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The effect of Enalapril drug on some histological aspects of testes tissue in the mature albino male mice

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Abstract

The study aimed to evaluate whether Enalapril has any effects on the testicular tissue of the albino male mice which received or did not receive treatment with Enalapril.

Mature mice were divided into three groups: control group which fed with 0.1mg of normal saline, the second group was orally fed with 10 mg/Kg of Enalapril drug while the third group was fed with 20 mg/Kg of drug, one time a day for 30 successive days by using gavage tube (0.1ml). The histological sections were performed and the slides were examined using the light microscope.

The present study result of light microscopic images of mice testes cross sections which treated with 20 mg/Kg of Enalapril showed coagulated necrosis on spermatogonia germ cells, stopping the maturation in testicular tissue and ischematic alternations. Furthermore, the group treated with 10 mg/Kg showed arresting of spermatozoa maturation, congestion of blood vessels and spreading of edema. In comparison with the control group which demonstrated normal interstitial tissue and absence of edema with spermatogenic maturation observing numerous spermatozoa within the tubule lumen. In conclusion, Enalapril might play a role in pathogenesis of testicular tissue and men infertility.

Keywords: Enalapril, testicular tissue, men infertility.

دراسة تاثيرعقار الأنالابريل في بعض النواحي النسجيه لنسيج الخصيه في ذكور الفئران البيض البالغة

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الخلاصة

تهدف الدراسه الى تقييم تأثير عقارالأنالابريل على نسيج الخصيه في ذكور الفئران البيض البالغه. قسمت الحيوانات الى ثلاثة مجاميع: مجموعة السيطرة التي عوملت ب 0.1 ml من المحلول الملحي و المجموعه الثانيه عوملت ب 10 ملغم/كغم من وزن الجسم من الانالابريل بينما المجموعه الثالثة عوملت ب 20 ملغم/كغم من العقار، جرعه واحدة في اليوم ولمدة ثلاثون يوماً متتاليه عن طريق استخدام انبوبة التغذيه الفميه الجبريه (0.1 مل).

أظهرت نتائج الدراسه الحاليه بعد الحصول على صورللشرائح النسجيه باستخدام المايكروسكوب لنسيج الخصيه أن استخدام 20 ملغم/كغم من الانالابريل أحدث تنخرتجلطي للخلايا المولده للمني وتوقف نضوج نسيج الخصيه وتغيرات إسكيميه. بالاضافة الى ما سبق اوضحت النتائج أن المجموعه المعامله ب 10 ملغم/كغم من العلاج اظهرت حصول توقف نضوج الخلايا المنويه و احتقان في الاوعيه الدمويه وانتشارالوذمه

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بالمقارنه مع مجموعة السيطرة التي أظهرت نسيج بيني طبيعي وغياب الوذمه ونضوج الخلايا المنويه المتجمعه بأعداد كبيرة داخل النبيبيبات المنويه.

من هذا يستنتج الانالابريل ربما يكون له دور في امراضية نسيج الخصيه مؤدياً الى انعدام الخصوبه infertility .

Introduction

Among the aetiological factors affected in male infertility, medications-related diseases must be considered [1]. Accordingly, Enalapril which is angiotensin-converting enzyme (ACE) inhibitors and the first-line drug for hypertension treatment must be investigated when the fertility is a relevant concern.

Enalapril is a drug used to treat high blood pressure, Kidney diseases [2], diabetes and heart failure [3]. It was patented in 1978 and came into medical use in 1984 [4]. It is a dicarbocyl-containing peptide with antihypertensive activity. Enalapril, as a promedication, is converted into its active form Enalaprilat [5].

Up to now very little studies have been conducted to investigate the impact of Enalapril on male fertility and the relationship between using Enalapril and testicular damage and male fertility is not clearly understood [6 and 7]. However, there have been no data reported on the effect of Enalapril on testicular tissue. To gain insight into this issue, we conducted a study that explored the influence of Enalapril on some Histological aspects of testes in male mice.

Materials and Methods:

Preparation of Enalapril solution

Doses of (10 and 20 mg/kg of body weight) were prepared by grinding tablet of the drug and then weighted according to the metabolism and weight of mice compared to the weight of the human. Each dose of the drug (10 &20 mg/ml) was dissolved in 100ml of distilled water. Finally, by using gavage tube (0.1ml), the drug was orally given to the animals one time a day for 30 successive days [8].

Experimental Animals:

Thirty adult Swiss albino male mice (*Mus musculs*) aged 10-12 weeks were obtained from the animal house of Al-kindy company for vaccines. The weight range was between 30-35gm. The animals were housed at lab temperature of 23 – 25°C, under natural 12 hrs light and 12 hrs dark and were fed *ad libitum* .They were divided into three groups: control group was treated with (0.1ml) of normal saline; group 2**:** animals were treated with 10mg /kg.b.wt/day of Enalabril and group 3 where animals were treated with 20mg /kg.b.wt/day of Enalabril.

Histological study:

Immediately after killing the animals by cervical dislocation, the abdominal cavity was opened in overturned (T) shape, and then the male reproductive organs (testes) were extirpated. The testes then were fixed in Bouin's fixative for 24hrs and then transferred into 10% normal buffer formalin until used [9]. The histological sections were performed according to procedure mentioned by Luna in 1968 [10] and then the sections were submitted to a microscopic examination for histological study at 40X magnification.

Results and Discussion:

The Previous data had suggested that Enalapril drug has a harmful effect on men fertility. However, it is difficult to evaluate the actual effect of these treatments as a result of the adverse impacts of hypertension on the function of the testes, related to endothelial dysfunction [11].

The result of light microscopic images of mice testes which treated with 20 mg/Kg of Enalapril showed coagulated necrosis on germ cells and ischematic alternation as shown in Fig 1 (**C** arrow). Furthermore, the group treated with 10 mg/Kg showed arresting of spermatozoa maturation, congestion of blood vessels and spreading of edema as presented in Figure-1 (**B** arrow). Previous study explained the Increase of edema after long term of using Enalapril to vasodilation and increased vascular permeability [12]. In comparison with the control group Figure-1 (A) which demonstrated normal interstitial tissue and absence of edema. It has been previously reported that vascular changes in the testicle lead to changes in spermatogenesis due to insufficient nutrition and oxygenation of the Sertoli cells [13] which may explain the alterations promoted by the Enalapril.

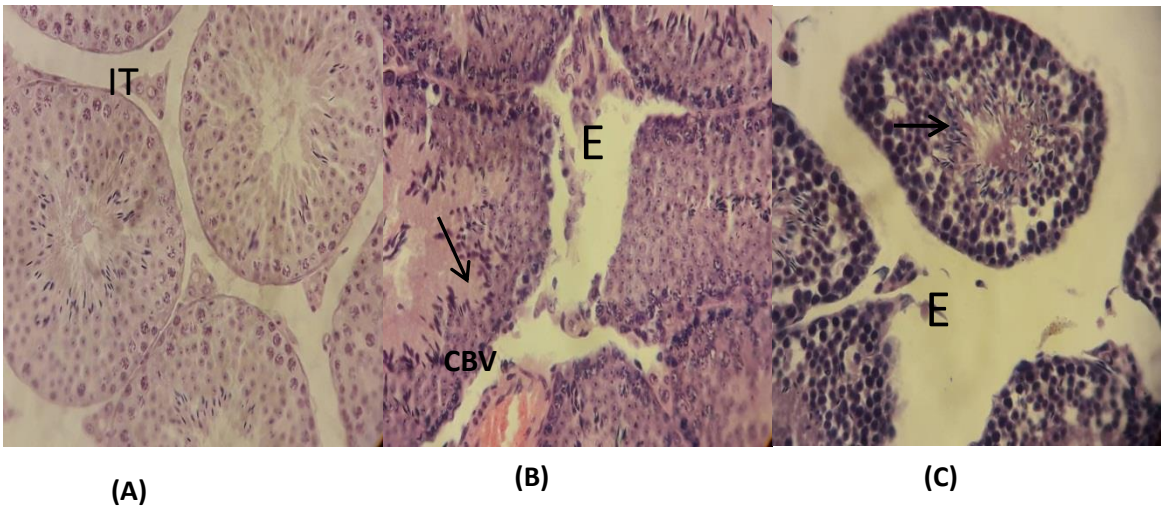

Figure 1-demonstrating light microscopic images in mice testes cross-sections of the control group (A) and Enalapril treated groups (B) and (C) were fed with 10 and 20 mg/Kg respectively. Image (B) shows maturation arrest (arrow); Congestion of blood vessels and (CBV) spreading of edema (E). Image (C) shows coagulated necrosis on spermatogonia desquamating into the lumen (arrow); and spreading of edema (E). The control image (A) demonstrates normal interstitial tissue and absence of edema. (Hematoxylin–eosin; magnification: 40X.

Moreover, Enalapril treatment results in ischemic alterations and stopping the maturation in testicular tissue. Furthermore, necrosis and degeneration of seminiferous tubule (N) can be noticed in the drug treated groups as shown in Fig 2 : (B and C arrows) as compared with spermatogenesis development which has been noticed on a sample from the control group and numerous spermatozoa are observed within the tubule lumen as observed in Fig 2 (A). These observations agreed with Turkili and others study in 2012 who reported ischemic alterations and maturation arrested in testicular tissue after using Enalapril [14].

In conclusion and in the light of previous studies and the present results, it can be said that Enalapril, independent of their hypotensive effects, has a negative impact on testicular tissue which in turn may effect on men fertility. However, for better understanding the action mechanism of these drugs on testicular tissue, further studies are needed to assess the morphometric parameters of the following structures: basement membrane, seminiferous epithelium and tubular lumen. Moreover, further researches are required to evaluate sperm viability and motility.

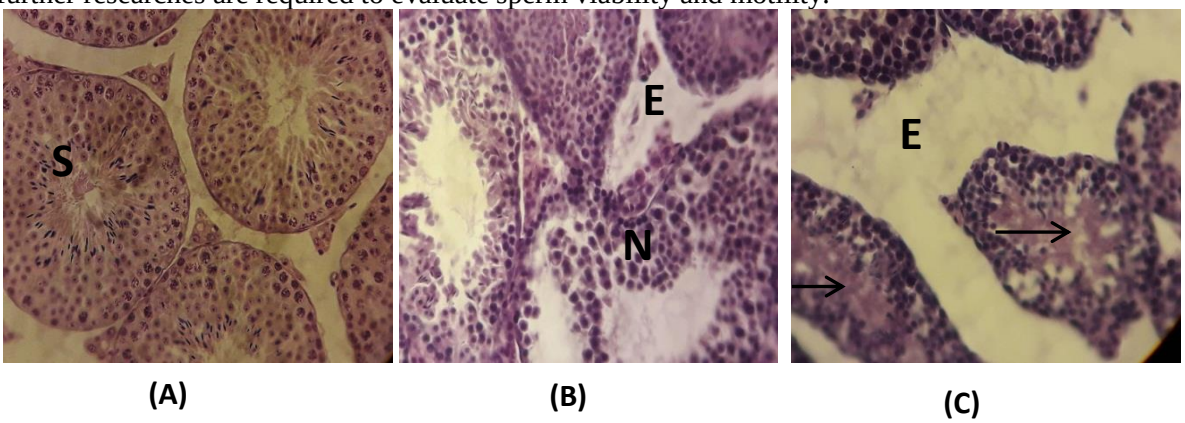

Figure 2-showing light microscopic images in mice testes Cross-section of the control group (A) and Enalapril treated groups (B) and (C) were fed with 10 and 20 mg/Kg respectively. Spermatogenesis development is noticed on a sample from the control group (A) and numerous spermatozoa are observed within the tubule lumen (S). After Enalapril treatment (B) and (C), it is seen that ischemic alterations are underway and that maturation in testicular tissue has stopped (arrows). Moreover, necrosis and degeneration of seminiferous tubule (N) can be noticed in the drug treated groups (B) and (C). (Hematoxylin–eosin; magnification:40X).

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