

A Relationship of Sex Hormone Levels and Erectile Dysfunction: Which Tests Should Be Done Routinely?

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Purpose: In this study, the relationship between sex hormone levels and erectile dysfunction (ED), as well as the necessity of routinely measuring sex hormone levels were evaluated. **Materials and Methods:** This study included one hundred patients admitted to a urology clinic for sexual dysfunction. To determine the hormone levels, following the history (included IIEF-5 score) and physical examination, triple blood samples were collected at intervals of 15 minutes between 08:00 and 10:00 am. Total and free testosterone, prolactin, follicle stimulating hormone and luteinizing hormone levels were studied. **Results:** Mean age was 43 (23 - 80) years. IIEF-5 score was less than 21 [9.8 - 4.3 (3 - 19)] in all study groups. There was a statistically significant correlation between tT and FSH, as well as between LH and FSH in Pearson ($r = -0.513$, $p < 0.001$, respectively) and also in Spearman tests ($r = -0.224$, $p = 0.042$ and $r = -0.459$, $p < 0.001$, respectively). However, there was no correlation between age and serum hormone levels ($p > 0.05$). Of the 100 patients, 18 (18%) had low tT, 77 (77%) had normal and 5 (5%) had high tT levels. No statistically significant correlation was found between decreased libido and tT levels ($p > 0.05$). Twelve (66.6%) of the 18 patients with low tT had normal libido. **Conclusion:** Analyzing the medical history in detail and performing a thorough physical examination can reduce the need for excessive studies and consultations, and enables patients to save time and costs.

Key Words: Hormones, diagnostic tests, erectile dysfunction, measurement and libido

INTRODUCTION

Erectile dysfunction is defined as the inability to

achieve or maintain an erection required for satisfactory sexual intercourse. It is a pathology that affects men's happiness, self-esteem and popular relations and may also contribute to serious psychological problems.^{1,2} According to the Massachusetts Male Aging Study, the prevalence of ED of all degrees is approximately 52% in men between 40 and 70 years.³ As most of the men are reluctant to discuss ED, more than 70% of ED cases remain undiagnosed.⁴ For this reason, most of the urologists perform an extensive screening of the patients admitted to urology clinics for ED.

Testosterone helps regulate sexual function; it organizes the sexual drive and stimulates masculine behavior.⁵ Testosterone is secreted episodically from the testicular Leydig cells in response to luteinizing hormone pulses, showing a diurnal pattern with a peak level in the early morning and a nadir in the evening. The unbound or active portion of testosterone accounts for approximately 2% of the total body stores, while the remaining 98% is bound to plasma proteins, primarily albumin and testosterone-estradiol-binding globulin.⁶ This unbound or free testosterone, which is equal to 2%, is physiologically active, with its effects exerted in the target cell where it may be converted to a more potent androgen, dihydrotestosterone, by 5-alpha reductase. Many factors can alter the amount of plasma proteins and, thus, affect the amount of biologically active free testosterone.⁷ Insufficient testosterone levels lead to a decrease in the relaxation of smooth muscle of corpus cavernosum.⁸

These diverse contributing factors necessitate the careful analysis of several parameters for diagnosing ED in patients. However, when the realities of costs and time are taken into con-

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sideration, only a routine examination is usually performed. While many of the diagnostic tests struggle to reduce costs. It is imperative that the evaluation remains sensitive enough to identify individuals with treatable endocrinopathies.⁷ In this respect, in our study, the relationship between sex hormone levels and ED, and the necessity of measuring hormone levels *routinely* for ED were evaluated.

MATERIALS AND METHODS

In this study, we evaluated 100 consecutive patients admitted to an andrology clinic for ED. Inclusion criteria were: being ≥ 18 years old, having a clinically diagnosed ED for the previous 6 months as evaluated by our institution and having a regular sexual life with a female partner. Patients with a history of previous pelvic surgery, pelvic irradiation, chronic neurological disease, hypogonadism, or excess alcohol consumption, as well as those who were on medication during the recruitment period were excluded from the study. All patients completed a detailed questionnaire, the validated Sexual Health Inventory for Men 5-item questionnaire, based on the International Index of Erectile Function questionnaire which covered all of the aspects of erectile dysfunction (IIEF-5).^{9,10} A physician examined all of the patients following the interview and requested the necessary tests be performed.

Following 10 hours without food, triple blood samples for hormone analyses were taken at 15-minute intervals between 8.00 and 10.00 AM.¹¹ Serum samples were kept at -70°C after a separation by centrifuge. Total testosterone (tT), free testosterone (fT), prolactin (PL), follicle stimulating hormone (FSH), and luteinizing hormone (LH) levels were studied with chemiluminescent immunoassay (ACS: 180-Chiron) and competitive radio immunoassay-(DSL) techniques. Measuring pituitary gonadotropins, FSH and LH can provide reliable clues to assist the physician in determining whether it is primary or secondary hypogonadism.

Based on the status of their libido, patients were divided into two groups as the normal libido group ($n = 58$) and the decreased libido group ($n =$

42). Libido groups were compared with age groups using chi-square tests. In addition, again using the chi-square test, libido groups were compared with groups classified according to tT, fT and PL levels. An unpaired, two-sample t-test, one-way ANOVA, logistic regression analyses and Spearman and Pearson's correlation analyses were used to compare the differences among the groups.

RESULTS

Mean age was 43 (23 - 80) years. The questionnaire took about 5 minutes to complete. IIEF-5 score was less than 21 [9.8 ± 4.3 (3 - 19)] in all study groups, which is indicative of ED. The IIEF-5 score was 17 to 21 in 6 of the 100 men (6%), suggesting mild ED; 11 to 16 in 40 (40%), suggesting mild to moderate ED; 8 to 10 in 18 (18%), suggesting moderate ED, and 7 or less in 36 (36%), suggesting severe ED.

The mean tT, fT, PL, FSH and LH levels were 14.5 ± 7.0 nmol/L (8.4 - 28.7 nmol/L, normal range), 72.5 ± 46.5 pmol/L (30.1 - 189.8 pmol/L), 12.9 ± 10.1 $\mu\text{g/L}$ (1.6 - 18 $\mu\text{g/L}$), 8.4 ± 10.9 IU/L (< 11 IU/L) and 6.2 ± 6 IU/L (0.5 - 6 IU/L), respectively. There was a statistically significant correlation between tT and FSH and also between LH and FSH in Pearson ($r = -0.513$, $p < 0.001$, respectively) and also in Spearman tests ($r = -0.224$, $p = 0.042$ and $r = -0.459$, $p < 0.001$, respectively). However, there was no correlation between age and serum hormone levels ($p > 0.05$).

Table 1 lists the mean values for tT, fT, and PL, as well as the rate of decreased libido according to the age groups. When the patients were classified according to decreased libido, only PL levels had a significant correlation with decreased libido (Table 2). There was an association between decreased libido and PL levels also on logistic regression analysis (Not shown on the tables, $p = 0.046$).

Of the 100 patients, 18 (18%) had low tT, 77 (77%) had normal and 5 (5%) had high tT levels. We did not find a significant correlation between decreased libido and tT levels by Student's t-test ($p > 0.05$). In addition to the information concerning testicular atrophy from the patients'

Table 1. The Mean Values of tT, fT, PL and the Rate of Decreased Libido in According to Age Group

Age groups (n)	tT	fT	PL	Decreased libido (%)
20 - 29 (10)	18.4	71.8	20.9	4 (40)
30 - 39 (10)	15.3	85	13.3	3 (30)
40 - 49 (32)	13.9	90.2	11.5	19 (60.6)
50 - 59 (26)	14.8	54.1	13.6	9 (33.3)
60 - 69 (17)	12.3	38.1	10.9	6 (35)
≥ 70 (5)	12.4	65.9	9.7	1 (20)
Total (100)	14.5	72.5	12.9	42 (42)
<i>p</i> value	0.392*	0.728*	0.193*	-

tT, total testosterone; fT, free testosterone; PL, prolactin.

*One way ANOVA.

Table 2. Mean Values of Age, tT, fT, PL, FSH and LH in According to Status of Libido

Libido	Age (yrs)	tT	fT	PL	FSH	LH
Decreased (n = 42)	47	14.7	69.4	16.5	7.6	5.3
Normal (n = 58)	50	14.2	76.3	10.2	8.9	6.8
<i>p</i> values	> 0.05	> 0.05	> 0.05	0.002	> 0.05	> 0.05

tT, total testosterone; fT, free testosterone; PL, prolactin; FSH, follicle stimulating hormone; LH, luteinizing hormone.

Table 3. The Percentages of Patients who had a Low, Normal and High Hormone Levels in According to Status of Libido

Libido	Low tT*	Normal tT*	High tT*	Low fT*	Normal fT*	High fT*	Low PL*	Normal PL*	High PL*
Decreased (n = 42)	6 (14)	34 (81)	2 (5)	15 (36)	23 (55)	4 (9)	-	32 (76)	10 (24)
Normal (n = 58)	12 (21)	43 (74)	3 (5)	-	58 (100)	-	1 (2)	50 (86)	7 (12)
<i>p</i> value [†]		0.076			0.085			0.190	

tT, total testosterone; fT, free testosterone; PL, prolactin.

*n (%).

[†] chi square test.

charts, the data from a questionnaire on libido were reviewed for those patients (n = 18) with low fT level. Since these patients had normal testicles on examination and normal fT and PL levels, they were not evaluated further. On the other hand, 12 (66.6%) of these 18 patients with low tT had normal libido. The percentage of patients who had low, normal and high hormone levels are shown on Table 3 with respect to decreased libido.

Serum PL levels were available in 93 of our 100

patients (91.2%) and were low in 1 (1.1%), normal in 76 (81.7%) and high in 16 (17.2%) patients. None of these patients with a high PL level had a pituitary pathology and 5 of these 16 patients had a low tT (31.3%).

DISCUSSION

Understanding the dynamics of endocrine

changes in the normally aging male is important not only because of the important role hormones play in the maintenance of sexual characteristics and sexual activity, but also for the diagnosis and management of endocrine and metabolic diseases. Data concerning the influence of age on androgens are inconsistent. Several researchers have reported a decrease in free and total testosterone concentrations, whereas others have failed to find age-related changes in testosterone.^{3,12} Although tT seems to decline slightly with age, we could not find any statistically significant correlation between age groups and the values of tT and fT.

This decline with age is related to decreased Leydig cell mass, decreased testicular perfusion with relative hypoxia and alterations in pituitary-hypothalamic function.¹³ FSH and LH show an increase with age, but PL has not been studied well in men. Davidson et al and Deslypere et al found no correlation between male PL levels and age, while Vekemans and Robyn reported a slight rise in PRL in 55 to 65 year-old men compared to those 20 years younger.¹⁴⁻¹⁶ In this study there was no correlation between age and PL levels.

In hypogonadic men, impaired erection response to visual sexual stimulation prompts consideration of androgens as enhancing erection, but not absolutely necessary.^{17,18} In 1% of ED cases caused by endocrinological problems, investigating serum testosterone levels once is sufficient when paired with a detailed history and physical examination.¹⁹ Johnson and Jarow found a low incidence of endocrinopathy (2.1%) and noted that decreased libido and/or testicular atrophy would predict this condition with 100% sensitivity.²⁰ They recommended laboratory testing only in patients with decreased libido and/or testicular atrophy. Slag et al studied 187 impotent patients and found no correlation between libido and hypogonadism in 35, while testicular atrophy correlated only with primary hypogonadism.²¹ In our study group (n = 100), only 42 patients had decreased libido and none of them had any type of endocrinopathy. Moreover, most of these patients had normal values of tT (80.5%) and PL (76%).

Fahmy et al reported that it is very difficult to establish a correlation between ED and serum testosterone levels; and demonstrated that low serum tT levels (<10 nmol/mL) indicate hypo-

gonadism.¹⁸ In the Massachusetts Male Aging Study, testosterone levels were confirmed to decline with age and free testosterone was found to be more predictive than tT.¹² It has been suggested that only the measurement of free testosterone is sufficient in ED, and it is not necessary to analyze other hormones.⁷ Buvat and Lemaire recommended measuring testosterone in all the men > 50 years and in only those men who are < 50 years old but having decreased libido and abnormal physical findings.²² But Ansong et al. found that routine serum tT and fT measurement were not sufficient for decreased libido and ED.¹³ However, we have found no significant correlation between ED and the values of tT and fT.

Although it seems more likely that decreased libido is a secondary phenomenon related to a defence mechanism in men with ED, in the present study, no statistically significant relation was found between ED and libido. PL levels were found to have a significant relation with decreased libido. Govier et al found a 16% incidence of hypogonadism and 57% of this group had neither decreased libido nor testicular atrophy.⁷

Baskin reviewed 600 patients and found a 3% incidence of hyperprolactinemia and 7 patients had pituitary tumors (6 with low testosterone).²³ Foster et al. found a 3.9% incidence of hyperprolactinemia with 2 pituitary tumors.²⁴ One patient with pituitary tumor had decreased libido and decreased serum testosterone, and 1 had decreased libido but normal serum testosterone. In practice, performing a history and physical examination in conjunction with measurement of testosterone may not be sufficient to diagnose hypogonadism or hyperprolactinemia in these patients.²⁵ Moreover, testosterone levels are not always depressed in endocrinological diseases.¹⁸ As such, we suggest that PL should be measured only in patients having any clinical signs and manifestation of endocrinopathy, not in all patients who present to a urology clinic for ED.

Measurement of hormones should be delayed until after taking a detailed history and performing a thorough physical examination. When these findings were evaluated with respect to other studies in the literature, measuring fT and especially PL should provide adequate information.

Taking a detailed medical history and per-

forming a thorough physical examination with history can decrease the need for excessive studies and consultations, saving patients time and unnecessary cost.

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