Experimental Study for the Effect of Methyl Rednisolone on the Sexual Hormones Levels

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Abstract

Methylprednisolone is one of the steroid drugs (Glucocorticoid), which is used in many medical conditions including allergy, ulcerative Colitis, Lupus, psoriasis, respiratory disorders and immune inhibitory. Fifty sex adult male rats weighing (225-250) gm where used, and randomly divided into four equal groups, which treated with daily by three different concentration from Methylprednisolone drug: (10, 30, 40) mg/kg/day. The blood samples is taken in the first and second week of dosage from all groups. The results of this study showed that the drug has obvious effect on the sexual hormones (Testosterone hormone, LH hormone, FSH hormone and Prolactin hormone) in sera of rats under investigation, In which the maximum change in the levels of hormones were showed in sera of groups with high dosage from drug (40 mg/kg) and the minimum change at the low dosage (20 mg/kg). The results are indicated there is significant decrease in testosterone levels, LH and FSH the decrease is continued until the second week. As for the Prolactin hormone, the results indicated there is a significant increased and increase is continued until the second week.

Keywords: Testosterone, LH, FSH, Prolactin.

Introduction

Methylprednisolone is considered as one of Glucocorticoids drugs. It's scientific name is: \(\text{11}\beta,17,21-\text{Trihydroxy-6a-methylpregna-1,4-diene-3,20-dione}\), while it's common name is Medrol, and it's molecular formula is \(\text{C}_{22}\text{H}_{30}\text{O}_{5}\) with 374.5 for molecular weight [1]. Methylprednisolone is quickly distributed to all body tissues like most of adrenal cortex steroids, in which move into the blood circulation and conjugated with plasma proteins, mainly with Globulin and Albumin in less ratio [2].

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Methylprednisolone is used in any of its various forms to treat cases prescribed to be treated with corticosteroid except for cases of shortage adrenal cortex in sufficiency, where it would be preferable to use Hydrocortisone with supplementary Fludrocortisone[3].

The side effects of Methylprednisolone can be summarized as follows: fluid and electrolyte disturbances, disorders in the skeletal muscle in the body and effect to stomach and intestine, delay the wounds healing, endocrines disturbance and eye increased the internal pressure of the eye [4].

Steroid hormones contain steroid nucleus and synthesized in the body from cholesterol, steroid hormones are a steroid that acts as hormones, it's endogenously derived from Cholesterol, the main classification of steroid hormones are corticosteroids (typically made in the adrenal cortex, hence corticoids) and sex steroids hormones which include androgens (male sex hormones), oestrogens (female or follicular hormones) and gestogens (corpus luteum hormone)[5]. Sex hormones belong to steroid hormones that are secreted by genital glands (testes and ovaries) and adrenal cortex and the placenta during pregnancy. Adrenal cortex hormones include Cortisol, Aldosterone and their derivatives; to this group is joined 1,25-dihydroxyl vitamin D3, the active form for D vitamin[6].

Testosterone is regarded one of the most important sex hormones secreted by human body, and produced in males by large amounts in testis by Leydig cells. The hormone is also produced in small amounts by adrenal gland cortex in both sexes[7]. It is also considered one of steroid hormones belongs to Androgens family derived from Cholesterol[8]. The mechanism of hormone secretion subject to the axis of hypothalamus – pituitary – testis and to feedback. When testosterone concentration in blood increases, it stops pituitary gland, which is highly sensitive to this hormone, by Gonadotropin releasing Hormone – GnRH, and then Luteinizing hormone - LH secretion is stopped as a result and Follicle stimulating hormone – FSH from the anterior lobe of pituitary gland, which is stops producing more testosterone in turn[9].

Follicle stimulating hormone and Luteinizing hormone are regarded to belong to Glycoprotein as well, and they are created in the Anterior pituitary gland[10]. Control over the secretion of two hormones is done by Hormone-releasing GnRH which is secreted from hypothalamus gland to stimulate pituitary gland hormones LH and FSH secretion; and hormone releasing GnRH is activated by Noradrenaline hormone and deterred by Dopamine. Control over LH and FSH hormones is done through pituitary gland and Genitals[11].
As for prolactin secreted from anterior lobe of pituitary gland by cells called Lactotrophs; as those cell discrete the greatest amount of the hormone, while it's produced in the least amounts by Mammary glands, Prostate, Endometrial, Leukocyte and Lymph[12].

Lactogenesis in mammals are related closely to Prolactin hormone as it stimulates the growing of Mammary glands[13], this pertains to females; as for males, it's important in the two processes of steroids producing and sperm creating through its intervention in process of releasing GnRH hormones by one side, on the other side it works in close liaison with Luteinizing hormone to regulate Lydig cells function[14].

Results and Discussion

High doses effect of Methylprednisolone upon the level of hormones (Testosterone, LH, FSH and Prolactin) was studies in the first and second weeks of administration. Table (1) shows the mean ± standard deviation for the hormones level in sera of blood of the animals under investigation.

Table(1): mean± standard deviation for Testosterone, LH, FSH and Prolactin sera of animals under investigation for the first and second weeks of administration.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Testosterone (ng/ml)</th>
<th>LH (mIU/ml)</th>
<th>FSH (mIU/ml)</th>
<th>Prolactin (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.92 ± 0.45 a</td>
<td>13.58 ± 1.16 a</td>
<td>1.59 ± 0.37 a</td>
<td>1.35 ± 0.28 d</td>
</tr>
<tr>
<td>G1</td>
<td>1.77 ± 0.22 bc</td>
<td>8.79 ± 0.52 b</td>
<td>0.94 ± 0.07 ab</td>
<td>2.44 ± 0.19 bcd</td>
</tr>
<tr>
<td>G2</td>
<td>0.86 ± 0.23 d</td>
<td>5.96 ± 0.29 cd</td>
<td>0.82 ± 0.18 b</td>
<td>3.58 ± 0.35 bc</td>
</tr>
<tr>
<td>G3</td>
<td>0.79 ± 0.07 d</td>
<td>2.77 ± 0.22 e</td>
<td>0.60 ± 0.13 b</td>
<td>4.32 ± 0.37 ab</td>
</tr>
<tr>
<td>LSD value</td>
<td>0.823 *</td>
<td>1.82**</td>
<td>0.631*</td>
<td>1.889*</td>
</tr>
</tbody>
</table>

*(P≤0.05), *(P≤0.01).

1st Week

<table>
<thead>
<tr>
<th>Groups</th>
<th>Testosterone (ng/ml)</th>
<th>LH (mIU/ml)</th>
<th>FSH (mIU/ml)</th>
<th>Prolactin (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.11 ± 0.32 a</td>
<td>13.49 ± 0.96 a</td>
<td>1.34 ± 0.15 a</td>
<td>0.32 ± 0.08 e</td>
</tr>
<tr>
<td>G1</td>
<td>0.94 ± 0.06 c</td>
<td>5.40 ± 0.16 b</td>
<td>0.48 ± 0.04 b</td>
<td>3.77 ± 0.32 d</td>
</tr>
<tr>
<td>G2</td>
<td>0.51 ± 0.07 cd</td>
<td>3.57 ± 0.26 bc</td>
<td>0.44 ± 0.15 b</td>
<td>6.11 ± 0.39 bc</td>
</tr>
<tr>
<td>G3</td>
<td>0.14 ± 0.03 d</td>
<td>1.62 ± 0.15 d</td>
<td>0.28 ± 0.05 b</td>
<td>8.93 ± 0.64 a</td>
</tr>
<tr>
<td>LSD value</td>
<td>0.562**</td>
<td>1.75**</td>
<td>0.544**</td>
<td>1.957*</td>
</tr>
</tbody>
</table>

**(P≤0.01).
Result shown in table (1) states that the mean ± standard deviation for Testosterone was (1.77 ± 0.22) ng/ml and (0.86 ± 0.23) ng/ml and (0.79 ± 0.07) ng/ml in the blood sera of groups G1, G2 and G3 respectively, while it was (2.92 ± 0.45) ng/ml in blood sera of the control group. The results show that there are differences in the level of Testosterone hormone as it shows significant decrease (P ≤ 0.01) in blood sera of all groups under experiment as shown in figure (1). It was noticed that decrease level augments as the concentration of the administered drugs dose increases. Table (1) also shows the mean ± standard deviation of Testosterone in the second week of administration as it was (0.94 ± 0.06) ng/ml and (0.51 ± 0.07) ng/ml and (0.14 ± 0.03) ng/ml in the blood sera of groups G1, G2 and G3 respectively while it was (4.11 ± 0.32) ng/ml in blood sera of the control group. Second week results shows a significant decrease (P ≤ 0.01) in blood sera of all the experimented groups as shown in figure (1).

The reason behind Testosterone decrease in the handled groups lies in the deterring occurs in testis functions, and as it is known that Glucocorticoid drugs, to which belongs the drug used in the research, deter the glucocorticoid receptors in Lydig cells (cells responsible for secreting Testosterone hormone) and Sertoli cells[17]. Quelling and paralyzing the process of creating the steroid in the testis is due to deterring that happens to the activity of enzymes that create steroids or due to overstrain resulted from LH hormone decrease in plasma[18]. Effect on Lydig cells might be done by many sides: the effect which occurs to the content the receptor human chorionic gonadotropin–hCG, the copying process of mRNA and the consistency or stimulation

![Figure (1): Mean ± standard deviation for Testosterone hormone level in first and second weeks of administration.](image-url)
occurs in the cytochrome content P450. The decrease in Testosterone level during the second week is due to the sensitivity increase of Lydig cells by increase of rat's age, then it is deterred more by treating with Glucocorticoid drugs[19].

It is shown in table (1) that mean ± standard deviation for LH hormone is (8.79 ± 0.52)mIU/ml and (5.96 ± 0.29)mIU/ml and (2.77 ± 0.22) mIU/ml in blood sera of groups G1,G2 and G3 respectively, while it is (13.58 ± 1.16)mIU/ml in blood sera of the control group, shows significant decrease (P≤ 0.01) in blood sera of all groups under experiment as shown in figure (2). It was noticed that decrease level augments as the concentration of the administered drugs dose increases. The results show difference in LH hormone level as it shows a significant decrease (P≤0.01) in blood sera of all groups under experiment as shown in figure (2). A decrease is noticed clear and significant in hormone level of blood sera of all groups under study, it increases by drug concentration increase. Table (1) also shows mean ± standard deviation of LH hormone during the second week of administration as results are (5.40 ± 0.16)mIU/ml and (3.57 ± 0.26)mIU/ml and (1.62 ± 0.15) mIU/ml in blood sera of groups G1, G2 and G3 respectively; and (13.49 ± 0.96)mIU/ml in blood sera of the control group. Results show that there are difference in LH hormone level as it shows a significant decrease (P≤0.01) in blood sera of all the groups under experiment during the second week, as shown in figure (2).

![Figure (2): Mean ± standard deviation for LH hormone level in first and second weeks of administration.](image)

Results show that LH hormone level is reduced comparing to control group as Glucocorticoid drugs may reduce the hormone batches which release hormone GnRH
secreted from hypothalamus gland[20]. It is known that GnRH is secreted per batches and when deterring occurs or reducing the secretion of this hormone, it will lead to reduction of hormone LH level, and that time factor also affects if LH hormone level keeps reducing in the second week. The cause may be attributed to the reduced response of Leydig cells to LH hormone as a result of cellular changes.

It is shown in table (1) that mean ± standard deviation for FSH hormone is (0.94 ± 0.07)mIU/ml and (0.82 ± 0.18)mIU/ml and (0.60 ± 0.13) mIU/ml in blood sera of groups G1, G2 and G3 respectively and (1.59 ± 0.37)mIU/ml in blood sera of the control group. Results also show that there are differences in FSH hormone level as they show a significant reduction (P≤ 0.05) in blood sera of group G2 and G3 while no significant changes are registered in blood sera of group G1 as shown in figure (3), and that the reduction is greater at high concentration of the drug. As for the second week of administration it is mean ± standard deviation for FSH hormone (0.48 ± 0.04)mIU/ml and (0.44 ± 0.15)mIU/ml and (0.28 ± 0.05) mIU/ml in blood sera of groups G1, G2 and G3 respectively and (1.34 ± 0.15)mIU/ml in blood sera of the control group.

The results show that there are differences in FSH hormone level, as it shows a significant decrease (P≤0.01) in blood sera of all the groups, as shown in figure (3).

Figure (3): Mean ± standard deviation for FSH hormone level in first and second weeks of administration.

Results concerning FSH hormone indicate the increase of the hormone level in blood sera of groups treated with high concentrations of the drug in comparison with control group. The reason may be attributed to the glucocorticoid drugs which reduce
the hormone batches which release hormone GnRH secreted from hypothalamus gland[21].

The table (1) shows mean ± standard deviation for Prolactin in first week of administration (2.44 ± 0.19)ng/ml and (3.58 ± 0.35)ng/ml and (04.32 ± 0.37) ng/ml in blood sera of groups G1,G2 and G3 respectively and (1.35 ± 0.28)ng/ml in blood sera of the control group . Results show that there are differences in Prolactin hormone level as it shows a significant increase (P ≤ 0.01) in blood sera of all the experimented groups except group G1 which is administered with the least concentration of the drug , as shown in figure (4). In the second week of the administration mean ± standard deviation of Prolactin is (3.77 ± 0.32)ng/ml and (6.11 ± 0.39)ng/ml and (8.93 ± 0.64) ng/ml in blood sera of groups G1,G2 and G3 respectively and (0.32 ± 0.08)ng/ml in blood sera of the control group . Results show that there are differences in Prolactin level , as it shows a significant increase (P≤0.01) in blood sera of all the experimented groups as shown in figure (4). This increase is occurred by the increased concentration of the studied drug dose .

![Figure (4): Mean ± standard deviation for Prolactin hormone level in first and second weeks of administration.](image)

Studies refer to that Prolactin is an active hormone for regulating fertility in males and that patterns of creating and deferring are determined by the hypothalamus gland and hormone level in blood circulation at maturity stage is determined too . Prolactin response is done through nerve cells , which are self-regulated and have a role in deterring GnRH hormone[22]. One of the factors that deter creating of Prolactin hormone is Lydig cells which exist in testis and essential in creating testosterone ; then
these cells deter Prolactin while Estrogen hormone is considered a Prolactin stimulating agent. Relation between Prolactin and Testosterone is almost an inverse relationship, as the increase in Prolactin level is associated with the decrease of Testosterone in mature males[21].

**Conclusions**

Methylprednisolone drug has a negative effect on sex hormones level through decreasing the levels of Testosterone, LH and FSH and raising the level of Prolactin and thus infertility might be caused.

**References**


