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Effects of prazosin in body weight and some hormones (TSH, T3, & T4) in rats (*Rattus* norvegicus)

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Abstract: This study was conducted at the laboratory of department of biology, faculty of science/university of Kufa , 40 male rats that was used.The present study was conducted to investigate the effect of Prazosin hydrochloride on some organs in male rats (*Rattus*norvegicus), after administration of prazosin hydrochloride at three doses (25,50,75)mg/kg b.wt. for eight-weeks, prazosin decreased the body weight from (22.00±3.74 to10.00±0.45), liver weight from (2.91 ±0.87 to4.43±0.263), and kidney weight from (1.14 ±0.116 to1.85±0.040). prazosin increased the thyroid stimulating hormone (TSH) from (0.7910±0.042 to 5.4885±0.066), thyroxine (T4) from (7.3875±0.2264 to 14.4575±0.147), and decreased triiodothyronine(T3) from (3.8275±0.1109 to 0.18153±0.007).
Keyword: alpha blocker, prazosin hydrochloride, Thyroid gland.

Introduction

Alpha blocker drugs:

Alpha blockers are characterize as one of the most therapies that used for treatment of several condition such as Raynaud's disease, hypertension, scleroderma , and one of the most therapies for treated chronic pelvic pain syndrome/ chronic prostatitis (CPPS/CP) and also be used to treat anxiety and panic disorder such as generalized anxiety, posttraumatic stress disorder (PTSD)[1]. Many reports suggested that certain patients might benefit from treatment with α-blocker drugs. Lately alpha blocker had side effects that severely limited their utility[2].

Prazosin hydrochloride is an alpha blocker work by blocking nerve ending called α-blockers. This will relaxes the smooth muscle of the urinary bladder and prostate. Prazosin substantially reduced trauma-related nightmares and globally rated severity of prosttraumatic stress disorder (PTSD) , it is also used to treat benign prostatic hyperplasia (BPH) in men which can be recognized by enlargements of prostate which causes difficulties with urination[3,4].Prazosin was discovered by investigation team led by at beginning as potential antihypertensive drug after that it was used to treat several disease such as lower urinary tract symptoms associated with urine retention and benign prostatic hyperplasia.

Prazosin is also beneficial in treating urinary hesitancy associated with prostatic hyperplasia, blocking alpha-1 receptors, which control constriction of both the prostate and urethra. While not a first line choice for either hypertension or prostatic hyperplasia, it is a choice for patients who present with both difficulties concomitantly[5].This medication has shown to be effective in treating severe nightmares in children and people with PTSD symptoms[6]. Veterans have also been treated successfully at Seattle's VA Puget Sound Health Care System (VAPSHCS) for sleep disturbance related to PTSD. Doses are lower for this purpose than for control of

blood pressure[6]. Alpha -agonists are known to excite thyroid hormone secretion[7], the medical efficiency of, alpha-adrenergic blockade in the handling of thyrotoxicosis ,results from a decline in peripheral adrenergic appearances[8]. The usage of ,alpha-blockers in the treatment of hypertension does affect thyroidfunction.

Methods:

Preparation of Prazosin Hydrochloride (Miniperss) solution:

The Prazosin was obtained from (pfizerlab, Germany) at concentration (5mg/kg),the Prazosin hydrochloride dose (25,50,75 mg/kg) were prepared by dissolving (10)g from Prazosin in (100)ml from distill water to make stock solution and different concentration from stock solution were prepared.

Experimental animals:

40 rats (*Rattus*norvegicus) of male sex weighing (210-290)g ,animals were housed in aplastic caged, under standard environment condition(temperature 25-28 ºC and 12 hr,light-dark cycle) and allowed access to standard laboratory water and feed. They were divided in to four groups[10] animals for each group.

Group 1: as a control, animals were treated with (0.5 ml/kg) of distilled water, give orally.
Group 2: The animals were treated with (0.5 ml) of volume dose from prazosin at concentration25 mg/kg for 8 weeks, give orally.
Group 3: The animals were treated with (0.5 ml) of volume dose from prazosin at concentration50 mg/kg for 8 weeks, give orally.
Group 4: The animals were treated with (0.5 ml) of volume dose from prazosin at concentration75 mg/kg for 8 weeks, give orally.

Measurement of weights:

The weight of male rats were measured depending on[9].

Determined of thyroid function test:

Determination of triiodothyronine (T3) and thyroxin (T4):

We determined by using elisa kits to determined T3,T4 and TSH in serum[10], it is supplied by Sigma-aldrich from (U.S.A).

Determination of calcitonineanderythropoietin

We determined the calcitonin in the serum of rats by using calcitonin& erythropoietin kits from Kamya biomedical company, the kit is a competitive inhibition of the immunoassay technique for the in vitro quantitative biological fluids.

Bio statistical analysis:

The results were expressed as (mean ± standard deviation), t- test was used for the comparison between control and other groups in the measured parameters[11].

Results and Discussion:

Effect of prazosin on the weights of body, liver and kidney:

The result in table (1) when compared that treated a male rats with prazosin at different doses (25, 50, 75mg/kg b.wt.) with control group shows significant decrease in the of body weight through the period of experiment .

Liver and kidney weight were increased in animals treated with Prazosin than in control animal. The results revealed no significant cdifferences in the weights of liver and a significant change at (P>0.05) in the weight of kidney of group that's give 25 mg/kg b.wt. of Prazosin but groups gives Prazosin 50 and 75mg/kg

b.wt. that result is a significant increase in liver and kidney weights when compared with control group, This decrease in weight of body in case of hyperthyroidism, increased in levels of T3,and T4the speeding up of the metabolism, lost weight without dieting. The heart rate and blood pressure may lead to, heart rhythms may be abnormal, and patients may sweat excessively, feel nervous and anxious, have difficulty sleeping[12,13],this decrease in body weight may be attributed to many factors such as ; the deficiency in testosterone level , testosterone plays a key role in the development of male reproductive tissues such as the testes and prostate as well as promoting secondary sexual characteristics such as increased muscle, bone mass and growth of body-hair[14,15]. In addition, testosterone is essential for health and wellbeing[16] as well as the prevention of osteoporosis[17].

Prazosin also found to cause many disorders such as asthenia, dizziness, drowsiness, headache, insomnia, syncope, vertigo , chest pain orthostatic hypotension, pharyngitis, diarrhea, general weakness and nausea[18]. All of these may be the cause of decrease in body weights of treated animal**.**

Table 1: Effect of prazosin on weights of male rats and their organs (liver &kidney) for 8 weeks.

Groups	Changes in body weight (gm)	Liver weight %	Kidney weight %
Control	22.00±3.74	2.91 ±0.87	1.14 ±0.116
PZ. 25 mg/kg	*15.00±0.32	3.11 ±0.337	*1.33 ±0.71
PZ. 50 mg/kg	*13.500±0.362	*3.7 ±0.337	*1.45 ±0.037
PZ. 75 mg/kg	*10.00±0.45	*4.43±0.263	*1.85±0.040
L.S.D. 0.05	2.436	0.903	0.451

No. of animals=10 for each group, Values are mean ±SE. *Significantly different at $p<0.05$.

Effect of prazosin on thyroid hormones (T3) , (T4) and TSH:

The results in figures (1) showed a significant decrement ($p<0.05$) in level of T3 and a significant increment ($P>0.05$) level of T4 in serum with in group treated with Prazosin for 8 weeks in contrast with control group.

The results show the animals treated with prazosin at three different doses (25,50,75) mg/kg b.wt. asignificant decrement ($p<0.05$) when compared with control. The results in figure (2) show the animals treated with Prazosin at low dose 25 mg/kg b.wt. significant increase at ($P>0.05$) in (T4) but no significant changed when contrast with groups of rats that's give high doses of Prazosin (50, and 75) mg/kg b.wt.the animals treated with Prazosin at high doses 50,75mg/kg b.wt. for each extract for 8 weeks showed significant increment($p>0.05$) in levels of (T4) when compared with control group.

These results in figure (3) may be attributed to effect of prazosin on pituitary gland in hypothalamus of brain , due to elevation in TSH, and at same time the prazosin effect on thyroid gland by stimulating it to secret more of T4, this called primary hyperthyroidism[19].

T4 is secreted about 20% more than in T3 in the bloodstream, hormones released from thyroglobulin but not secreted are deiodinated from iodothyrosinedehalogenase to permit all of iodide to be reabsorbed and recycled. TSH, through stimulation of these processes, stimulates thyroid gland to synthesize thyroid hormones and rise its volume. Elevated levels of T4 and T3 inhibit the secretion of TRH and TSH, with a negative feedback mechanism. Medicines that inhibit T4 and T3 synthesis increase TSH circulating levels, which encourages thyroid gland hyperplasia (goiter). Thyroid hormone release can also be stimulated secondarily through blood vessels by nerve fibers of cervical sympathetic ganglia (Dott.sa Carmela,2012).Hyperthyroidism is also known as thyrotoxicosis. It ischaracterized by hypermetabolism and elevated serum levelsof free thyroid hormones. There is enlargement of the thyroidgland and exophthalmos (bulging eyes) [20].

This present study agreement with the results that obtained by[21], on propranolol and prazosin revealed, the propranololdecrease T3 levels, by lowering the conversation of T4 to T3, and prazosin causes elevation in T4 and TSH, or may be attributed by Thyroiditis, subacute thyroiditis is caused by inflammation of the thyroid gland and produces an abrupt onset of thyrotoxic symptoms as excess hormone released from the inflamed gland, it often lead to complication and results in temporary hyperthyroidism

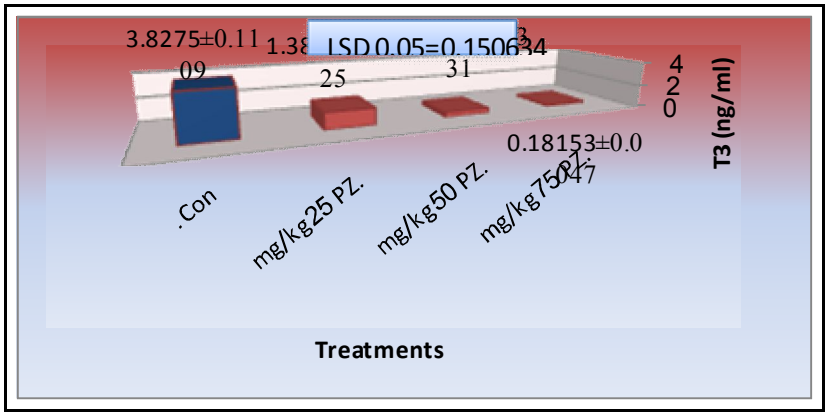

Figure (1): Effect of prazosin at in the serum levels Triiodothyronin in male rats.Values are mean ±SE. *significantly different at p<0.05

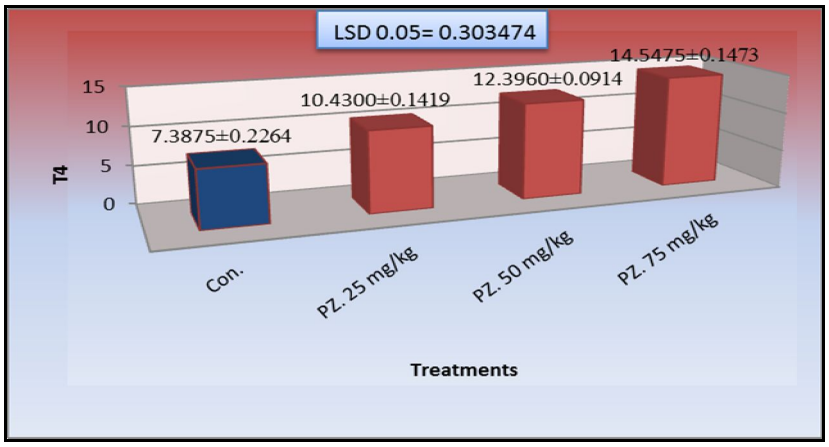

Figure (2): Effect of prazosin at in the serum levels Thyroxine in male rats.Values are mean ±SE. *Significantly different at p<0.05.

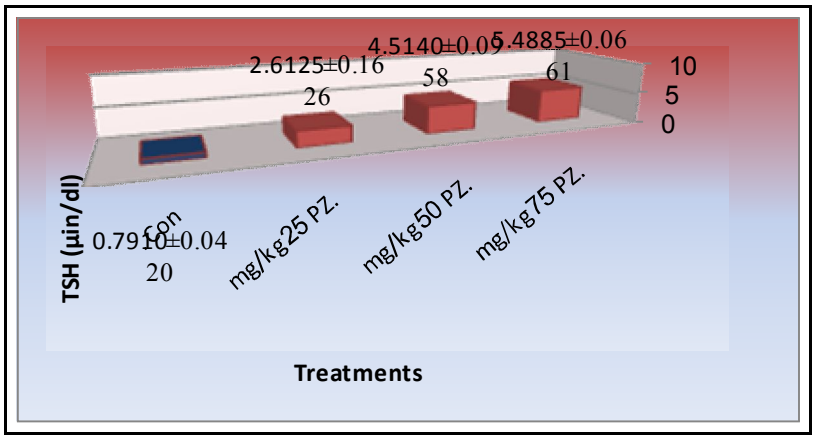

Figure (3): Effect of prazosin at in the serum levels TSH in male rats. Values are mean ±SE. *Significantly different at p<0.05.

Effects of prazosin on erythropoietin and calcitonin hormones:

The results in figures (4) and(5) showed a significant decrement ($p<0.05$) in level of erythropoietin and level of calcitonin in serum with in group treated with Prazosin for 8 weeks in contrast with control group.

The results show the animals treated with Prazosin at low dose 25 mg/kg b.wt. significant decreased at ($P<0.05$) in (Erythropoietin and Calcitonin) when compared with control group but no significant changed

when contrast with groups of rats that's give high doses of Prazosin(50, and 75) mg/kg b.wt.The animals treated with Prazosin at high doses 50,75mg/kgb.wt. for each extract for 8 weeks showed significant decrement ($p<0.05$) in (Erythropoietin and Calcitonin) levels when compared with control group,This study demonstrates that prazosin, a quinazoline derivative that is now thought to be a selective postsynaptic el-adrenergic receptor blocking agent, exerts and inhibitory effect on the erythropoietic rate of normoxic mice, which, in turn, induces a moderate decrease in the hematocrit. Since the drug is also able to depress the oxygen-dependent EPO production in hypoxemic rats, it is conceivable that prazosin affects erythropoiesis indirectly, through its negative effect on the secretion of the regulating hormone, prazosin induced a sustained decrease of the hematocrit value despite continuation of the hypobaria induced hypoxemia, oxygen consumption was not significantly different between normoxic and hypoxic mice, being unaffected by prazosin. The critical point decreased in hypoxic compared with normoxic rats, but was unaffected by prazosin.

Calcitonin (thyrocalcitonin) is a hormone produced by clear cells in the thyroid gland. The main action of calcitonin is on the bone. It increases deposition of calcium and phosphate in the bone and regulate the ca^{+2} levels in the blood, so effectively it inhibits calcium resorption by binding to a specific receptor on the osteoclasts, and inhibits their action. In the kidneys, it decreases the re-absorption of both calcium and phosphate on the proximal tubules. Its overall effect is to decrease the plasma calcium concentration.

Patients with primary hyperparathyroidism may be more sensitive to the hypercalcaemic action of thiazides[22,23] because ofloss of the normal counter-regulation of parathyroid hormone secretion during thiazide-induced hypercalcaemia[24]. experimental work by[25] has demonstrated that isoproterenol or adrenaline, but not phenylephrine, can acutely increase parathyroid hormone levels without changing serum calcium concentrations, while propranolol decreases parathyroid hormone levels.

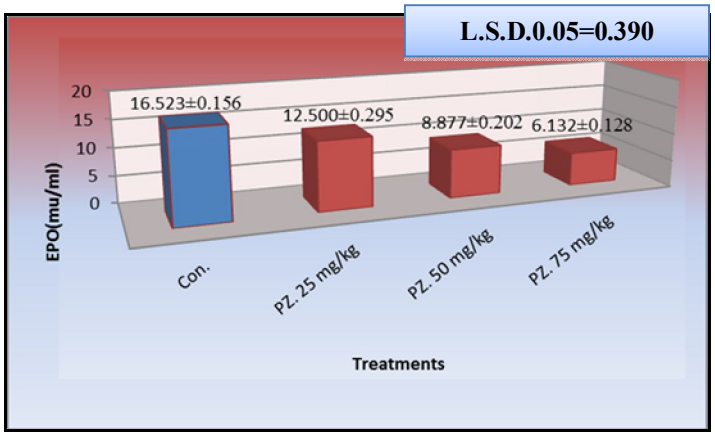

Figure (4): Effect of prazosin at in the serum levels Erythropoietin in male rats.Values are mean ±SE. *Significantly different at p<0.05.

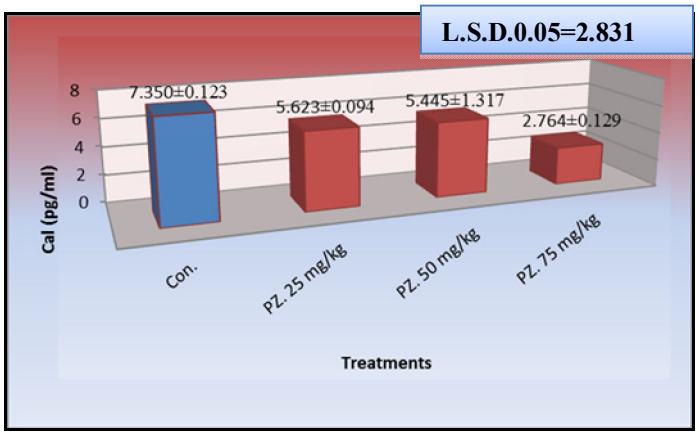

Figure (5): Effect of prazosin at in the serum levels Calcitonin in male rats.Values are mean ±SE. *Significantly different at p<0.05.

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