atropine with glycopyrrolate showed more positive results as compared to therapy with atropine alone, in the management of mild to moderate cases of organophosphate poisoning.

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