JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

TRAMADOL HYDROCHLORIDE INDUCED ALTERATIONS IN REPRODUCTIVE PHYSIOLOGY OF ALBINO MICE

[1]R. L. Rahatgaonkar
Department of Zoology,
Shri R.L.T. College of Science, Akola

Abstract: The present study was carried out on male Albino mice to observed the adverse effects of chronic dose of Tramadol Hydrochloride at a dose of 0.05mg/kg administered intramuscularly daily once for 60 days. Alterations in tissue biochemical parameters like protein, cholesterol, ascorbic acid, glycogen, acid phosphatase were investigated. Alterations in body and tissue weight were also recorded. Long term administration of tramadol hydrochloride significantly lowered down the tissue weight as well as proteins, ascorbic acid and acid phosphatase etc in tissue. However, the level of tissue cholesterol was increased in testis. The study suggests that the repeated use of Tramadol hydrochloride may pose anti-androgenic effects.

Key words: Tramadol Hydrochloride, Biochemical parameters, anti-androgenic effects.

INTRODUCTION

Addiction to narcotic drugs is common now a days and several investigators have reported that these drugs inhibit gonadotrophin secretions and causes sterility in female, where as in males, they reduced the level of plasma testosterone and affect the secretary functions of accessory sex organs resulting the condition similar to castration. Wilkinson and Youngali(1986),Johnston et.al (1994) and Hopwood et.al. (1998). Sreenivasan and Vijayan(1996) have demonstrated that opiates and opioids exert an inhibitory action on the intramuscular metabolism. Opioids and analgesics are known to modify the gonadotrophin secretion in rats. Karla(1984) and Malvan(1986).According to Barb et.al(1988) and Evans et.al (1993)the opioid drugs being CNS influencing drugs inhibit the release of FSH and LH from pituitary by acting through hypothalamus , blocking the neural stimulation to the gonadotropins releasing hormone resulting into the alterations in biochemical parameters of reproductive physiology including morphological changes. Therefore, the present study was undertaken to find out the impact of administration (im) of Tramadol Hydrochloride on reproductive physiology of male albino mice.

MATERIALS AND METHODS

The present study was carried out on male swiss albino mice weighing about 30±2 g. They were kept under standard laboratory condition with proper diet and water *ad libitum*. The mice were divided in to two groups i.e. Group I : Control : were administered (im) with 0.2ml saline water as vehicle daily once up to 60 days and Group II : Experimental : were administered (im) with 0.05 mg/kg dose of Tramadol Hydrochloride daily once up to 60 days. Only healthy mice were used for experimental purpose. After 30 and 60 days of treatment control and experimental male mice were weighed and then sacrificed and dissect out to remove testis, epididymis and seminal vesicle. The tissues removed were blotted quickly and weighed. The tissue biochemical parameters like cholesterol were estimated by the method of Liberman Burchard (1959), proteins by the method of Lowry et.al. (1951), Glycogen and Ascorbic acid by Montgomery(1957), Acid Phosphatase by Fiske and Subbarrow(1925).

RESULTS AND DISCUSSION

Table:1 Body weight and organ/tissue weight of Albino mice administered with Tramadol Hydrochloride for 60 days

S.N	Body weight and organ/tissue weight	Days of Treatment		
		Control/Expt.	30 Days	60 Days
1	Body Weight(g)	Control	32.08±1.12	34.28±1.06
		Experimental	29.60±1.56	26.08±0.92
2	Testis (mg)	Control	118.03±6.35	129.65±3.37
		Experimental	96.11±4.79	79.43±2.78
3	Seminal Vesicle (mg)	Control	22.90±1.22	25.64±5.58
		Experimental	18.69±1.10	24.44±5.46
4	Epididymis (mg)	Control	21.38±3.28	25.10±4.84
		Experimental	22.77±2.27	27.67±2.70

Results are means ± of SE of six replicates.
Figures in parenthesis indicate percentage change over control.

Table:2 Alterations In Tissue Protein and Cholesterol (mg/gm) of Albino mice administered with Tramadol Hydrochloride for 60 days

S.N	Biochemical Parameter	Tissue	Days of Treatment		
			Control/Expt.	30 Days	60 Days
1	Protein	Testis	Control	13.39±1.32	17.36±0.95
			Experimental	13.06±2.00	16.82±0.80
2		Seminal Vesicle	Control	14.02±1.04	14.92±1.10
			Experimental	12.84±0.96	11.84±0.98
3		Epididymis	Control	16.08±1.12	17.09±0.95
			Experimental	14.75±0.84	14.56±1.01
4	Cholesterol	Testis	Control	9.68±1.04	10.07±1.01
			Experimental	10.94±0.97	12.14±1.12
5		Seminal Vesicle	Control	8.12±1.05	8.54±1.10
			Experimental	7.59±0.56	7.05±0.85
6		Epididymis	Control	9.56±1.08	10.01±0.79
			Experimental	8.45±1.02	9.75±1.65

Results are means ± of SE of six replicates.
Figures in parenthesis indicate percentage change over control.

Table:3 Alterations In Tissue Glycogen, Ascorbic Acid (mg/gm) and Acid Phosphatase(IU) of Albino mice administered with Tramadol Hydrochloride for 60 days

S.N	Biochemical Parameter	Tissue	Days of Treatment		
			Control/Expt.	30 Days	60 Days
1	Glycogen	Testis	Control	13.39±1.32	17.36±0.95
			Experimental	13.06±2.00	16.82±0.80
2		Seminal Vesicle	Control	14.02±1.04	14.92±1.10
			Experimental	12.84±0.96	11.84±0.98
3		Epididymis	Control	16.08±1.12	17.09±0.95
			Experimental	14.75±0.84	14.56±1.01
4	Ascorbic Acid	Testis	Control	10.08±1.07	12.07±1.10
			Experimental	8.65±0.97	7.14±1.04
5		Seminal Vesicle	Control	8.12±1.05	8.54±1.10
			Experimental	7.59±0.56	7.05±0.85
6		Epididymis	Control	9.56±1.08	10.01±0.79
			Experimental	8.45±1.02	9.75±1.65
7	Acid	Testis	Control	5.02±1.01	5.46±1.09

	Phosphatase		Experimental	4.65±0.97	3.14±0.56
8		Seminal Vesicle	Control	3.12±0.96	3.21±1.05
			Experimental	3.04±0.52	2.95±0.80
9		Epididymis	Control	4.18±0.17	4.80±0.32
			Experimental	1.45±0.18	0.95±0.14

Results are means ± of SE of six replicates.
Figures in parenthesis indicate percentage change over control.

No mortality was observed during the experimental period. Body weight was recorded regularly. The mice administered with vehicle(Group I) showed steady gain in body weight up to 60 days, whereas the mice treated with Tramadol hydrochloride showed loss in body weight (Table-1) due the anti-androgenic activity of Tramadol hydrochloride with their anti-anabolic action. A similar observation was reported in morphine and nicotine treated albino rats by Chinoy and Seethalakshmi (1978).The Tramadol hydrochloride administered male albino mice showed significant increase in cholesterol content in testis than control mice, however after 60 days treatment the cholesterol content decreases in epididymis and seminal vesicle. (Table-2). High accumulation of cholesterol content in the testis of drug treated mice may be attributed to the lowered steroidogenesis, which is dependent on availability of pituitary gonadotropins stated by Hopwood et.al.(1998). This observations is supported by Kasson and Hsuch(1985) and Meyer and Curr (1987) on the similar studies with nicotine. Long term administration of Tramadol hydrochloride (im) lowered the protein content of all organ under study, when compared with control mice, similar result were recorded by Chinoy and Seethlakshmi(1978) and Means(1975). According to them decrease in organ weight and low protein content indicates the retarded testicular growth as FSH is essential for protein synthesis in gonads. Glycogen, a stored form of glucose, plays a crucial role in male reproductive physiology by providing energy for various cellular processes, including spermatogenesis, steroidogenesis, and cell differentiation. Its metabolism is essential for maintaining testicular health and function. In the present investigation, the level of tissue glycogen decreases in epididymis and testis after 60 days of drug administration (Table-3) However, the decrease in level of free ascorbic acid in seminal vesicle and epididymis as compared to testis due to increased oxidative stress and the drug's impact on antioxidant systems can induce oxidative stress, leading to the generation of reactive oxygen species (ROS). These ROS can damage cells and tissues, including those in the reproductive organs. Ghada Abdel Kader et.al (2021). Both Acid Phosphatase and Alkaline Phosphatase are important enzymes in the male reproductive system, with roles in sperm maturation, cellular maintenance, and response to various factors like toxins. In the present investigation the concentration of tissue Acid Phosphatase was found to be decrease after 60 days of drug treatment (Table-3).This is in accordance with the method of nourishment of sperms Patil et.al(1998) and Chinoy and Seethalakshmi(1978). Similar findings was reported by Ghosh et.al(1990).

CONCLUSION

The present investigation indicate that the Tramadol hydrochloride drug has deleterious effects on the reproductive organs of albino mice and causes alterations in tissue biochemical parameters such as protein, cholesterol, ascorbic acid, glycogen and acid phosphatase indicate its anti-androgenic effects. However, less depletion of ascorbic acid in epididymis and seminal vesicle in drug treated mice indicating its role in preventing more deleterious effects of the Tramadol hydrochloride.

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