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Effect Of Pyrethroid Pesticides On Behaviour Of Adult Mice

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Abstract

Pesticides are described as chemical substances that are used for the eradication of rodents, insects, weeds and unwanted organisms. Since before 2000 BC, humans have utilized pesticides to protect their crops. Almost all conventionally grown vegetables have been sprayed with pesticides. Pyrethroid is an organic compound similar to the natural pyrethrins produced by the flowers of pyrethrums. Pyrethroids constitute the majority of commercial household insecticides. However, owing to their very nature, that is, to disable and/or kill, they still pose a threat to the nontarget species. Aim of the present study was to elicit the effect of commonly used pyrethroid pesticide on the behavior of the non target species. Adult swiss albino mice weighing 20- 25 gm (average age of 80-100 days) were used after approval of institutional ethical committee. A 2nd generation pyrethroid pesticide – Cypermethrin wss used. On performing open field exploratory and elevated plus maze test on mice, behavioural changes such as anxiety and depression were observed. Conclusion drawn by this study is that pesticides should be used with care and in recommended dose. Excess accumulation of pesticide residues in food products is harmful to us, especially to children and infants.

Keywords: Pesticides, Cypermethrin, Neurotoxicity, Behavioural changes

Introduction

A pyrethroid is an organic compound similar to the natural pyrethrins produced by the flowers of pyrethrums. Pyrethroids constitute the majority of commercial household insecticides. In the concentrations used in such products, they may also have insect repellent properties. The new generation pesticides are designed such that they are short lived in the environment and do not accumulate in the human and animal tissues. However, owing to their very nature, that is, to disable and/or kill, they still pose a threat to the nontarget species. Several pesticides used as herbicides, insecticides, and fungicides are known to be endocrine-disrupting chemicals. Mixture of pyrethroids, and other pesticides in a study showed to induce hormonal imbalances even when exposed within the reference values (Straube et al., 1999)[1]. In USA Environmental Protection Agency (EPA) must ensure that all pesticides used on food meet FQPA's (Food Quality Protection Act) stringent safety standard. Accumulated pesticide residues in food products have been related with a broad variety of human health hazards, ranging from short- term to long term toxic effects. The preventive measures to control pesticide residues in the developing countries are not implemented practically due to shortage of funds and lack of specific government regulations. The present study is planned to elicit the effect of commonly used pesticide on non-target species.

Mode Of Action

Pyrethroids are axonic excitotoxins, the toxic effects of which are mediated through preventing the closure of the voltage gated sodium channels in the axonal membranes. The sodium channel is a membrane protein with a hydrophilic interior. This interior is a tiny hole which is shaped to strip away the partially

charged water molecules from a sodium ion and create a favourable way for sodium ions to pass through the membrane, enter the axon, and propagate an action potential. When the toxin keeps the channels in their open state, the nerves cannot repolarize, leaving the axonal membrane permanently depolarized, thereby paralyzing the organism.

The first genertation pyrethroids , introduced by a team of Rothamsted Research scientists in the 1960s, include bioalletrin, tetramethrin, resmethrin and bioresmethrin. They are more active than the natural pyrethrum but are unstable in sunlight.

By 1974, the Rothamsted team had discovered a second generation of more persistent compounds : permethrin, cypermethrin and deltamethrin. They are more resistant to degradation by light and air, thus making them suitable for use in agriculture, but they have significantly higher mammalian toxicities.

Material And Methods

Animal Used

Adult swiss albino mice weighing 20- 25 gm (average age of 80-100 days) are used after approval of institutional ethical committee. These animals are obtained from animals house of the Department of Anatomy, IMS, BHU, Varanasi.

Drug Used

A 2^{nd} generation Pyrethroid pesticide – Cypermethrin is used.

Methodology

LD 50 (lethal dose 50) represents the amount of drug, which killed 50% of population of animal species employed for the test. The oral LD 50 dose of cypermethrin is found to be 3ml/kg bw of 25% of drug diluted in distilled water. In the present study low doses of drug are used, which are 1/5 and 1/10 of LD 50 dose.

The mice are randomly assigned into four groups. Groups I is control group while II to IV are treated groups. Group I is given 3 ml/kg/bw of tap water throughout the duration of the experiment.

Groups II - IV are further subdivided into two subgroups, respectively, each of six animals. Distilled water is used to dilute the drug to concentrations of 2.5% and 5%. The mice in Group IIa, IIIa, and IVa are treated with 3 ml/kg/bw of 5%, while those in IIb, IIIb, and IVb with 3 ml/kg/bw of 2.5% of the agent orally for a duration of 10, 15 and 20 days each.

Result

Animal behaviour study

After the daily administration of the chemicals to the animals, behaviours such as aggressiveness, suspended tail, erected furs, drowsiness and itching were observed and recorded for up to 2 h post administration.

Behaviour test

Effect of cypermethrin on Elevated Plus Maze Test:

This is an important test for observing behavioural abnormalities like anxiety and depression in the experimental animals. Elevated plus maze test consisted of two open arms (30×5 cm, surrounded by a 0.25 cm-high border) and two closed arms (30×5 cm, surrounded by 15 cm-high walls), with the two pairs of identical arms, which emerged from a central platform (5×5 cm), positioned opposite each other. The apparatus was elevated 45 cm above the floor and was made up of plywood. The test was initiated by placing a mouse on the central platform of the maze, facing one of the open arms, and letting it move freely. Mouse behaviour was continuosly recorded for a session of 5 minutes. The maze was carefully cleaned with alcohol after every test. (1) Closed arm duration: the total amount of time the mouse spent in the closed arms. (2) Open arm duration: the total amount of time the mouse spent in the open arms. (3) Closed arm entry: the frequency of mouse entry with all four paws into the closed, protected arms. (4) Open arm entry: the frequency of mouse entry with all four paws into the open, unprotected arms. Table 1.1 shows values obtained for control and treated groups with respect to different variables. Data and corresponding student t test statistical analysis is summarized in table 1.2. For closed arm time, we observed that in comparison between control and treated groups a highly significant correlation was shown ($p<0.001$). Overall comparison of these groups for closed arm time was found to be statistically significant ($p<0.05$).

For open arm time, we observed that on comparing control group with treated groups, all treated groups had significant correlation with control group

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($p<0.001$) except group IIb ($p>0.05$) and group IIIb ($p>0.05$). Overall p value in closed arm time is found to be statistically significant ($p<0.05$).

For frequency of entry in closed arms parameter, we observed that on comparing control with treated groups, all the values came to be significant ($p<0.001$) except for group IIb and IIIb ($p>0.04$). Overall p value for this parameter was found to be statistically significant ($p<0.05$).

For frequency of entry in open arms, on comparing control group with treated groups, all the values showed significant correlation ($p<0.05$). Overall p value for this parameter was found to be statistically significant ($p<0.05$).

So plus maze test has shown that control group is found to spend significantly more time in open arms and has more number of entries in open arms as compared to treated groups. Non- significant correlation of groups IIb and IIIb with control group for most of the parameters shows that cypermethrin if given in lesser dose and for lesser duration is not harmful.

Table 1.1 **Elevated plus maze test**

	Close arm duration	Open arm duration	Entry close arm	Entry open arm
GroupI(Control)	1.87±0.66	3.12±1.11	3.67±1.45	17.89±2.89
Group IIa	3.88±0.45	1.11±0.34	9.36±1.23	6.45±1.22
Group IIIa	4.16±0.67	0.83±0.45	12.11±1.23	3.42±1.21
Group IVa	4.51±0.12	0.48±0.39	12.28±1.39	2.11±1.11
Group IIb	2.87±0.56	2.12±0.34	4.34±1.12	13.56±2.56
Group IIIb	2.89±0.22	2.11±0.38	5.67±1.49	9.12±2.12
Group IVb	3.76±0.21	1.23±0.34	7.29±1.45	6.47±1.23

Table 1.2 Comparison between groups of plus maze test by Student 't' test

Comparison	Close arm duration	Open arm duration	Entry close arm	Entry open arm
Controls & IIa	<0.001	<0.001	<0.001	<0.001
Controls & IIIa	<0.001	<0.001	<0.001	<0.001
Controls & IVa	<0.001	<0.001	<0.001	<0.001
Controls & IIb	0.017	0.061	0.391	0.020
Controls & IIIb	0.004	0.061	0.040	<0.001
Controls & IVb	<0.001	0.003	<0.001	<0.001
Over all*	<0.001	<0.001	<0.001	<0.001

Overall value is calculated by student 'f' test.

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Discussion :

Preliminary student t test analyses performed on the mean obtained for the elevated plus maze test clarified the significance of various parameters observed on comparing the control and treated groups. Consistent with previous studies our study confirmed the sensitivity of plus maze test for analyzing behavioural abnormalities like anxiety and depression in the experimental animals. (Cole J.C and Rodgers R. J, 1995 , A. Dalvi and Rodgers R. J, 2001, Sheila L. Handley and Siddika Mithani 1984)[2-5]. Numerous studies have investigated the toxic effects of cypermethrin in mammals, revealing increase in salivation, lack of coordination, muscle tremor and convulsions (Manna S.,et al., 2005). These signs of toxicity indicate that the target for this compound is the central nervous system in mammals.(Manna S.,et al., 2005 and Macan J.,et al.,2006)[6,7] as observed in the present study.

Cypermethrin when given to white rabbits showed reduced feed and water intake in treated animals as compared to control groups.(Lakkawar AW.,et al., 2004)[8]

A health survey on 199 workers engaged in dividing and packaging pyrethroids was conducted in Chinese Academy of preventive medicine, Beijing, China. Burning sensations and tightness or numbness on the face appeared in two thirds of the subjects and one third had sniffs and sneezes. Abnormal facial sensations, dizziness, fatigue, and miliary red papules on the skin were more evident in summer than in winter. (F HE,et.al., 1988)[9]

Developmental neurotoxicity of Pyrethroid insecticides in Zebrafish embryos was studied in Department of Biochemistry and Microbiology, Rutgers, The State University of New Jersey . Pericardial edema, craniofacial malformations, curvature of the body axis and spasms were observed as teratogenic lesions in Zebrafish. (Amy DeMicco, et al., 2009)[10]

The neurotoxic effects of Pyrethroid pesticides were reviewed at School of Biomedical Sciences, University of Nottingham Medical School, Queen's Medical Centre, Nottingham. these insecticides cause developmental neurotoxicity and neuronal death in mammals was suggested.(David E. Ray , et.al., 2006)[11]

Embryotoxic and teratogenic effects of Pesticides in Chick embryos were studied at Department of Zoology, Faculty of Science, The Maharaja Sayajirao University of Baroda, Vadodara, India. Pyrethroids induced explicit alterations in the embryonic growth and development was observed in chick embryos which resulted in malformations particularly to the axial and appendicular skeletal structures. (Gowri K. Uggini, et.al., 2010)[12]

A histomorphologic analysis of pyrethroid pesticides on cerebrum and cerebellum of adult albino rats was conducted in Department of Human Anatomy and Cell Biology, Delta State University, Abraka, Delta State, Nigeria. Behaviors exhibited by the animals included itching, twitch contraction, dilation of pupils, erected furs, tail suspension and increased salivation. Histological examination of the brain tissues revealed mild to marked distortion of the cyto-architectural patterns with multifoci of necrosis, severe gliosis involving predominantly astrocytes and olingodendrocytes both in the cerebral and cerebellar tissues.(Odokuma Emmanuel Igho, et.al., 2014)[13]

Present study also suggested behaviors such as aggressiveness, suspended tail, erected furs, drowsiness and itching in adult mice after treatment with cypermethrin.

A lot of external morphological deformities and visceral malformations in the offspring pubs of exposed male and pregnant female wistar rats were observed, which signify the potential of such insecticide to induce reproductive toxicity and teratogenesis. (M.E Assayed,et.al., 2010)[14]. This study was conducted at the Department of Forensic Medicine and Toxicology, Faculty of Veterinary Medicine, Menoufiya University, Sadat City Branch, Egypt.

Conclusion

It is clear from the present study that pyrethroid pesticides have neurotoxic effect on non-target species if not used in recommended dose. Further studies are required to elucidate its effect on other species as well.

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References

1. Straube E, Straube W, Kru¨ger E, Bradatsch M, Jacob-Meise M, Rose HJ. 1999. Disruption of male sex hormones with regard to World Health Organization. 2007. Principles for evaluating health risks in children associated with exposure to chemicals. Environ. Health Criteria 237:1–351.
2. Cole JC, Rodgers RJ. Ethological comparison of the effects of diazepam and acute/chronic imipramine on the behaviour of mice in the elevated plus-maze. Pharmacol, Biochem Behav 1995;52:473 ± 8.
3. Dalvi A, Rodgers RJ. Behavioural effects of diazepam in the murine plusmaze: flumazenil antagonism of enhanced head-dipping but not the disinhibition of open arm avoidance. Pharmacol, Biochem Behav 1999;62:727 ± 34.
4. Dalvi A., Rodgers RJ. Anxiolytic effects of valproate and diazepam in mice are differentially sensitive to picrotoxin antagonism. Pharmacol, Biochem and Behav 68 (2001) 23±32 Sheila L. Handley and Siddika Mithani. Effects of alpha-adrenoceptor agonists and antagonists in a maze-exploration model of 'fear'-motivated behavior. Naunyn-Schmiedeberg's Arch Pharmacol (1984) 327:1 -5
5. Sheila L. Handley and Siddika Mithani. Effects of alpha-adrenoceptor agonists and antagonists in a maze-exploration model of 'fear'-motivated behavior. Naunyn-Schmiedeberg's Arch Pharmacol (1984) 327:1 -5
6. Manna S, Bhattacharya D, Mandal TK, Das S. Neuropharmacological effects of alfa-cypermethrin in rats. Indian J. Pharmacol. 2005;37:18–20. [Google Scholar]
7. Macan J, Varnai VM, Turk R. Health effects of pyrethrins and pyrethroids. Arh Hig Rada Toksikol. 2006;57:237–43. [PubMed] [Google Scholar]
8. Lakkawar AW, Chattopadhyay SK, Somuanshi R. Experimental cypermethrin toxicity in rabbits- a clinical and patho-anatomical study. Folia Vet. 2004;48:3–8. [Google Scholar]
9. F HE, J SUN. Effects of pyrethroid insecticides on subjects engaged in packaging pyrethroids. Br. J. ind. Med. 1988;45:548-551
10. Amy DeMicco, Keith R. Developmental Neurotoxicity of Pyrethroid Insecticides in Zebrafish Embryos. Toxicol Sci.113(1), 177–186 (2010)
11. David E. Ray , Jeffrey R. Fry. A reassessment of the neurotoxicity of pyrethroid insecticides. Pharmacol. Ther. 111 (2006) 174 – 193
12. Gowri K. Uggini, Prabhudas V. Patel. Embryotoxic and Teratogenic Effects of Pesticides in Chick Embryos: A Comparative Study Using Two Commercial Formulations, Published online 6 July 2010 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/tox.20627
13. Igho O.E, Afoke I.K. A histomorphologic analysis of pyrethroid pesticide on cerebrum and cerebellum of adult albino rats. J Exp Clin Anat | Vol. 13 | Issue 2 | Jul-Dec 2014
14. Assayed M.E, Khalaf A.A. Protective effects of garlic extract and vitamin C against in vivo cypermethrin-induced teratogenic effects in rat offspring. Food Chem.Toxicol 48 (2010) 3153–3158

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