Endocrine disturbances in induced Fenvalerate toxicity in rats and its amelioration with *Withania somnifera*

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Abstract

The present study was carried out to investigate endocrine disturbances in female rats with 20% EC fenvalerate. Significant (P<0.05) decrease in T3, T4 and E2 levels in all fenvalerate treated groups when compared to control groups. In between groups significant variation was observed. Significant improvement was observed only in lower dose levels of toxin with ameliorating agent.
Keywords: Endocrine, Toxicity, Fenvalerate, Wistar Rat, Amelioration.

Introduction

Fenvalerate is a synthetic pyrethroid insecticide commonly used in agriculture and other domestic applications due to its high insecticidal activity and low mammalian, avian and phytotoxicities (Giri et al., 2002). Although fenvalerate is considered to have low acute toxicity to mammals, it is having severe neurotoxic effects and estrogenic activity causing endocrine disorders. Hence fenvalerate is enlisted as one of the neuroendocrine disrupting chemicals (EDCs) and has aroused world wide concern. EDCs are known to act at multiple sites through multiple modes of action, but the mechanism of action is poorly understood (Junhe et al., 2006). Persual of literature revealed limited information regarding toxicopathologicaleffects of fenvalerate with special reference to endocrine system. (Mani et al., 2002). Keeping in view of its wide spread use, the present study was taken up to investigate endocrine disturbances.

Materials and Methods

Studies were conducted on healthy adult female wistar rats weighing more than 150g. All the rats were housed in standard polypropylene rat cages (Three rats / cage) at 25o ±10 C and a 12:12 hour interval light / dark cycle through out the experimental period for 6 weeks by taking necessary precautions. During the experiment, they were maintained under standard laboratory hygienic conditions, providing laboratory animal feed and water ad libitum. The approval of the institutional animal ethical committee was obtained prior to commencement of the experiment. After 10 days of aclimatization the animals were randomly assigned to experimental group. Fenvalerate (20% EC) was given orally to rats at the dose rate of 1/10 LD 50 (42.5 mg/ Kg b.wt), 1/20 LD 50 (21.25 mg/ Kg b.wt) and 1/40 LD 50 (10.125 mg/ Kg b.wt) respectively to the groups II, III and IV. In addition to fenvalerate, ashwagandha was given orally at a dose rate of 200 mg/ Kg b.wt. to the groups V, VI and VII. Group I and VIII were kept as oil control and ashwagandha control respectively. Serum was collected at every fortnight intervals to study endocrine disturbances.

Results

Serum samples were collected from all groups at each sacrifice and were used for the estimation of T3 , T4 and TSH using kit obtained from Omega Diagnostics, Alva (Scotland) and Estrogen (E2) using C.L.I.A. technique.

Thyroid Hormone:

T3 (Tri iodo thyronine) : The mean values of T3 levels (ng / ml) in groups I to VIII were 1.79, 0.39, 0.54, 0.68, 0.66, 0.89, 1.49 and 3.57 respectively and given in Table 1. There was a significant (P<0.05) decrease in T3 levels in all fenvalerate treated groups when compared to control groups. In ameliorated groups no significant difference was observed except group VII where significant increase was when compared corresponding toxin treated group (IV).

Tetra iodo thyronine (T4) or Thyroxine: The mean values of T4 levels (ng / ml) in groups I to VIII were 134.83, 36.42, 65.42, 105.75, 64.43, 79.0, 107.67 and 164.92 respectively and given in Table 2. There was a significant (P<0.05) decrease in T4 levels in all fenvalerate treated groups when compared to control

Table-1: Mean values of T3 levels (ng / ml) in rats of different experimental groups.

Group	Age in weeks			Mean ± SE
	2	4	6	
G1	1.79	1.52	2.1	1.79 ± 0.17b
G2	0.58	0.15	0.45	0.39 ± 0.13a
G3	0.6	0.52	0.49	0.54 ± 3.28a
G4	0.82	0.69	0.53	0.68 ± 8.39a
G5	0.89	0.45	0.62	0.66 ± 7.94a
G6	1.21	0.71	0.76	0.89 ± 0.22a
G7	1.36	1.6	1.52	1.49 ± 7.05b
G8	2.89	3.6	4.23	3.57 ± 0.39c

Table-2: Mean values of T4 levels (ng / ml) in rats of different experimental groups.

Group	Age in weeks			Mean ± SE
	2	4	6	
G1	130	138	136.5	134.83 ± 2.45d
G2	38	33.75	37.5	36.42 ± 1.34a
G3	75	80.25	81	65.42 ± 15.21b
G4	107.25	105	105	105.75 ± 0.75c
G5	63.5	64.55	65.25	64.43 ± 0.51b
G6	79.5	78	79.5	79.00 ± 0.50b
G7	107	107.25	108.75	107.67 ± 0.55c
G8	155	169.5	170.25	164.92 ± 4.96e

Mean values with different subscripts differ significantly (P<0.05), One way ANOVA, SE –Standard error

groups. In ameliorated groups no significant difference was observed except group VII where significant increase was when compared corresponding toxin treated group (IV).

Thyroid stimulating hormone (TSH): The mean values of TSH levels (µ IU / ml) in groups I to VIII were 0.1, 0.12, 0.3, 0.3, 0.17, 0.3, 0.3 and 0.17 respectively. There was no significant (P<0.05) difference in TSH levels of any groups.

Estrogen (E2): The mean values of E2 levels (pg / ml) in groups I to VIII were 153.07, 130.86, 140.44, 143.89, 79.08, 127.09, 132.42 and 140.91 respectively. The detailed data was presented in Table 3. There was a significant decrease in the serum estrogen hormone levels in all the experimental groups compared to the oil control. In ameliorated groups there was significant decrease compared to toxin treated groups.

Discussion

Significant reduction in T3 and T4 levels was observed in all fenvalerate fed and ameliorated groups without any significant change in TSH levels and it was in accordance with Akhtar et al. (1996). In contrary Kaul et al. (1996) observed significant increase in T3 and T4 levels. Significant increase in T3 levels was noticed in lower dose levels of fenvalerate and ashwagandha treated groups (group VII) when compared to corresponding toxin treated group and it might be due to efficacy of ashwagandha in regulating thyroid function (Panda and Kar, 1997 and 1998) at lower doses of toxin.

In the present study significant reduction in estrogen levels was observed in all fenvalerate and ameliorated groups. This was in accordance with Garg et al. (2004). In contrary Ping et al. (2006) observed increased estrogen levels. Pyrethroid insecticides mimic the hormone estrogen and proliferation is another characteristic feature of estrogen. Go et al. (1999) tested a series of synthetic pyrethroids to determine their ability to disrupt estrogen signaling in experiments using a cell culture line of human breast cancer cells (MCF-7), using expression of pS2 and MCF-7 cell proliferation assays. It might be one of the reasons for proliferation of epithelial cells in organs like liver, lung, intestine and uterus that were observed in the present study. Keeping in view, further research is needed to elucidate chronic toxicity of fenvalerate, the underlying interruption mechanism in estrogen and thyroid homeostasis and its downstream events. In addition studies are deserved by using different herbal products in combination for amelioration.

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Table-3: Mean values of E2 levels (pg / ml) in rats of different experimental groups.

Group	Age in weeks			Mean ± SE
	2	4	6	
G1	147.6	152.3	159.31	153.07±3.4e
G2	136.2	128.72	127.65	130.86±2.69b
G3	141.2	137.82	142.31	140.44±1.35cd
G4	143.8	142.6	145.28	143.89±0.77d
G5	89.21	78.12	69.92	79.08±5.59a
G6	131	128.61	121.61	127.09±2.79bc
G7	136.28	132.31	128.68	132.42±2.19bc
G8	141.28	142.69	138.76	140.91±1.15f

Mean values with different subscripts differ significantly ($P<0.05$), One way ANOVA, SE –Standard error

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