Hormonal Disturbances among the Infertile Men in Baghdad-Iraq

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Abstract

The aims of this work are to determine the prevalence and pattern of endocrinological abnormalities in infertile men in our environment. The study was conducted on 70 infertile men with different subgroups. 43 were azoospermic, 14 with mildoligospermic and 13 with severoligospermic in addition to 20 healthy and fertile men as control. Hormonal assessments were done on those with abnormalities of their sperm count. Fifty-one (72.86%) of 70 subjects were with abnormal hormonal levels and 19 (27.14%) were with normal levels. Prolactin elevation was detected in 30 infertile men (42.86%) from all subgroups. This elevation was either alone (13 infertile men, 18.57%) or combined with abnormal levels of other hormones (24.29%). Other hormonal abnormalities were also detected in all subgroups. FSH was detected at high levels in 26 (37.1%) of 70 infertile men. Decreased level of testosterone, FSH and LH was also detected but in low percentage (1.43% each). The statistical analysis of these levels showed that FSH and prolactin were with high significant levels in azoospermic, LH in severoligospermic and LH plus prolactin in mildoligospermic.

Keywords: Infertility, FSH, LH, testosteron, azoospermia

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Introduction

Hormonal disturbances are results in approximately 15% of married couples and males are responsible in about 50% of them.\(^{1}\) Fertility in men required normal functioning of the hypothalamas, pituitary glands and testes and the complete male germ cells development is dependent on the balanced endocrine secretion of these glands.\(^{2}\)

The gonadotropins- FSH and LH- are secreted from the anterior pituitary in response to gonadotropin releasing hormones- GnRhd- secreted from the medial basal hypothalamus. The level of these hormones are under negative feed back control by the gonada.\(^{3}\) The primary role of these hormones in male is to stimulate the production of testosterone by the Leydig cells and to regulate spermatogenesis in Sertoli cells.\(^{4}\) The failure of the production of the gonadotropins will result in disruption of testicular function leading to infertility.\(^{5}\)

Therefore, hormones measurement can help determine whether the patient has gonadotropin deficiency, primary testicular failure, spermatogenic failure or androgen resistance. The current study is focused on the correlation between hormones level, semen profile and personal and health record.

Materials and Methods

1. Subjects

The infertile men who attended the Infertile Clinic at Kamal Alsamarai Hospital, Alkadimyah Hospital and private clinics/Baghdad/Iraq between June 2008 to May 2009 were recruited into the study. They were asked to complete a comprehensive questionnaire relating to their medical and personal history, lifestyle habits and exposure to gonadotoxins (such as radiation therapy and drugs used for cancer chemotherapy).

A complete semen analysis was performed in all cases according to the World Health Organization Guidelines.\(^{6}\) Semen samples were obtained after a 3- to 7-day period of sexual abstinence. At least two abnormal semen analyses had to be presented before a diagnosis of oligozoospermia could be made. Azoospermia was verified in at least two ejaculates by pellet analysis after semen centrifugation (1000 \(\times\) g for 20 min). In addition, blood samples were obtained for hormonal evaluations.

2. Hormonal evaluations

Serum concentrations of follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL) and testosterone were measured by ELISA using Enanthos 2020 system and according to the manufacturer’s instructions. Normal reference ranges for men were: FSH 1.7-12 mIU/L, LH 4.6-10 mIU/L, PRL 1.5-7.5 ng/mL and testosterone 3-9 ng/mL.
Results

Fifty-one (72.86%) of 70 subjects were found with abnormal hormonal levels and 19 (27.14%) were with normal levels. None of subgroups included in this study showed homogenized hormonal results (Table 1). Prolactin elevation was detected in 30 infertile men (42.86%) from all subgroups. This elevation was either alone (13 infertile men, 18.57%) or combined with abnormal levels of other hormones (24.29%). In azoospermic, the elevation of prolactin was detected in 19 (44.19%) of 43 azoospermic men. Nine of these (20.93%) were with prolactin elevation alone and the rest (10 men, 23.26%) were combined with other hormonal abnormalities.

In severe oligospermic, prolactin elevation alone was detected in 2 men (15.38%) of 13 oligospermic and in 2 men (15.38%) combined with abnormal levels of other hormones. However, the prolactin elevation in the severe oligospermic represent 30.77%.

In mild oligospermic sub group the elevation level of prolactin was detected in 7 (50%) of 14 mild oligospermic men. Two of these (14.28%) were with prolactin elevation alone, the rest (5 infertile men, 53.72%) of these were with elevated prolactin combined with abnormal level of other hormones. Other hormonal abnormalities were also detected in all subgroups. FSH was detected at high levels in 26 (37.1%) of 70 infertile men. 19 (27.1%) of them were detected in the azoospermic subgroup. Eight (18.6%) of 43 azoospermic were detected with FSH elevation alone, 2 with LH elevation alone, 1 with FSH and testosterone elevation, 1 with diminished testosterone and 1 with FSH elevation and diminished testosterone levels. Such abnormalities were also detected in severe and mild oligospermic subgroups. In severe oligospermic men, one of 13 subjects were with LH elevation alone, one with FSH and LH elevation, one with FSH and testosterone elevation.

Table 1  Hormonal profile of the azoospermic, severe oligospermic, mild oligospermic men and control.

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Mean ± SD</th>
<th>FSH</th>
<th>LH</th>
<th>Prolactin</th>
<th>Testosterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoospermic</td>
<td></td>
<td>*12.3 ± 2.04</td>
<td>8.62 ± 2.9</td>
<td>*10.35 ± 1.5</td>
<td>5.57 ± 2.8</td>
</tr>
<tr>
<td>Severoligospermic</td>
<td></td>
<td>*10.2 ± 2.1</td>
<td>9.39 ± 1.8</td>
<td>6.47 ± 1.2</td>
<td>6.91 ± 2.6</td>
</tr>
<tr>
<td>Mildoligospermic</td>
<td></td>
<td>9.36 ± 2.6</td>
<td>*10.91 ± 3.2</td>
<td>*9.41 ± 2.9</td>
<td>6.92 ± 1.8</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>8.45 ± 3.21</td>
<td>8.18 ± 1.82</td>
<td>6.0 ± 1.5</td>
<td>7.9 ± 1.32</td>
</tr>
</tbody>
</table>

*p <0.05, high significant
and one with decreased LH and testosterone levels. In mildoligospermic, one of 14 subjects was with FSH and LH elevation and one with FSH and testosterone elevation levels. The statistical analysis of these levels showed that FSH and prolactin were with high significant levels in azoospermic, LH in severoligospermic and LH plus prolactin in mildoligospermic (Table 2).

Table 2 The spectrum of reproductive hormones levels in infertile men

<table>
<thead>
<tr>
<th>Hormones level</th>
<th>Infertility subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Azoospermia No.43</td>
</tr>
<tr>
<td>FSH elevation alone</td>
<td>8</td>
</tr>
<tr>
<td>LH elevation alone</td>
<td>2</td>
</tr>
<tr>
<td>Prolactin elevation alone</td>
<td>9</td>
</tr>
<tr>
<td>FSH+LH elevation</td>
<td>2</td>
</tr>
<tr>
<td>FSH+ prolactin elevation</td>
<td>4</td>
</tr>
<tr>
<td>LH+ prolactin elevation</td>
<td>1</td>
</tr>
<tr>
<td>FSH+LH+prolactin elevation</td>
<td>3</td>
</tr>
<tr>
<td>FSH+ testosterone elevation</td>
<td>1</td>
</tr>
<tr>
<td>Prolactin+testosterone elevation</td>
<td>1</td>
</tr>
<tr>
<td>Decreased testosterone+elevated prolactin</td>
<td>1</td>
</tr>
<tr>
<td>Decreased testosterone alone</td>
<td>1</td>
</tr>
<tr>
<td>Decreased FSH+LH</td>
<td>0</td>
</tr>
<tr>
<td>Decreased LH+ elevated prolactin</td>
<td>0</td>
</tr>
<tr>
<td>Decreased testosterone + elevated FSH</td>
<td>1</td>
</tr>
<tr>
<td>Infertile men with normal levels</td>
<td>9</td>
</tr>
</tbody>
</table>

Discussion

It is extremely important in the evaluation of male infertility to consider the reproductive hormone levels. It was reported that these hormones have a major role in male spermatogenesis.\(^{(7,8,9)}\) LH effects spermatogenesis indirectly in that it stimulates androgenous testosterone production while FSH targets Sertoli cell.\(^{(10)}\) Previous studies on male infertility in Iraq were found that the elevated FSH is a reliable indicator for germinal epithelial damage, decreased Sertoli cells function and azoospermia\(^{(11,12)}\). In our study, serum FSH was found with high level alone in 8 (18.6%) of 43 azoospermic but not in oligospermic males and combined with other hormones high levels in 14 (20%) of 70 infertile men. LH elevation alone was also
detected in 2 of 43 azoospermic and in one of 13 severoligospermic and combined with FSH elevation in 2 azoospermic, one severoligospermic and one mildoligo-spermic. Elevation of FSH and LH was reported to be an indication of testicular failure in which there is loss of negative feedback by testicular products which lead to increase the levels of FSH and LH causing in failure of sperm production.\(^{(13)}\) While low levels of FSH and LH lead to decrease gonadotropin stimulation of potentially normal testes leading to a secondary hypogonadism.\(^{(10)}\) The cause appears to be a partial gonadotropin deficiency in which there is adequate LH to stimulate testosterone production with resultant spermatogenesis but insufficient testosterone to promote virilization.\(^{(14)}\) FSH elevation alone or LH elevation alone were also reported in infertile men.\(^{(3,4,5)}\) FSH elevation alone may indicate disturbance of seminiferous tubules function probably due to deficient secretion of inhibin and sex steroids.\(^{(8)}\) Such inhibin deficiency was early reported to be associated with pituitary tumor.\(^{(15)}\) Inhibin produced by Sertoli cell and regulate and control FSH level by the feedback mechanism.\(^{(16)}\) Decreases in spermatogenesis are accompanied by decreased production of inhibin and this reduction in negative feedback is associated with elevation of FSH level.\(^{(10)}\) Isolated increased levels of FSH constitute an important, sensitive marker of the state of the germinal epithelium.\(^{(17)}\) While LH elevation alone suggest the presence of a cross-reacting substance such as hCG.\(^{(10,17)}\) The break through in our results is the elevated level of prolactin. 30 (42.86%) of 70 infertile men were with elevated level of prolactin. 19 (63.33%) of them are in azoospermic subgroup. Prolactin elevation alone was detected in 13 infertile men nine of them in azoospermic subgroup. This make the prolactin elevation the major cause of men infertility in Iraq - especially in azoospermic- followed by elevation of FSH alone.

This does not indicate absence of effect of hormone decreases. Decreased level of testosterone, FSH and LH was also detected but in low percentage (1.43% each). Prolactin is generally only though of as factor in female fertility, but in fact, also play a role in male fertility. Elevation of prolactin in male can cause decreased testosterone level or abnormal sperms.\(^{(3,15)}\) Such elevation also tends to inhibit the production of gonadotropin releasing hormone-GnRH- from hypothalamus which is essential for stimulating the production and release of both FSH and LH from the anterior pituitary.\(^{(3)}\) Moreover, the exposure to constant GnRH results in inhibition of FSH and LH.\(^{(3,7)}\)

Hyperprolactinemia is considered a pituitary disorder. Elevation of prolactin levels in men are usually the result of overactive prolactin cells in the pituitary gland which is a kind of tumor called prolactinoma.\(^{(15)}\) Other factors were also implicated in prolactin production and regulation such as thyrotropin releasing hormone-TRH\(^{(18)}\), serotonin (trigger
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the prolactin production\(^{(19)}\), dopamine which block prolactin\(^{(20)}\), iron deficiency\(^{(21)}\) and 21-hydroxylase deficiency.\(^{(14)}\) Whether the high percentage of hyperprolactinemia recorded in our work due to pituitary gland tumor or to another resenaone need further investigations especially with high contamination caused by gulf wares.

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References


