Some Biochemical Alternations Associated with Oral Contraceptives And Atherosclerosis in Albino Rats.

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Abstract

An excess intake of vitamin D$_2$ can result in mobilization of calcium in the skeleton and increase the serum calcium level. This calcium is taken up by soft tissues such as arteries. The risk of calcium builds up in arteries, a significant component of atherosclerotic plaque. Many researches clarify the relationship between oral contraceptives and atherosclerosis. This study aims to evaluate the changes in some biochemical parameters as well as the histopathological examination of liver and aorta following the administration of hormonal oral contraceptives (O.Cs) with different concentrations of estrogen (ethinylestradiol) (E.E) and progestogen DL-norgestrel (norethindrone) (NOR.) to the atherosclerotic rats. In addition to this, the study clarifies the role of low dose oral contraceptives. 48 adult female albino rats were divided into six comparable groups of 8 animals each. Group I (Gr. I) was considered as control, group II (Gr. II) was intramuscularly (i.m.) injected with vit. D$_2$ 350.000 I.U/kg B.W., group III (Gr. III) administered O.C (35$\mu$g E.E/0.5 mg NOR.), group IV (Gr. IV) received (vit. D$_2$ 350,000 I.U vit. D$_2$ /kg B.W plus O.C 35$\mu$g E.E/0.5 mg.), group V(Gr.V) received (vit. D$_2$ 350,000 I.U/kg B.W plus O.C 35$\mu$g E.E/1mg NOR.), group VI (Gr.VI) received (vit. D$_2$350,000 I.U /kg B.W.plus O.C 70$\mu$g E.E/0.5 mg NOR.) daily for an experimental period eight weeks.

Serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), and serum alkaline phosphatase (ALP) displayed significant increase in the following groups (higher progestogen concentrations in O.Cs plus vit. D$_2$ treated group, at low-dose O.C plus vit. D$_2$ treated group, at higher estrogen dose within O.C plus vit. D$_2$ treated group, vit. D$_2$ treated, and at low-dose O.C treated group). Serum triglycerides recorded significant increase in group treated with higher estrogen dose within O.C plus vit. D$_2$ treated group, low-dose O.C plus vit. D$_2$ treated group, higher progestogen concentrations in O.Cs plus vit. D$_2$ treated group, vit. D$_2$ treated group, and at low-dose O.C treated group respectively. Serum total cholesterol increased significantly in higher progestogen concentrations in O.Cs plus vit. D$_2$ treated group, at low-dose O.C plus vit. D$_2$ treated group, vit. D$_2$ treated group, low-dose O.C treated group and at higher estrogen dose within O.C plus vit. D$_2$ treated group at 8 weeks in comparison with control. Histopathological studies of livers showed severe at the higher progestogen concentration in O.C plus vit. D$_2$ treated group and at low dose O.C plus vit. D$_2$ treated group. Liver displayed moderate degenerative changes in higher estrogen dose within O.C plus vit. D$_2$ treated group, in vit. D$_2$ treated group and in low dose O.C treated group. Media calcinosis in aorta was more obvious at the higher progestogen concentrations in O.Cs plus vit. D$_2$ treated group. Also it develops at low dose O.C treated group.

In conclusion atherosclerosis may develop at low dose O.C due to progestogen content.

Keywords: Hypervitaminosis vit. D$_2$, O.Cs, Atherosclerosis, Liver, Aorta
Introduction:
The control of a population explosion is an important part in our national development plan. Hormones are still the most popular contraceptives for such explosion, however their use proved to be responsible for various adverse reactions.

Krauss et al, (1977) found changes in serum high-density lipoproteins, which played a protective role, in atherosclerosis in women on oral contraceptive drugs.

Al-shebib et al, (1982) concluded that hypercholesterolaemia and atheroma could be induced in rabbits by progestosterone injection after longer periods of use. Krauss et al (1983) pointed out that changes in serum lipids were associated with the use of two low-dose estrogen progesten and could occur with use of such agents for a 2-month period.


This investigation aims to evaluate the changes in some biochemical parameters as well as the histopathological examination of liver and aorta following the administration of hormonal oral contraceptives with different proportions of estrogen ethinylestradiol and progestogen norethindrone to the atherosclerotic rats. In addition to this, the study clarifies the role of low dose oral contraceptives.

Materials and Methods

Experimental drugs
1 ml ampoules of vitamin D2 (Viosterol 600,000 IU in oil) were obtained from the Memphis Chemical Co. (Cairo) Egypt.

Ethinylestradiol and norethindrone were obtained from Chemical Industries Development (CID) Laboratories (Giza) Egypt.

Experimental design

Animals
48 adult female albino rats weighing 120-150gm, were kept under good hygienic conditions and a well balanced diet. The animals were divided into six comparable groups of 8 animals. Group I (Gr.1) was considered as control, group II (Gr. II) was I/M injected with 350,000 vit. D2/kg B.W., group III (Gr. III) administered 35 µg E.E/0.5 mg NOR, group IV (Gr. IV) received (vit. D2 350.000 I.U/vit. D2/kg B.W plus O.C 35 µg E.E/0.5 mg.), group (Gr.V) received (vit. D2 350.000 I.U/kgB.W. plus O.C 35 µg E.E/1mg NOR.), group VI (Gr.VI) received (vit. D2 350.000 I.U/kg B.W. plus O.C 70 µg E.E/0.5 mg NOR.) daily for an experimental period eight weeks.

Body weights
Body weights of rats were recorded before treatment, weekly for 2, 4, 6 and 8 weeks.

Blood sampling
Blood samples were collected from retro-orbital plexus (Schermer, 1967). Serum total cholesterol was determined according to (Waston, 1960), serum triglyceride was estimated according to (Wahlefeld, 1974), (AST), (ALT) were determined according to (Reitman and Frankle, 1957), ALP was determined according to (Kind and King, 1954). The data were statistically analyzed used student’s t-test according to (Sendecor and Coebram, 1969). In addition histopathological studies were carried out by collecting the specimens from liver and aorta. These specimens were fixed in 10% formalin 5 micron
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thick paraffin sections were prepared, stained with hematoxylin & eosin and examined microscopically.

**Results and Discussion**

Serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), and serum alkaline phosphatase (ALP) displayed significant increase in the following groups (higher progestogen concentrations in O.Cs plus vit. D2 treated group, at low-dose O.C plus vit. D2 treated group, at higher estrogen dose within O.C plus vit. D2 treated group, vit. D2 treated, and at low-dose O.C treated group) at 8 weeks in comparison with control tables (4,5&6). Histopathological studies of livers showed clear changes at the higher progestogen concentration in O.Cs plus vit. D2 treated group and at low-vit. D2 treated group. Liver displayed moderate degenerative changes in dose O.C plus higher estrogen dose within O.C plus vit. D2 treated group, and in vit. D2 treated group. Also in low dose O.C only. Histopathological examination appeared as dissociation of hepatic cords, dilation and congestion of central vein and portal tract, and fatty infiltration. Moreover necrosis of some hepatic cells figures (10,7,13, 1&4).

Vit.D has a highly toxic effect on liver and elevated (AST), (ALT) and (ALP) Canada de Zunzunegui et al, 1984. O.Cs elevates serum transferase activities and impaired secretory liver function (Nareman, et al 1991).

The accumulation of vit.D and hormonal contraceptives in liver caused marked increase in (AST), (ALT) and (ALP).

The elevation in serum cholesterol and triglycerides in vit. D treated group was in harmony with Vijayakumar and Kurup (1974). While the same group gained less weight (Bajwa et al 1971and Takahashi, 1993). An excess intake of vitamin D can result in mobilization of calcium in the skeleton and increases the serum calcium level. This calcium is taken up by soft tissues such as arteries. Vit. D2 over dosing is mediated through its intermediate ,25-hydroxy –D, rather than its active metabolite 1,25 –dihydroxy –D .It means that the toxicity of vit. D2 is believed to be the result of high circulating 25-OHD levels. Thus calcium transport and bone resorption goes on at high and unchecked rate , giving hypercalacemia (Fraser, 1995 & Basu and Tapan1996).

Concerning our data the increase in the serum total cholesterol and gaining body weight by oral contraceptives treatment, may be referred to the effect of progestosterone content which serves as precursor to all other steroids ( Kutsy, 1973). The World Health Organization (WHO) reported a relationship between different progestogens in low estrogens oral contraceptives on venous thromboembolic disease from 1989-1993 in 21 centers globally. Petitti et.al 1998 recorded that progestogen type might affect myocardial infarct-ions. Our results indicated that, the estrogen part elevated serum triglyc-erides in the absence of increased cholesterol levels and gained less weight than the other groups. This result in agreement with (McGill et. al, 1977). Harris and Hughes 1998 reported that O.C use increased circulating levels of 25-hydroxyvitamin D (25OHD) in young women. This finding confirmed our results that medial calcinosis develops at low dose O.Cs Groups treated with vit. D plus O.Cs lead to increase the circulating 25-OHDevels which lead to increase the formation of medial calcinosis.

Media calcinosis in aorta was more obvious at the higher progestogen concentration in O. Cs plus vit. D2.
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treated group and at low-dose O.C plus vit. D_2 treated group. Media calcinosis was moderate at higher estrogen dose within O.C plus vit. D_2 treated group, and at vit. D_2 treated group. Also it develops at low dose O.C treated group.

In conclusion atherosclerosis may develop at low dose O.C due to progestogen content.

**Acknowledgment:**

The authors thankful to Dr/ R.M. Al-Allawy Prof. Dr. in Biochemistry in NODCAR for his sharing in suggestion the point.

**Table(1):** Average values ± of body weights (gm) in normal rat groups intramuscularly injected with vit. D 350.000IU/kg BW and administered different concentrations of estrogen, ethinyle estradiol, (E-E) and progesterone, norethindrone, (NOR) and their corresponding controls for 8 weeks

<table>
<thead>
<tr>
<th>Time intervals</th>
<th>Groups</th>
<th>Control</th>
<th>Vit.D_2 350,000IU/kg BW</th>
<th>O.C (35μgE.E / 50mgNOR )</th>
<th>Vit.D_2+OC(35μgE.E/ 50mgNOR)</th>
<th>Vit.D_2+OC(35μgE.E / 1mgNOR)</th>
<th>Vit.D_2+OC(70μgE.E/ 50mgNOR)</th>
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<tbody>
<tr>
<td>Zero-time</td>
<td>Gr. I</td>
<td>129.37±1</td>
<td>131.25±1</td>
<td>129</td>
<td>128.62±0.7</td>
<td>127±1</td>
<td>127.5±1</td>
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<td>Gr. II</td>
<td>146.25±1</td>
<td>140.25±1</td>
<td>148</td>
<td>145.6±1</td>
<td>160±3</td>
<td>135±5</td>
</tr>
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<td>Gr. III</td>
<td>167.5±1</td>
<td>150.87±1</td>
<td>166.26±1</td>
<td>158±0.6</td>
<td>186±2</td>
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<td>Gr. IV</td>
<td>183.5±1</td>
<td>170±1</td>
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<td>176.25±1</td>
<td>200±3</td>
<td>177.5±5</td>
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<td>180.37↓</td>
<td>225*</td>
<td>216.66±3</td>
<td>240**</td>
<td>190↓</td>
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<td></td>
<td>VI</td>
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</tbody>
</table>

Number of rats in each group n=8.

Insignificant difference from the corresponding control at p>0.05

*Significant difference from the corresponding control at p<0.05

**Highly significant difference from the corresponding control at p<0.01

***Very highly significant difference from the corresponding control at p<0.001
Table(2): Average values of serum total cholesterol (mg%) in rat groups intramuscularly injected with vit. D$_3$ 350,000IU/kg BW and administered different concentrations of estrogen, ethinyle estradiol, (E-E) and progesterone, norethindrone, (NOR) and their corresponding controls for 8 weeks

<table>
<thead>
<tr>
<th>Time intervals</th>
<th>Groups</th>
<th>Gr. I</th>
<th>Gr. II</th>
<th>Gr. III</th>
<th>Gr. IV</th>
<th>Gr. V</th>
<th>VI</th>
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<td>Control</td>
<td>350,000 IU/kg BW</td>
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<td>35 μg E.E / 50mgNOR</td>
<td>35 μg E.E / 50mgNOR</td>
<td>35 μg E.E / 50mgNOR</td>
<td>35 μg E.E / 50mgNOR</td>
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<tr>
<td>Zero-time</td>
<td>60 ±2.2</td>
<td>59.4 ±1.87</td>
<td>60 ±2</td>
<td>58.5 ±2</td>
<td>57.7 ±1.5</td>
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<tr>
<td>Two-weeks</td>
<td>60.3 ±1.5</td>
<td>65 ±6</td>
<td>62.6 ±2</td>
<td>63 ±2</td>
<td>63.7 ±3.4</td>
<td>62 ±2</td>
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</tr>
<tr>
<td>Four-weeks</td>
<td>59.2 ±2</td>
<td>70 ±5</td>
<td>65.4 ±3</td>
<td>75 ±5</td>
<td>83.8 ±6.4</td>
<td>64.3 ±1.5</td>
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<tr>
<td>Six-weeks</td>
<td>59 ±1</td>
<td>74 ±6</td>
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<td>90 ±4</td>
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<td>Eight-weeks</td>
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<td>80** ±4</td>
<td>73** ±2.5</td>
<td>88** ±4</td>
<td>100** ±3</td>
<td>70 ±3</td>
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Number of rats in each group n=8 .
Insignificant difference from the corresponding control at p>0.05
**Significant difference from the corresponding control at p<0.05
***Highly significant difference from the corresponding control at p<0.01

Table(3): Average values of serum triglycerides (mg%) in normal rat groups intramuscularly injected with vit. D$_3$ 350,000IU/kg BW and administered different concentrations of estrogen, ethinyle estradiol, (E-E) and progesterone, Norethindrone, (NOR) and their corresponding controls for 8 weeks

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<th>Gr. III</th>
<th>Gr. IV</th>
<th>Gr. V</th>
<th>VI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>35 0.000IU/kg BW</td>
<td>(35μg E.E / 50mgNOR)</td>
<td>(35μg E.E / 50mgNOR)</td>
<td>(35μg E.E / 50mgNOR)</td>
<td>(35μg E.E / 50mgNOR)</td>
<td>(35μg E.E / 50mgNOR)</td>
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<td>35 ±1.5</td>
<td>34 ±2</td>
<td>34 ±1.5</td>
<td></td>
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<tr>
<td>Two-weeks</td>
<td>33.8 ±1</td>
<td>39.5 ±1.8</td>
<td>37 ±1</td>
<td>55 ±2</td>
<td>63 ±3.4</td>
<td>75 ±3</td>
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<tr>
<td>Four-weeks</td>
<td>34 ±0.8</td>
<td>42.5 ±1.5</td>
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<td>65 ±3</td>
<td>81 ±4</td>
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<tr>
<td>Six-weeks</td>
<td>34.7 ±1</td>
<td>48.4 ±5</td>
<td>39 ±1.5</td>
<td>80 ±5</td>
<td>120 ±5</td>
<td>150 ±6</td>
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<tr>
<td>Eight-weeks</td>
<td>35 ±1</td>
<td>50** ±5</td>
<td>43** ±2</td>
<td>100** ±4</td>
<td>150*** ±6</td>
<td>206*** ±10</td>
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Number of rats in each group n=8 .
Insignificant difference from the corresponding control at p>0.05
**Significant difference from the corresponding control at p<0.05
***Highly significant difference from the corresponding control at p<0.01

***Very highly significant difference from the corresponding control at p<0.001
**Table (4)**: Average values of serum aspartate aminotransferase (SAST) U/L in normal rat groups intramuscularly injected with vit. D$_2$ 3500.000IU/kg BW and administered different concentrations of estrogen, ethinyle estradiol, (E-E) and progestogen , Norethindrone, (NOR) and their corresponding controls for 8weeks

<table>
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<tr>
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<td>Gr. I</td>
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<td>Control</td>
<td>Vit.D$_2$ 350.000 IU/kg BW</td>
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<tr>
<td>Zero-time</td>
<td>23.5 ±1.5</td>
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<tr>
<td>Two-weeks</td>
<td>22.2 ±1.5</td>
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<td>Four-weeks</td>
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<td>Six-weeks</td>
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<tr>
<td>Eight-weeks</td>
<td>23 ±2</td>
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Number of rats in each group n=8.

Insignificant difference from the corresponding control at p>0.05

*Significant difference from the corresponding control at p<0.05

**Highly significant difference from the corresponding control at p<0.01

***Very highly significant difference from the corresponding control at p<0.001

**Table (5)**: Average values of serum alanine aminotransferase (U/L) (SALT) in rat groups intramuscularly injected with vit. D$_2$ 3500.000IU/kg BW and administered different concentrations of estrogen, ethinyle estradiol, (E-E) and progesterone, norethindrone, (NOR) and their corresponding controls for 8weeks

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<td>Eight-weeks</td>
<td>17.2 ±3</td>
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Number of rats in each group n=8.

Insignificant difference from the corresponding control at p>0.05

*Significant difference from the corresponding control at p<0.05

**Highly significant difference from the corresponding control at p<0.01

***Very highly significant difference from the corresponding control at p<0.001
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Table(6): Average values of serum alkaline phosphatase U/mL (SALP) groups intramuscularly injected with vit. D 350,000IU/kg BW and administered different concentrations of estrogen, ethinyle estradiol, (E-E) and progesterone, norethindrone, (NOR) and their corresponding controls for 8 weeks

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<th>Time intervals</th>
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<th>Gr. II</th>
<th>Gr. III</th>
<th>Gr. IV</th>
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<tr>
<td>Zero-time</td>
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<td>±2.3</td>
<td>±7</td>
<td>±6</td>
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</table>

Number of rats in each group n=8 .
Insignificant difference from the corresponding control at p>0.05
*Significant difference from the corresponding control at p<0.05
**Highly significant difference from the corresponding control at p<0.01
***Very highly significant difference from the corresponding control at p<0.001
Fig. (1): liver of female rat I/M injected with vit. D$_2$ 350,000 IU/Kg Bw. 8 weeks. Showing congestion, and fatty infiltration. H&E x100

Fig. (2): Aorta of female rat I/M injected with vit. D$_2$ 350,000 IU/Kg Bw. for 8 weeks. Showing mild degenerative changes in the media. H&E x400

Fig. (3): Aorta of female rat I/M injected with vit. D$_2$ 350,000 IU/Kg Bw. for 8 weeks. Showing focal calcinosis changes in the media. H&E x100

Fig. (4): liver of female rat administered O.C (35μg E. E/0. 5mg NOR) for 8 weeks. Showing congestion and fatty infiltration. H&E x100

Fig. (5): Aorta of female rat administered O.C (35μg E. E/0. 5mg NOR) for 8 weeks. Showing early fibrilar degenerative changes at the media. H&E x400

Fig. (6): Aorta of female rat administered O.C (35μg E. E/0. 5mg NOR) for 8 weeks. Showing marked fibrilar degenerative changes at the media. H&E x400

Fig. (7): liver of female rat administered O.C (35μg E. E/0. 5mg NOR+ I/M injected with vit. D$_2$ 350,000 IU/Kg Bw) for 8 weeks. Showing congestion, fatty infiltration and necrotic changes. H&E x100

Fig. (8): Aorta of female rat administered O.C (35μg E. E/0. 5mg NOR+ I/M injected with vit. D$_2$ 350,000 IU/Kg Bw) for 8 weeks. Showing moderate calcinosis in the media. H&E x100

Fig. (9): Aorta of female rat administered O.C (35μg E. E/0. 5mg NOR+ I/M injected with vit. D$_2$ 350,000 IU/Kg Bw) for 8 weeks. Showing medial calcinosis. H&E x100
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Fig. (10): liver of female rat administered O.C (35μg E. E/ 1mg NOR+ I/M injected with vit. D₂ 350,000 IU /KgBw) for 8 weeks. Showing congestion, fatty infiltration and necrotic changes. H&E x 100.

Fig. (11): Aorta of female rat administered O.C (35μg E. E/ 1mg NOR+ I/M injected with vit. D₂ 350,000 IU /KgBw) for 8 weeks. Showing hyalinization (necrobiotic changes) precedes calcinosis. H&E x 400.

Fig. (12): Aorta of female rat administered O.C (70μg E. E/ 0.5mg NOR+ I/M injected with vit. D₂ 350,000 IU /KgBw) for 8 weeks. Showing focal medial calcinosis. H&E x 100.

Fig. (13): liver of female rat administered O.C (70μg E. E/ 0.5mg NOR+ I/M injected with vit. D₂ 350,000 IU /KgBw) for 8 weeks. Showing congestion and fatty infiltration. H&E x 100.

Fig. (14): Aorta of female rat administered O.C (35μg E. E/ 1mg NOR+ I/M injected with vit. D₂ 350,000 IU /KgBw) for 8 weeks. Showing medial calcinosis. H&E x 100.

Fig. (15): Aorta of female rat administered O.C (35μg E. E/ 1mg NOR+ I/M injected with vit. D₂ 350,000 IU /KgBw) for 8 weeks. Showing medial calcinosis. H&E x 100.

Fig(13): liver of control female rat at 8weeks
H&E x 100

Fig(14): Aorta of control female rat at 8weeks
H&E x 100
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بعض المتغيرات الكيميائية الحيوية المصاحبة لتناول موائع الحمل التي تستعمل عن طريق الفم ومرض تكسش الششرابين (تصلب الششرابين) في فنان المحقق

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ينتج عن ذيادة تناول فيتامين D2 ذيادة معدل الكالسيوم في الدم ويؤدي ذلك إلى ترسبيه في الأنسجة الرقيقه مثل الأوعية الدموية. وقد أجريت أبحاث كثيرة وضحت العلاقة بين تناول موائع الحمل (الهرمونات الأستمرارية المختلفة) التي تستعمل عن طريق الفم ومرض تكسش الششرابين.

ولذا فقد تناول البحث تقييم بعض المتغيرات الكيميائية الحيوية وفحص المتغيرات المرضا في الكبد والشربان الأوطر الناتجة عن تناول موائع الحمل (مرجى من الأستروجين والبروجسترون) بتركيزات مختلفة لفتوران مصابه بمرض تكسش الششرابين عن طريق أطعمة فيتامين D2.

ثمنية ذائدة وأيضا توضيح دور موائع الحمل التي تستعمل عن طريق الفم ذات الجرعه المخضرم.

وقد تم تقسيم عدد 44 من إناث الفنر إلى 6 مجموعات كل مجموعه تحتوى على 8 فنر. وتعتبر المجموعة الأولى مجموعه ضابطة ومجموعة الثانية تحقق عضليا (بجرعة 0.5 ملغ فيتامين D2 وحده دولي + كجم من وزن الجسم + 35 ميكرو جم من الأستروجين). المجموعة الثالثة تتجاوز عضليا (بجرعة 35000 فيتامين D2 وحده دولی + كجم من وزن الجسم + 35 ميكرو جم من الأستروجين/0.5ملجم من البروجسترون). المجموعة الرابعة تحقق عضليا بجرعة 35000 فيتامين D2 وحده دولي / كجم من وزن الجسم + 35 ميكرو جم من الأستروجين/0.5ملجم من البروجسترون. المجموعة الخامسة تحقق عضليا (بجرعة 35000 فيتامين D2 وحده دولي / كجم من وزن الجسم + 35 ميكرو جم من الأستروجين/1ملجم من البروجسترون). المجموعة السادسة تحقق عضليا (بجرعة 35000 فيتامين D2 وحده دولي / كجم من وزن الجسم + 70 ميكرو جم من الأستروجين/0.5ملجم من البروجسترون). بعد فترة تتراوح ثمانية أسابيع تم أخذ عينات من دم الفنر للدراسة مستوى بعض الأنزيمات والدهنيات في الدم وأيضا تم أخذ عينات شمعه لكل من الكبد والشربان الأوطر لدراسة التغييرات المرضيه.

وبهذاؤولهمت النتائج زياده ذو دلالة إحصائيه في مستوى مصل خمائر أنيزمات أمينوتير انس فرايز ومستوى مصل الفسفاته القلوي في المجموعات الأتية (مجموعة تعامل فيتامين D + مانع الحمل ذات الجرعه العالية من البروجسترون، ومجموعة تعامل فيتامين D + مانع الحمل ذات الجرعه المنخفضة، ومجموعة المعاملة مع الفيتامين D + مانع الحمل ذات الجرعه العالية من الأستروجين، والمجموعة المعاملة بفيتامين D ثم المجموعه المعاملة بمانع الحمل ذات الجرعه المنخفضه) وأيضا الجلسيرادات الثلاثيه
Some Biochemical Alternations Associated……

فقد سجلت النتائج ذيادة ملحوظة في المجامع التالية (المجموعة المعالمة بفيتامين D+مانع الحمل ذات الجرعة العالية من الاستروجين)، والمجموعة تعامل بفيتامين D+مانع الحمل ذات الجرعة المنخفضة، والمجموعة المعالمة بفيتامين D ثم المجموعة المعالمة بمانع الحمل ذات الجرعة المنخفضة

وبالنسبة للكوليستيرول فقد سجلت النتائج ذيادة ذات معنى أخصائي في المجامع التالية (مجموعة تعامل بفيتامين D + مانع الحمل ذات الجرعة العالية من البروجستيرون), ومجموعة تعامل بفيتامين D+مانع الحمل ذات الجرعة المنخفضة والمجموعة المعالمة بفيتامين D ثم المجموعة المعالمة بمانع الحمل ذات الجرعة المنخفضة ثم المجموعة المعالمة بفيتامين D + مانع الحمل ذات الجرعة العالية من الاستروجين).

وأوضح الفحص المجهرى وجود تغييرات مرضية في خلايا الكبد تكون شديدة في المجموعة المعالمة بفيتامين D + مانع الحمل ذات الجرعة العالية من البروجستيرون، و أيضاً المجموعة تعامل بفيتامين D+مانع الحمل ذات الجرعة المنخفضة، وتكون التغييرات المرضية متوسطة في المجموعة المعالمة بفيتامين D + مانع الحمل ذات الجرعة العالية من الاستروجين، ومجموعة المعالمة بمانع الحمل ذات الجرعة المنخفضة.

وقد ذكر النتائج أن حيوية منع الحمل ذات الجرعة المنخفضة قادرة لوحدها لأحداث مرض تصلب الشرايين (تكليس الشرايين) ويرجع هذا إلى البروجستيرون الموجود بها.