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MINERAL AND HORMONAL CHANGES AFTER ADMINISTRATION OF SOME ANTIRHEUMATICS TO ADULT RATS

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ABSTRACT

Dexamethasone sodium phosphate (0.13 mg/kg b. wt) and diclofenac sodium (6.7 mg/kg kg b.wt.) were injected intramuscularly day after day for two weeks to two groups of mature male rats respectively.After the end of the experiment, all rats of the treated and control groups were killed and blood samples were collected. Testosterone, corticosteroids prolactin, sodium and potassium levels were determined in the serum.Dexamethasone and diclofenac sodium significantly decreased testosterone level whereas, they elicited a significant increase in the levels of corticosteroids and prolactin. Serum sodium and potassium showed a significant increase and decrease as a result of treatment with dexamethasone and diclofenac respectively.

INTRODUCTION

The choice of drugs for the relief of pain depend on the severity of the symptom. Analgesics can be used alone by most patients having symptoms which need drugs with an anti-inflammatory as well as analgesic properties[1].

Antirheumatics are either steroidal as dexamethasone or non steroidal as enolic acids ar carboxylic acid derivatives[2].

Data concerning the effect of antirheumatics on male fertility are contradictory. Some authors claimed a reduction in male fertility, others reported an improvement in male fertility. Saksena et al.[3] reported a decreased testosterone level after indomethacin adminstraion, while Fusches and Chantharaksi(4) found an increase in testosterone level in rats treated with indomethacin.

Relatively little has been done in this respect in male rats. It is therefore, the purpose of this study to investigate the role played by some antirheumatics on testosterone level. The experiments also deals with their action on corticosteroids and prolactin hormones together with serum sodium and potassium. This will give us a wide biocehmical study about the effects of those anti-rheumatics.

MATERIAL AND METHODS

Drugs:

1- Diclofenac sodium (voltaren)[R] ampoules. Each ampoule contain 3 ml each ml contain 25.0 mg. Swiss pharma S.A.E. Cairo under licence from Ciba Geigy Ltd. Basle, Switzerland.

2- Dexamethasone sodium phosphate (Dexamethasone)[R] ampoules. Each ampoule contain 8 mg in 2 ml, it is produced by AMRIYA Pharmaceutical industries Alexandira Egypt, under licence of Weimner pharma. (MBH, Rastatt, West Germany).

Animals:

Forty five adult male albino rats of average weight 162 ± 8 gm, were used in this study. The animals ere housed in steeel boxes and were kept under hygienic conditions and allowed food and water ad-libitum.

Rats were divided into three equal groups of 15 each, they were treated as follows:

Group 1: were kept as control and injected with 0.6 ml saline i.m. day after day for two weeks.

Group 2: were injected with dexamethasone sodium phosphate at a dose of 0.13 mg/kg b.wt.i.m. contained in 0.6 ml saline day after day for two weeks.

Group 3: were injected with diclofenac at a dose of 6.7 mg/kg b.wt.i.m. in 0.6 ml saline day after day for two weeks.

Blood samples were collected after decapitation of all groups after two weeks. Then centrifugated at 3000 r.p.m. for 15 minutes. Serum samples were separated and kept in a deep freezer at -20.C until assayed.

Testosterone determination was performed in serum using RIA technique[5], using testosterone kits (Diagnostic products Corporation (DPC) Los Angelos, USA).

Corticosteroids were determined according to Kley and Krusjemper[6], using RIA technique. Corticosteroids kits were purchased from Clinical Assay (Division of Travenol USA).

Prolactin was determined using RIA technique [7], using prolactin kits (Radioassay system laboratories. Inc. 20770 Leapwood Aven. Carson, California, USA. Sodium and potassium were determined according to the method of John[8].

Statistical analysis:

Data obtained in this study were statistically analysed using Student "t" test[9].

RESULTS AND DISCUSSION

Many different factors have been implicated as possible causes of male infertility, among these factors the use of antirheumatic drugs which are used in the treatment of many inflammatory conditions widely prevailed allover the world.

Administration of dexamethasone and voltaren intramuscularly into adult male albino rats for two weeks (Table 1) decreased testosterone level in serum. These results were consistent with the recorded declining effect of dexamethasone in the testes of rat (10,11)

The declined effect may be due to inhibition of the hypothalamo-pituitary gonadal axis[12], or due to reduction of LH receptors concentration on leyding cells[13].

The decreased testosterone in serum of rat after voltaren administration was not observed by Fadl Allah[10].

The decreased testosterone level might be most probably due to inhibition of testicular responsiveness to gonadotrophins and inhibition of 17 α-hydroxylase in leyding cells[14].

Serum corticosteroids were recorded in (Table 1). There was a significant increase in corticosteroids after the administration of dexamethasone and voltaren in the two groups. The elevated level of corticosteroids may inhibit the LH release, thus decrease testosterone production[15] This rise in corticosteroids level. may also be a relfection of ACTH release from the pituitary gland due to direct or indirect action of the administered drugs[16].

Administration of dexamethasone and voltaren into adult male rats increased prolactin production (Table 1). Prolactin has been shown to increase during different types of stresses[17], and the increased prolactin level decreased testosterone production and several theories have been proposed to explain the suppression of gonadal function in hyperprolactinemia. These include (a) suppression of gonadotrophin secretion, (b) increase in adrenal secretion (c) blockade of effects of gonadotrophins at the gonadal level[18].

Regards, the changes of sodium and potassium levels (Table 1) after antirheumatic drugs administration, the data revealed an increased sodium level, likewise, potassium followed an opposite trend to sodium.

These findings can be explained as the salt and water metabolism are controlled by mineralocorticoids. All the active corticosteroids execpt androgens, increase the reabsorption of sodium i.e., increase its level in the blood and decreases its secretion to sweat and intestinal secretions. In addition to sodium increase, corticosteroids increase potassium excretion i.e., decreases its level in the blood[19].

Thus we can conclude that dexamethasone and voltaren altered the endocrine function of the testis reflected by decreased testosterone level, also, a stress effect may be noticed leading to elevation of both prolactin and corticosteroids.

Moreover, anti-rheumatic drugs may alter the normal levels of sodium and potassium in the blood due to changes in corticosteroids.

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Table (1): Effect of i.m. injection of dexamethasone, diclofenac sodium every other day for 2 weeks on serum levels of testosterone, corticosteroids, prolaction, sodium and potassium of mature male rats.

Treatment	Testosterone ng/dl	Corticosteroids ng/ml	Prolactin ng/ml	Sodium mEq/L	Postassim mEq/L
Control 0.6 ml saline	256.32 ± 15.0	2.76 ± 0.12	29.24 ± 0.88	130.7 ± 0.98	4.3 ± 0.32
Dexamethasone 0.13 mg/kg b.wt.	230.54 ± 22.0*	4.48 ± 0.3*	40.62 ± 2.4*	148.6 ± 1.2*	2.8 ± 0.28*
Diclofenac 6.7 mg/kg b.wt.	202.86 ± 19.0*	5.1 ± 0.64*	46.34 ± 3.1*	143.4 ± 1.46*	2.4 ± 0.3*

* Significant at $P < 0.05$.

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التغيرات في المعادن والهرمونات بعد اعطاء الدكساميثازون والداى كلوفيناك لذكور الفئران البالغة

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تم حقن الدكساميثازون صوديوم فوسفات عن طريق العضل فى ذكور الفئران البالغة يوم بعد يوم بجرعة قدرها ١٣رمجم/كجم من وزن الفئران لمدة أسبوعين وكذلك تم حقن الداى كلوفيناك صوديوم (الفولتارين) بنفس الطريقة ولنفس المدة فى مجموعة أخرى قدرها ٦ر٧ مجم/كجم من وزن الفئران.

وبعد نهاية التجربة تم ذبح جميع الفئران المعالجة والضوابط وتم جمع الدم. وتم قياس مستوى هرمونات التستوستيرون، والكورتيزونات وهرمون اللبن والصوديوم والبوتاسيوم فى مصل الفئران.

وقد أظهرت النتائج أن الدكساميثازون أحدث نقص معنوى فى مستوى التسترستيرون وزيادة ملحوظة فى مستوى الكورتيزونات وهرمون اللبن كما أن الدكساميثازون والداى كلوفيناك أحدثا زيادة معنوية فى مستوى الصوديوم ونقصاً معنوياً فى مستوى البوتاسيوم.