Original Paper

Urologia Internationalis

Urol Int 2012;88:454–458
DOI: 10.1159/000336137

Received: September 21, 2011
Accepted after revision: December 23, 2011
Published online: February 23, 2012

Hormonal Evaluation in Premature Ejaculation

Metin İshak Öztürk Orhan Koca Murat Tüken Muzaffer Oğuz Keleş
Abdullah İlktaç M. Ihsan Karaman

Department of Urology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

Key Words
Premature ejaculation · International Index of Erectile Function · Endocrine abnormalities

Abstract
Introduction: Premature ejaculation (PE) is a frequently encountered sexual dysfunction in men. It significantly impairs quality of life of the affected male and his partner. The aim of this study is to investigate the role of hormonal factors in patients with PE. ***Patients and Methods:*** 107 male patients aged between 26 and 64 years (mean 45.1 ± 10.36) who consulted our outpatient clinics with complaints of PE and 94 healthy males (48.1 ± 11.81 years) as a control group were included in the study. ***Results:*** When mean serum hormone concentrations of both groups were compared, levels of prolactin and free T4 were found to be significantly higher in the PE group relative to the control group ($p < 0.05$). At least one of the hormonal parameters was abnormal in 36 cases (33.6%) with PE, compared to only 22 (23.4%) of the controls. The number of hyperprolactinemic cases was found to be significantly increased in the PE group ($p < 0.05$). ***Conclusion:*** We feel that during the evaluation of this problem, which affects great numbers of men and their partners throughout the world, consideration of potential effects of hormonal factors might be beneficial.

Introduction

Premature ejaculation (PE) is a frequently encountered type of male sexual dysfunction. Although its incidence varies according to the criteria used for the definition of PE, it usually ranges between 22 and 38% [1]. Apart from erectile dysfunction (ED), it is known to affect adult males in all age groups at similar rates [2]. PE significantly impairs quality of life of the affected male and his partner. Genetic factors are known to have an effect on the lifelong PE etiology. However, neurologic, endocrinologic, psychologic and urologic factors might conceivably be involved in the etiology of acquired PE [3].

Hormones do affect an individual's sexuality throughout his life (and even in the early phases of fetal life) [4]. However, hormonal mechanisms involving sexual function, and dysfunction, and their degree of impact have not been fully elucidated. Investigation and revealment of hormonal disorders (if any) in patients with sexual dysfunction is important as among patients with sexual dysfunction, these cases respond to treatment more favorably. In most of the cases, sexual dysfunction also resolves with no further treatment when the hormonal abnormality is corrected [4].

The role of hormones in the male reproductive physiology has been analyzed in many trials; however, only a few studies have investigated their place in ejaculatory

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0042–1138/12/0884–0454$38.00/0

Accessible online at:
www.karger.com/uin

Orhan Koca, MD
Haydarpaşa Numune Eğitim ve Araştırma Hastanesi II. Üroloji Kl, Üsküdar
TR–34718 Istanbul (Turkey)
Tel. +90 216 414 4502
E-Mail drorhankoca@hotmail.com

mechanism and their impact on intravaginal ejaculatory latency time (IELT). However, there is an increasing (albeit gradually) body of evidence suggesting hormonal abnormalities as etiologic factors in PE [5, 6]. Pinpointing the place of hormonal causes in PE will enable us to understand its pathophysiology as well as contribute to the development of new treatment modalities. The aim of this study is to examine the place of hormonal factors in patients with PE.

Patients and Method

107 male patients aged between 26 and 64 years (mean 45.1 ± 10.36) who consulted our outpatient clinics with complaints of PE and 94 healthy males (mean age 48.1 ± 11.81, range 24–63) as a control group selected from our hospital staff were included in the study. Male participants in both groups were sexually active and had engaged in regular sexual activity for the last 6 months. A detailed sexual life history relevant to the objective of the study was obtained from each participant. Physical examination, routine laboratory tests, and serum thyroid-stimulating hormone (TSH), free T3, free T4, prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH) and total testosterone measurements were completed in all patients. Blood samples were obtained in the morning while the patient was resting. Subjects who had used drugs that might change hormonal values and IELT (antidopaminergics, testosterone preparations, anti-hypo/hyperthyroidism drugs, serotonin reuptake inhibitors, etc.) were excluded from the study. For abnormal values, a second blood sample was taken at a later date. Abnormal estimates confirmed twice were accepted as pathologic.

TSH, FT4, FT3, prolactin, LH, FSH, and total testosterone values were measured using immunoassay methods. The lower and upper limits of normal for the measured hormones were as follows: TSH: 0.4 and 4 mIU/l; free T4: 0.93 and 1.7 ng/dl; free T3: 1.80 and 4.60 pg/ml; prolactin: 4.1 and 20 ng/ml; LH: 1.7 and 8.6 mIU/ml; FSH: 1.5 and 12.4 mIU/ml; and total testosterone: 280 and 800 ng/dl.

The International Index of Erectile Function Erectile Domain (IIEF-ED) score (the sum of responses to questions 1–5 and 15) for evaluation of erectile function was evaluated. For the measurement of IELT, patients were provided with a stopwatch which had to be used by their partners. Statistical analysis was performed using Student t test; $p < 0.05$ was considered as statistically significant.

Results

The mean ages of the subjects evaluated in the PE (n = 107) and control (n = 94) groups were 45.1 ± 10.4 years (26–64), and 48.1 ± 11.8 years (24–63), respectively. Age distribution was homogenous in both groups (table 1).

The mean IIEF-ED score in patients with PE was found to be 21.4. In the control group, the mean IIEF-ED score was 24.3. A significant intergroup difference was found for the IIEF-ED score ($p < 0.05$) (table 1).

Based on IIEF–ED assessment, scores in PE group were >26 in 30 (28.0%; absence of ED), 17–25 in 56 (52.3%; mild ED) and 11–16 in 21 (19.6%; moderate ED) patients, while in the control group 44 men (46.8%) were without ED, 44 (46.8%) had mild or moderate ED, and 3 (3.2%) had severe ED.

Mean serum prolactin and free T4 concentrations were found to be significantly higher in the PE group ($p < 0.05$). Serum levels of other hormones measured did not differ between groups.

Hyperprolactinemia was detected in 19 participants (17.8%) in the PE group, while hypoprolactinemia was not seen in any of them. In the control group we identified 7 hyperprolactinemic (7.4%) and 2 (2.1%) hypoprolactinemic participants.

Hypotestosteronemia was found in 7 (36.8%) out of 19 patients with hyperprolactinemia. In the PE group, mean serum testosterone (400.6 ± 182.9 ng/dl) levels of hyperprolactinemic patients were detected to be significantly lower than the corresponding mean value (471.8 ± 122.4 ng/dl) in those without ($p < 0.05$). The total mean testosterone level in hyperprolactinemics without PE was calculated to be 456.6 ± 113.4 ng/dl, while it was estimated to be 382.4 ± 108.6 ng/dl in those without PE and hyperprolactinemia (table 2).

LH-FSH elevation was found in 6 patients (5.6%) with PE, and isolated LH elevation was detected in 4 cases (3.7%) with PE. Eleven patients (10.3%) were hypotestosteronemic. Besides, 7 (63.6%) of 11 hypotestosteronemic patients demonstrated LH and/or FSH elevation (hypergonadotropic hypogonadism). In the control group, however, 4 participants (4.3%) had LH-FSH elevation, while isolated LH or FSH elevation was seen in 2 patients each. Four (57.1%) out of 7 (7.4%) hypotestosteronemic participants had LH and/or FSH elevations.

Lower than normal levels of TSH were detected in 9 patients (8.4%) with PE, and all of these patients had higher serum free T4 levels. Two patients (1.86%) with higher TSH levels demonstrated normal serum free T4 concentrations. Lower TSH levels were detected in 4 participants (4.25%) in the control group who all demonstrated free T4 levels higher than normal. Only 1 (4.25%) out of the 4 patients with increased TSH levels had serum free T4 concentration that was lower than normal.

At least one of the hormonal parameters of 36 cases (33.6%) with PE was abnormal, while we found only one

Table 1. Comparisons between PE and control group parameters

	PE	Control	p
Age, years	45.13 ± 10.36	48.12 ± 11.81	>0.05
LH, mIU/ml	5.28 ± 2.93	5.72 ± 1.96	>0.05
FSH, mIU/ml	5.50 ± 4.99	5.39 ± 2.81	>0.05
Testosterone, ng/dl	458.46 ± 137.5	478.91 ± 130.3	>0.05
Prolactin, ng/ml	14.36 ± 7.02	11.90 ± 6.35	<0.05
TSH, mIU/l	1.24 ± 0.78	1.43 ± 1.23	>0.05
Free T3, pg/dl	3.29 ± 0.60	3.42 ± 0.49	>0.05
Free T4, ng/dl	1.43 ± 0.66	1.28 ± 0.32	<0.05
IELT, s	44.12 ± 23.42	315.64 ± 184.4	<0.05

Values are means ± SD. T3 = T3 thyroid hormones; T4 = T4 thyroid hormones.

Table 2. Comparative serum testosterone levels in cases with or without hyperprolactinemia in both groups

	Hyperprolactinemia (+)	Hyperprolactinemia (–)	p
PE	400.60 ± 182.90	471.76 ± 122.35	<0.05
Control	456.6 ± 113.4	382.4 ± 108.6	<0.05

Table 3. Most frequently seen endocrinopathies and number of affected male patients in both groups (%)

	PE group	Control group	p
Total number of patients with hormonal disorders	36 (3.64)	22 (23.4)	>0.05
Hypergonadotropism (LH and/or FSH elevation)	10 (9.34)	8 (8.51)	>0.05
Hypotestosteronemia	11 (10.28)	7 (7.44)	>0.05
Hyperprolactinemia	19 (17.75)	7 (7.44)	<0.05
Hyperthyroidism	9 (8.4)	4 (4.25)	>0.05

hormonal abnormality in only 22 participants (23.4%) in our control group. Statistically, no significant differences were observed when all cases with endocrinopathies were compared ($p > 0.05$). In the patient group, only the number of hyperprolactinemic cases increased significantly ($p < 0.05$) (table 3). Multiple endocrinopathies were detected in the PE (8.41%) and control groups (4.25%).

The mean IELT of patients with PE was 44.1 s, while in the control group it was found to be 315 s ($p < 0.05$) (table 1). The mean IELT of patients with PE associated with an endocrinopathy was 43.2 s, while it was detected to be 44.6 s in cases with PE without any endocrinopathy. There were no significant differences between the two groups.

Discussion

PE is the most dominant type of sexual dysfunction affecting men worldwide [7]. Although many etiologic factors have been blamed for its occurrence, influential factors have not yet been clearly revealed [8]. As is the case with other types of sexual dysfunction, evidence suggesting a potential role of hormonal disorders have been accumulating with increasing frequency [5, 6]. The objective of this study is to investigate the role of hormonal abnormalities in the etiology of PE.

The impact of thyroid hormones on sexual function and reproductive physiology is well known [9]. In recent years, some publications have suggested they have a potential effect on PE [4, 10]. Although the mechanism involved between hyperthyroidism and PE has not been not elucidated fully, increased sympathetic activity, serotoninergic neurotransmission and alterations in the estrogen/androgen ratio have been assumed to be influential [4]. Waldinger et al. [11] reported a lack of association between lifelong PE and TSH levels. Cihan et al. [9] suggested the presence of a significant association between serum TSH levels and mean IELT values. Cihan et al. also emphasized an existence of higher levels of anxiety in hyperthyroid PE patients relative to those found in healthy controls. They also concluded that performance anxiety secondary to hyperthyroidism leads to uncontrolled involuntary early ejaculation. In addition, they noted significant improvement in anxiety levels, and prolongation of IELT in patients with ameliorated thyroid dysfunction. In our study, consistent with the study by Cihan et al. [9], lower TSH levels were seen twofold more frequently in the PE group.

In patients with hyperthyroidism PE is generally seen, while patients with hypothyroidism frequently complain of delayed ejaculation [4]. In our study we did not encounter any case with hypothyroidism in the PE group.

With our current knowledge it is very difficult to clearly explain the mechanism of action of testosterone on ejaculatory latency time. However some theories have been proposed. Accordingly, an aggressive, dominant

and irritable way of conduct triggered by higher testosterone levels might lead to PE [5, 12]. Another theory asserts that decrease in ejaculate volume due to lower testosterone levels delays the onset of ejaculatory reflex leading to prolonged ejaculation latency [5]. Keleta et al. [13] demonstrated decrements in 5-hydroxytryptamine levels in the brains of testosterone-fed rats. Indeed, 5-hydroxytryptamine is an important central neurotransmitter known for its ejaculation-delaying effect [14]. In a patient series consisting of 2,437 ED patients, Corona et al. [5] revealed associations between various levels of testosterone and diverse ejaculatory problems, and reported that interrelationships between hypertestosteronemia and PE, as well as between hypotestosteronemia and delayed ejaculation are more frequently seen. Although this correlation was deduced completely from the findings of a specific patient group with ED, it has a crucial significance. In our study, regarding mean testosterone levels, any statistically significant difference between groups with or without PE was not observed. However, studies evaluating levels of bioavailable testosterone, which was not analyzed in our study, will contribute to our body of knowledge.

The prolactin molecule was discovered in 1933 [15]. Interestingly, the physiological role of prolactin in men has not been fully elucidated for the last 78 years [15]. However, severe hyperprolactinemia was implicated as an etiologic factor in ED and decreased libido [16, 17]. El-Sakka et al. [18] examined 1,249 patients with sexual dysfunction and demonstrated the presence of an association between hyperprolactinemia and PE. Also, in our study, we detected hyperprolactinemia in a significantly higher number of subjects relative to the control group. Even if mean ages of the PE and control groups are different from the mean ages cited for the above-mentioned study, detection of a significant correlation between hyperprolactinemia and PE in both trials is important.

Although mechanisms of sexual dysfunction in cases with hyperprolactinemia have not been elucidated fully, conceivably hypogonadism is frequently seen in these patients, and at least in some of them hypogonadism is responsible for sexual dysfunction [16]. In our study, mean testosterone levels in hyperprolactinemic patients were found to be statistically significantly lower than those with normal levels. This phenomenon which was cited in the literature, and also demonstrated in our study, might appear as a controversial assertion. Indeed hypogonadism is frequently observed in cases with hyperprolactinemia and hypogonadism is generally associated with delayed rather than premature ejaculation. This phenomenon suggests the presence of another mechanism playing a role in the etiology of PE.

In our study there was no statistically significant difference between the mean IELT values of patients with hormonal disorders and patients with normal hormonal parameters. In this case it can be suggested that investigation of hormonal disorders in PE etiology is unnecessary. On the other hand, patients with sexual dysfunction secondary to hormonal disorders constitute a more favorable group. Indeed in many cases, sexual dysfunction improves with the amelioration of hormonal disorders [4]. Besides, identification and correction of the hormonal abnormality contribute favorably to sexual and general health status of men as well.

In patients with sexual dysfunction, requirement of routine hormonal evaluation might be decided based on the cost-effectiveness of this evaluation. Johri et al. [19] detected 3 cases with hyperprolactinemia among 138 patients, and estimated that the cost of each test was USD 1.32; therefore, to come across 1 case with hyperprolactinemia, USD 60.7 needs to be spent. Although these results are debatable, we believe that in consideration of potential detection of other underlying diseases, alleviation of hormonal problems leading to improvement in sexual dysfunction without any additional therapy in many cases might justify the expense incurred.

The single-center study design, relatively small sample size and undetermined IELT subsequent to improvement in hormonal status constitute weak points of this study.

We think that the results of this study provide support for investigation of hormonal factors in the etiology of PE. However, as our study included only a limited number of patients and because the differences between the patient and control groups are not very distinctive, it is obvious that there is a need for larger studies.

References

1 McCarty EJ, Dinsmore WW: Premature ejaculation: treatment update. Int J STD AIDS 2010;21:77–81.
2 Linton KD, Wylie KR: Recent advances in the treatment of premature ejaculation. Drug Des Devel Ther 2010;4:1–6.
3 Rowland D, McMahon CG, Abdo C, Chen J, Jannini E, Waldinger MD, Ahn TY: Disorders of orgasm and ejaculation in men. J Sex Med 2010;7:1668–1686.
4 Carani C, Isidori AM, Granata A, Carosa E, Maggi M, Lenzi A, Jannini EA: Multicenter study on the prevalence of sexual symptoms in male hypo- and hyperthyroid patients. J Clin Endocrinol Metab 2005;90:6472–6479.

5 Corona G, Jannini EA, Mannucci E, Fisher AD, Lotti F, Petrone L, Balercia G, Bandini E, Chiarini V, Forti G, Maggi M: Different testosterone levels are associated with ejaculatory dysfunction. J Sex Med 2008;5:1991–1998.
6 Corona G, Jannini EA, Lotti F, Boddi V, De Vita G, Forti G, Lenzi A, Mannucci E, Maggi M: Premature and delayed ejaculation: two ends of a single continuum influenced by hormonal milieu. Int J Androl 2011;34:41–48.
7 Keel CE, Dorsey PJ, Acker W, Hellstrom WJ: New concepts in the diagnosis and treatment of premature ejaculation. Curr Urol Rep 2010;11:414–420.
8 McMahon CG: The etiology and management of premature ejaculation. Nat Clin Pract Urol 2005;2:426–433.
9 Cihan A, Demir O, Demir T, Aslan G, Comlekci A, Esen A: The relationship between premature ejaculation and hyperthyroidism. J Urol 2009;181:1273–1280.
10 Corona G, Petrone L, Mannucci E, Jannini EA, Mansani R, Magini A, Giommi R, Forti G, Maggi M: Psycho-biological correlates of rapid ejaculation in patients attending an andrologic unit for sexual dysfunctions. Eur Urol 2004;46:615–622.
11 Waldinger MD, Zwinderman AH, Olivier B, Schweitzer DH: Thyroid-stimulating hormone assessments in a Dutch cohort of 620 men with lifelong premature ejaculation without erectile dysfunction. J Sex Med 2005;2:865–870.
12 Archer J: Testosterone and human aggression: an evaluation of the challenge hypothesis. Neurosci Biobehav Rev 2006;30:319–345.
13 Keleta YB, Lumia AR, Anderson GM, McGinnis MY: Behavioral effects of pubertal anabolic androgenic steroid exposure in male rats with low serotonin. Brain Res 2007;1132:129–138.
14 Waldinger MD, Schweitzer DH, Olivier B: On-demand SSRI treatment of premature ejaculation: pharmacodynamic limitations for relevant ejaculation delay and consequent solutions. J Sex Med 2005;2:121–131.
15 Corona G, Mannucci E, Jannini EA, Lotti F, Ricca V, Monami M, Boddi V, Bandini E, Balercia G, Forti G, Maggi M: Hypoprolactinemia: a new clinical syndrome in patients with sexual dysfunction. J Sex Med 2009;6:1457–1466.
16 Buvat J: Hyperprolactinemia and sexual function in men: a short review. Int J Impot Res 2003;15:373–377.
17 Corona G, Mannucci E, Fisher AD, Lotti F, Ricca V, Balercia G, Petrone L, Forti G, Maggi M: Effect of hyperprolactinemia in male patients consulting for sexual dysfunction. J Sex Med 2007;4:1485–1493.
18 El-Sakka AI, Howayda H, Hisham S: Pattern of endocrinal in patients with sexual dysfunction. J Sex Med 2005;2:551–558.
19 Johri AM, Heaton JP, Morales A: Severe erectile dysfunction is a marker for hyperprolactinemia. Int J Impot Res 2001;13:176–182.