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INVESTIGATING PROMETHAZINE'S ANTIDOTAL ROLE IN DICHLORVOS POISONING

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Abstract

Dichlorvos, an organophosphate insecticide, is widely utilized to combat household and stored product insects. Its efficacy extends to a range of pests in greenhouse and outdoor fruit and vegetable crops. The mode of action involves the inhibition of synaptic acetylcholinesterase, which also accounts for its toxicity. Tragically, dichlorvos pesticide self-poisoning constitutes a significant clinical challenge in the developing world, resulting in approximately 200,000 fatalities annually. Organophosphate poisoning, with dichlorvos as a notable contributor, poses a pressing concern in Nigeria, given its prevalent use by farmers and households for pest control.

In this context, we conducted a research study to investigate the potential antidotal effects of promethazine, a first-generation antihistamine and neuroleptic medication, in cases of dichlorvos poisoning in rats.

Introduction

Dichlorvos (2,3-dichlorovinyl dimethyl phosphate) is one of the classes of insecticides referred to as organophosphates (OP) used to control households and stored products insects. It is effective against mushroom flies, aphids, spider mites, caterpillars, thrips, and white flies in greenhouse, outdoor fruits, and vegetable crops (Lotti, 2001).It acts by inhibiting synaptic acetylcholinesterase which is also its mechanism of toxicity. Dichlorvos pesticide self-poisoning is an important clinical problem in the developing world, and kills an estimated 200,000 people every year (Michael, *et al.*, 2008). Organophosphate poisoning therefore is an existing serious concern in Nigeria as poisoning by this compound is on the increase. This is as a result of its frequent use by farmers for pest control as well as household pest control. Promethazine is a neuroleptic medication and first-generation antihistamine of the phenothiazine family used to treat allergy symptoms, nausea and vomiting after surgery and to prevent motion sickness.This research study therefore, set out to assess the possibleantidotal effect of promethazine an antihistamine on dichlorvos poisoning in rats.

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Methodology

65 rats weighing between 220g- 300g obtained from the Department of Pharmacology animal house were used for this study. The rats were bred and maintained under suitable conditions, allowed an acclimatization period of two (2) weeks, housed in hygienic cages in groups of five and allowed free access to feed obtained from vital feeds UAC PLC and water *adlibitum*. The beddings were changed and cages cleaned out on alternate days.

Animals were handled according to the Helsinki declaration on animal care.The animals weredivided into 13 groups, each consisting of 5 rats. The groups included those for treatment and the control groups. Drugs were administered intraperitoneally via a 1ml syringe.

Determination of Antidotal Effect of Promethazine

This test was carried out onsixty-five (65) adult wistar rats. The animals were grouped into five (5) with five (5) rats in the control group (A) while the remaining four groups (B, C, D & E) were sub-divided into three (3) groups each. Each subgroup had five (5) rats. The drugs (Promethazine and Atropine) were administered either 5 minutes before dichlorvos poisoning (pre-treatment) or 5 minutes after dichlorvos poisoning (post-treatment). Drug administration was done intraperitoneally as follows

(i) Group A, the negative control, was given 15mg/kg dichlorvos. Subsequently this dose was used to initiate poisoning in the test animals. (Hutson*et al*, 1972)

(ii) Group B was post treated with three (3) doses of promethazine, 0.375mg/kg, 0.75mg/kg and 1.5mg/kg administered five (5) minutes after dichlorvos (15mg/kg) poisoning. (Liu*et al*, 2008)

(iii) Group C received a combination of promethazine 0.375mg/kg + atropine 1.6mg/kg, promethazine 0.75mg/kg + atropine 1.6mg/kg and promethazine 1.5mg/kg + atropine 1.6mg/kg respectively five (5) minutes after dichlorvos poisoning. (Ellenhorn*et al*, 1997)

(iv) Group D was post treated with atropine alone. Three doses of atropine, 0.4mg/kg, 0.8mg/kg, and 1.6mg/kg were administered five (5) minutes after dichlorvos poisoning. (Aaron *et al*, 2001)

(v) Group E was pre-treated with promethazine alone. 0.375mg/kg, 0.75mg/kg and 1.5mg/kg respectively five (5) minutes before dichlorvos poisoning.

The groups were observed for straub tail, muscle fasciculation, defecation/ urination, salivation, latency of tremors, and these reactions were recorded (Yavuz*et al*, 2007)

Results

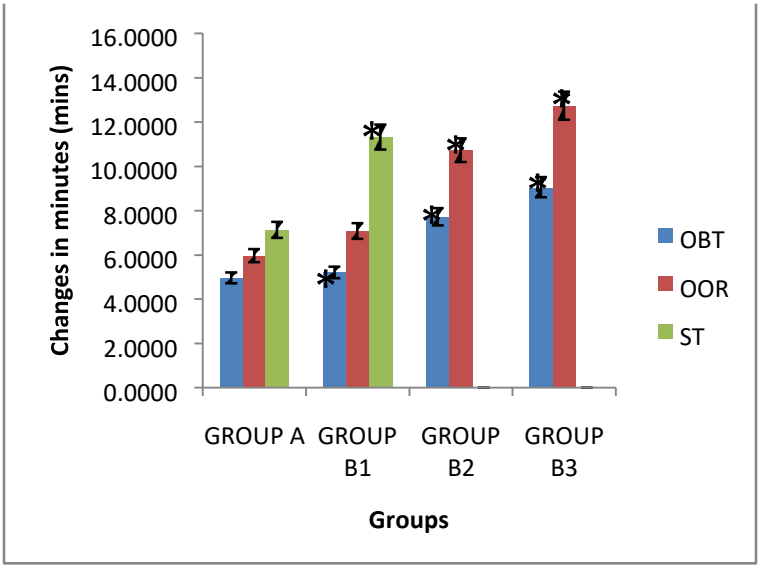

Figure 1: Effect of low, medium and high doses of Promethazine post-treatment on the onset of body tremors (OBT), onset of other reactions (OOR) and survival time (ST).

KEY:

Group A – Effects with dichlorvos 15mg/kg only.

Group B1 – Post treatment with Promethazine 0.375mg/kg Group B2 – Post treatment with Promethazine 0.75mg/kg

Group B3 – Post treatment with Promethazine 1.5mg/kg

Results are expressed as mean±SEM, the superscript (*) means significant difference with respect to Group A (dichlorvos only)at $p<0.05$.

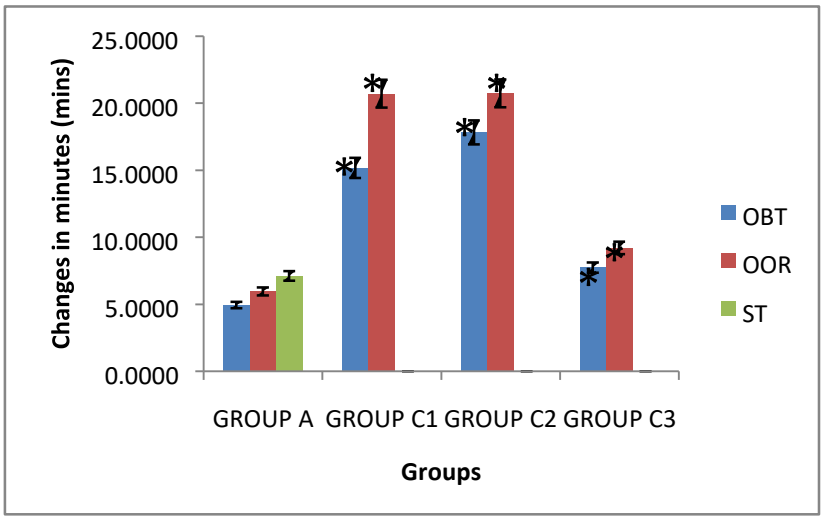

Figure 2: Effect of low, medium and high doses of Promethazine +Atropine combination on the onset of body tremors (OBT), onset of other reactions (OOR) and survival time (ST).

Key:

Group A – Effects with dichlorvos 15mg/kg only.

Group C1 – Post- treatment with Promethazine 0.375mg/kg and Atropine 1.6mg/kg

Group C2 – Post treatment with Promethazine 0.75mg/kg and Atropine 1.6mg/kg

Group C3 – Post treatment with Promethazine 1.5mg/kg and Atropine 1.6mg/kg

Results are expressed as mean±SEM, the superscript (*) means significant difference with respect to Group A (dichlorvos only)at $p<0.05$.

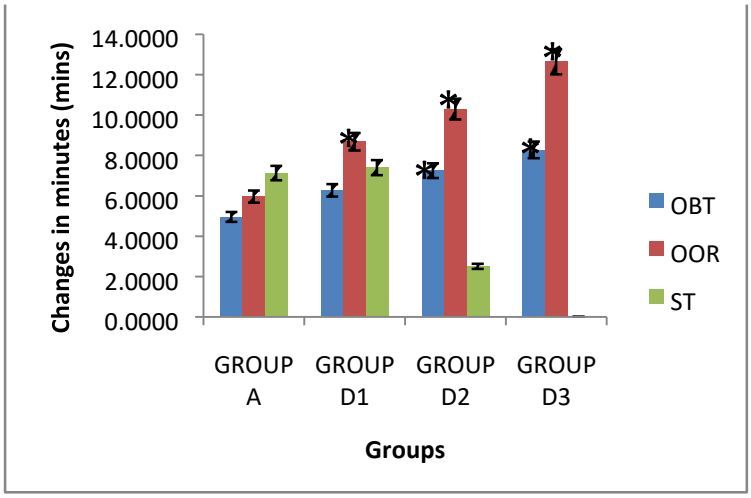

Figure 3: Effect of low, medium and high doses of Atropine post-treatment on the onset of body tremors (OBT), onset of other reactions (OOR) and survival time (ST).

Key:

Group A – Effects with dichlorvos 15mg/kg only.

Group D1 – Post-treatment with Atropine 0.4mg/kg

Group D2 – Post-treatment with Atropine 0.8mg/kg

Group D3 – Post-treatment with Atropine 1.6mg/kg

Results are expressed as mean±SEM, the superscript (*) means significant difference with respect to Group A (dichlorvos only)at $p<0.05$.

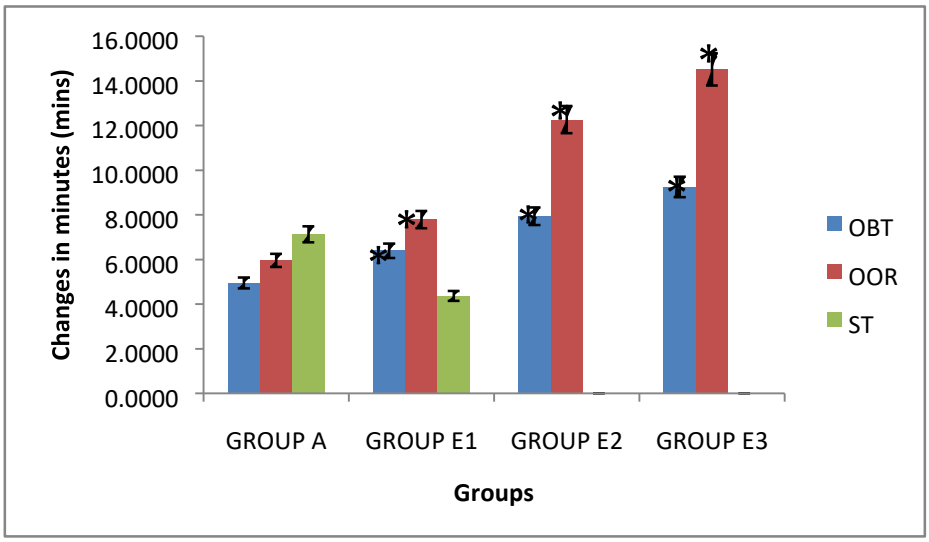

Figure 4: Effect of low, medium and high doses of promethazine pre- treatment on the onset of body tremors (OBT), onset of other reactions (OOR) and survival time (ST).

Key:

Group A – Effects with dichlorvos 15mg/kg only.

Group E1 – Pre-treatment with Promethazine 0.375mg/kg

Group E2 – Pre-treatment with Promethazine 0.75mg/kg

Group E3 – Pre-treatment with Promethazine 1.5mg/kg

Results are expressed as mean±SEM, the superscript (*) means significant difference with respect to Group A (dichlorvos only)at $p<0.05$.

Discussion

Pre-treatment with Promethazine 5 minutes before dichlorvos (15mg/kg) poisoning showed that the onset of body tremor was delayed across all the subgroups. The onset of body tremor was more evident in the subgroup given the highest dose of 1.5mg/kg.The onset of other reactions such as salivation, lacrimation, urination, straub tail was also delayed and statistically significant ($p<0.05$) when compared with the control.The mortality rate in Group E1 was 40% while Group E2 and Group E3 recorded 0%. In the subgroup with 40% mortality, the survival time was also delayed.

A comparison between the post and pre-treatment models with promethazine alone revealed that at low dose, onset of body tremors was faster in the post-treatment model while the effect on onset of other reactions was similar. The survival time was also better in the post-treatment model when compared to that of the pre-treatment model. At medium dose, onset of tremors and onset of other reactions such as salivation, lacrimation and straub

tail were similar in both treatment models. At high dose, all the parameters evaluated gave similar outcomes for both pre and posttreatment models studied.

A number of alternative therapies for organophosphate poisonings have been well explored in the past that could potentially be useful in emergency situations of antidote shortages. For instance, it has been demonstrated that glycopyrrolate, an antimuscarinic agent, is equally effective with less central nervous system side effects and a greater control of salivary, tracheobronchial, and pharyngeal secretions (Yusuf*et al,* 2000). However, glycopyrrolate does not cross the blood brain barrier and it is not expected to control central cholinergic toxicity which is a drawback to how effective glycopyrrolate is in reversing organophostate poisoning. Moreover, early death due to OP poisoning appears to be a centrally mediated process (Rajapukse*et al,* 2011).

The pharmacological evolution of antihistamines revealed three generations of products differing at the levels of specificity, half-life and duration of action, safety and toxicity. The first generation antihistamines have the advantage over the others due to their diverse pharmacological activities which are desirable in OP poisoning. The pharmacological benefits of first generation antihistamines are numerous.

They are centrally acting, exhibitantimuscarinic and anticholinergic activities, crossing the blood brain barrier, are widely available, easily accessible and less expensive with time tested safety over other antidotes. They also commendably reduce edema, which is one of the major factors in OP poisoning related death. However, their lack of receptor specificity may also impede their eventual use.

Conclusion

This study therefore concludes that Promethazine may be useful as an antidote in dichlorvos poisoning. Promethazine/Atropine combination may be more effective for antidotal treatment of dichlorvos poisoning than either alone. However, their lack of receptor specificity may limit their use due to the resultant side effects.

References

Aaron, C.K., (2001). Organophosphates and carbamates. In: Ford MD, Delaney KA, Ling LJ, Erickson T, (ed). Clinical toxicology. WB Saunders Company; Philadelphia: *pp. 819– 828.*

Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning, 2nd ed. Matthew J. Ellenhorn, Seth

Schonwald, Gary Ordog, and Jonathan Wasserberger.Baltimore, MD: Williams and Wilkins, (1997), 2047 pp., $199, ISBN 0–683-30031–8

Hutson, D.H. and Hoadley, E.C.,(1972). The metabolism of [14C-methyl] dichlorvos in the rat and mouse.Xenobiotica 2:107.

Liu, J. H., Chou, C. Y….., Liu, Y. L., (2008) Acid-base interpretation can be the predictor of outcome among patients with acute organophosphate poisoning before hospitalization. *Am J Emerg Med*. 26(1):24-30.

Lotti, M., (2001). Clinical toxicology of anticholinesterase agents in humans. In: Krieger R, (ed). Handbook of pesticide toxicology. Volume 2. Agents. 2nd ed. Academic Press; San Diego: pp. 1043–1085.

Michael, E., Nick, A. B., Peter, E., Andrew, H. D., (2008). Management of acute organophosphorus pesticide poisoning. Lancet. 16; 371(**9612**): 597–607.

Rajapakse, B. N., Thiermann, H., Eyer, P., Worek, F., Bowe, S. J….., Dawson, A. H., (2011) Evaluation of the Testmate ChE (cholinesterase) field kit in acute organophosphorus poisoning. *Ann Emerg Med*. 58(6):559564.e6.

Yavuz, Y., Yurumez, Y……, Ciftci, J., (2007) Effect of diphenhydramine on myocardial injury caused by organophosphate poisoning. *ClinTox*. 46:67-70.

Yusuf, H. R.,Akhter, H.,Rahman, M. H., Chowdhary, M. K., Rochat, R. W.,*Lancet*, (2000), 355, 12201224.Organophosphorus pesticides. In: International programme on chemical safety.