



Associations Between Sex Hormones and Lower Urinary Tract Symptoms in Middle-aged Men

Orta Yaş Erkeklerde Seks Hormonları ve Alt Üriner Sistem Semptomları Arasındaki İlişki

Yasemin Üstündağ Budak, Kağan Huysal, Erkan Karadağ*, Hakan Demirci**, Muhammet Güzelsoy*, Soner Çoban*

Bursa Yüksek İhtisas Training and Research Hospital, Clinic of Biochemistry, Bursa, Turkey

*Bursa Yüksek İhtisas Training and Research Hospital, Clinic of Urology, Bursa, Turkey

**Bursa Yüksek İhtisas Training and Research Hospital, Clinic of Family Medicine, Bursa, Turkey

Abstract

Purpose: The aim of this study was to investigate the association between serum sex hormone levels and lower urinary tract symptoms in men. **Material and Method:** Forty-nine men with lower urinary tract symptoms aged 25-45 years (mean: 37.9 ± 2.0 years) and 25 healthy men aged 25-45 years (mean: 35.9 ± 2.0 years) as controls participated in this study. Estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone, dehydroepiandrosterone sulfate, insulin-like growth factor-binding protein 3 (IGFBP3), insulin-like growth factor -1 (IGF1), and sex hormone-binding globulin levels were measured using commercially available assay kits. All participants were asked to complete the International Prostate Symptom Score questionnaire.

Results: Demographic data were similar between patients and controls. Among the sex steroids studied, only FSH and E2 showed a statistically significant association with lower urinary tract symptoms ($p < 0.05$). Besides, neither IGF1 nor IGFBP3 were associated with lower urinary tract symptoms.

Discussion: Excess E2 may play an important role in the occurrence of lower urinary tract symptoms. E2 receptors located in the prostate tissue may take part in the development of benign prostatic hyperplasia.

Keywords: Estradiol, insulin like growth factor, lower urinary tract symptoms, prostate, sex hormones

Öz

Amaç: Bu çalışmanın amacı erkeklerde serum seks hormon seviyeleri ve alt üriner sistem semptomları arasındaki ilişkiyi incelemektir.

Gereç ve Yöntem: Alt üriner sistem semptomu olan 25-45 yaş arası (ortalama: $37,9 \pm 2,0$ yıl) 49 erkek ve aynı yaş aralığında (ortalama: $35,9 \pm 2,0$ yıl) 25 kontrol olgusu çalışmada yer aldı. Estradiol (E2), folikül uyarıcı hormon (FSH), luteinleştirici hormon, dehidroepiandrosteron sülfat, insülin benzeri büyüme faktörü bağlayıcı protein-3 (IGFBP3), insülin benzeri büyüme faktörü-1 (IGF1) ve seks hormonu bağlayıcı globulin ölçümleri yapıldı. Tüm katılımcılar Uluslararası Prostat Semptom Skoru anketini doldurdular.

Bulgular: Hasta ve kontrol grubuna ait demografik veriler benzerdi. Çalışılan hormonlardan FSH ve E2 değerleri alt üriner sistem semptom skorları ile anlamlı korelasyon gösterdi ($p < 0,05$). IGF1 ve IGFBP3 sonuçları alt üriner sistem semptomları ile ilişkili bulunmadı.

Tartışma: Estradiol yüksekliğinin alt üriner sistem semptomlarının görülmesinde etkili bir rolü olabilir. Prostat E2 reseptörleri benign prostat hiperplazisi gelişmesinde rol alabilir.

Anahtar kelimeler: Estradiol, insülin benzeri büyüme faktörü, alt üriner sistem semptomları, prostat, seks hormonları

Introduction

Lower urinary tract symptoms (LUTS) are storage, voiding and post-micturition symptoms affecting the lower urinary tract. LUTS may point to serious pathology of the urogenital tract (1). Many adults experience LUTS, and the prevalence of these symptoms increases with age (2). It has been shown that LUTS significantly diminish quality of life in affected men (3). Male LUTS are highly

prevalent, occurring in 15% to 60% of males over the age of 40 years in the United States and Europe (4,5,6,7). The prevalence of LUTS is reported as fairly high (ranging from 17.8% to 85.2%) among Turkish patients (8,9). The etiopathogenesis of LUTS is complex and there is more than one hypothesis (10,11,12). Embryologically, genital and urinary systems are related in the sense that they share common passages and are sensitive to sex hormones (13) and androgen receptors are widely distributed in bladder and

urethra epithelium cells (14). Estrogens and androgens are known to be important in occurrence of LUTS in men. Components of the insulin-like growth factors (IGF) axis have been found to be associated with the risk of benign prostatic hyperplasia (BPH) and LUTS in previous studies (15,16,17,18,19). It has been shown that high levels of insulin-like growth factor-binding protein 3 (IGFBP3) are inversely correlated with LUTS (20).

LUTS has been studied rather extensively in geriatric males at present. In this study, we aimed to focus on middle-aged males and to investigate a possible association between the severity of LUTS and serum levels of sex hormones, insulin-like growth factor -1 (IGF-1) and IGFBP3.

Materials and Methods

Study Population

Forty-nine men with LUTS and 25 healthy men as controls participated in the study. None of the patients had a diagnosis of BPH. All subjects had normal hematocrit, thyroid-stimulating hormone, and prolactin levels as well as normal liver function tests. Subjects were excluded if they had a history of a reproductive disorder or use of medications known to interfere with androgen synthesis/action or glucose homeostasis. Self reports of major comorbidities, including heart conditions, vascular conditions, stroke, transient ischaemic attack, diabetes mellitus, cancer, high blood pressure, high cholesterol and previous urinary tract infection were considered. All patients gave written informed consent to participate in this study which was approved by the Ethics Committee of Bursa Yüksek İhtisas Hospital.

Patient Group

Patients complaining of LUTS who attended the outpatient clinics of the department of urology at Şevket Yılmaz Training and Research Hospital from January 2010 to March 2010 were asked to complete the International Prostate Symptom Score (IPSS). This scoring system is used to assess the severity of symptoms in BPH (21). A total of 49 men aged 25-45 years (mean: 37.9±2.0 years) with LUTS (IPSS ≥9) were included in this prospective study. Considering diurnal variation in hormone values, analyses controlled for the interval between waking and sampling the subjects' blood. Estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone, dehydroepiandrosterone sulfate (DHEA-SO4), IGFBP3, IGF1 and sex hormone-binding globulin (SHBG) were determined using commercially available assay kits (Dade Behring Inc. -Newark, DE, USA) with an immulite 1000 auto-analyser (Dade Behring Inc. - Newark, DE, USA).

Statistical Analysis

Data were evaluated using SPSS version 13.0 (SPSS Inc, Chicago, IL). Descriptive statistical values (arithmetic means, standard deviation) were calculated. Correlation between serum hormone levels and IPSS was studied using Spearman's correlation coefficient (r). Comparisons were made by student's t-test. A p value of less than 0.05 was considered statistically significant.

Results

Demographic data of the study group is demonstrated in Table 1. General characteristics, including age, height, weight and body mass index (BMI) variables were statistically similar between patients and controls.

Table 1. Demographic data of the participants

Variable	Control	Patient
Age (years)	35.9±6.1	37.9±2.0
IPSS*	1±1	15±6
Height (m)	174±8.0	170±9.5
Weight (kg)	81.0±10.4	78.6±10.4
BMI (kg/m ²)	26.8±3.1	27.0±3.5
Values are presented as mean ± standard deviation. *IPSS: International Prostate Symptom Score, BMI: Body mass index		

Table 2. Biochemical data of the participants

Variable	Control	Patient	p
FSH (mIU/mL)	6.2±4.8	6.0±3.1	p=0.766
LH (mIU/mL)	5.2±2.9	4.9±2.3	p=0.877
E2 (pg/mL)	29±14	33±11	p=0.376
DHEA-SO4 (mg/dL)	121.1±47.8	200.8±94.3	p<0.001
SHBG (ng/mL)	17.7±8.3	27.4±10.9	p<0.001
IGFBP3 (mg/mL)	6.6±3.7	10.1±62.2	p=0.261
IGF1 (ng/mL)	166.8±63.9	153.4±62.2	p=0.435
Values are presented as mean ± standard deviation. FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, E2: Estradiol, DHEA-SO4: Dehydroepiandrosterone sulfate, SHBG: Sex hormone-binding globulin, IGFBP3: Insulin-like growth factor-binding protein 3, IGF-1: Insulin-like growth factor-1			

Table 3. Correlations between International Prostate Symptom Score, and other clinical and laboratory parameters

Variable	IPSS	
	Correlation (r)	p
Age (years)	0.39	0.806
Height (m)	-0.338	0.157
Weight (kg)	-0.157	0.520
BMI (kg/m ²)	0.037	0.884
FSH (mIU/mL)	-0.304	0.032
LH (mIU/mL)	0.084	0.563
E2 (pg/mL)	0.287	0.043
DHEA-SO4 (mg/dL)	-0.029	0.851
SHBG (ng/mL)	-0.030	0.842
IGFBP3 (mg/mL)	-0.046	0.763
IGF-1 (ng/mL)	-0.184	0.220

IPSS: International Prostate Symptom Score, BMI: Body mass index, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, E2: Estradiol, DHEA-SO4: Dehydroepiandrosterone sulfate, SHBG: Sex hormone-binding globulin, IGFBP3: Insulin-like growth factor-binding protein 3, IGF-1: Insulin-like growth factor-1

Biochemical data of the participants are presented in Table 2. There was a remarkable difference in DHEA-SO4 and SHBG between the patients and controls.

Correlations between IPSS scores and clinical and laboratory tests related to the patient group are given in Table 3. Among them, FSH had a statistically significant negative correlation while E2 showed a statistically significant positive correlation with IPSS scores.

Discussion

Excess E2 may play an important role in the occurrence of LUTS or, stimulus to E2 receptors located in the prostate tissue may take part in the development of BPH (22,23). The results of the present study showed that E2 levels are elevated in LUTS-positive patients. The role of androgens is better studied in case of LUTS but E2 produced from metabolism of androgens or its metabolites is still an issue of discussion. We well know that most of the patients with LUTS recover by using antiandrogen medications but some do not respond to this treatment approach. Therefore, some additional mechanisms are suspected to explain the pathophysiology of LUTS; excess E2 is supposed to be one of them.

Although IGF axis has been shown to be associated with LUTS, the results of the present study did not support this idea. Limited number of the subjects in the study group may be one of the explanations of the situation, but another reason may be characteristics of the participants. In contrast to previous studies, our study group was composed of young males with an average BMI values. Insulin resistance is common among obese persons, and thus, a possible association between IGF and LUTS might have been missed in the study.

In addition to being a precursor of androgens and estrogens, DHEA-S is an active hormone with effects on its own (24). Only a few studies in the literature have evaluated DHEA-SO4 in patients with LUTS, and the results were controversial (25,26,26,27). Rabijewski et al. (25) found that in middle-aged men, the more severe LUTS were associated with low DHEAS. However, Litman et al. (27) showed that this relationship disappeared after statistical adjustment for age. We did not observe any correlation between serum levels of DHEA-SO4 and IPSS scores. Small sample size may have limited our ability to detect modest effects and high DHEA-SO4 levels in patients may account for unknown confounding causality. Most notably, our study has a small sample size. Thus, findings should be interpreted with caution.

Conclusion

In conclusion, LUTS in men may be in association with E2. Further research are needed to understand the possible role of E2 in enlargement of the prostate.

Ethics

Ethics Committee Approval: The study were approved by the Bursa Yüksek İhtisas Local Ethics Committee, Informed Consent: Consent form was filled out by all participants. Peer-review: Externally peer-reviewed.

Authorship Contributions

Medical Practices: Erkan Karadağ, Hakan Demirci, Muhammet Güzelsoy, Soner Çoban, Concept: Yasemin Üstündağ Budak, Kağan Huysal, Erkan Karadağ, Design: Yasemin Üstündağ Budak, Kağan Huysal, Erkan Karadağ, Data Collection or Processing: Yasemin Üstündağ Budak, Kağan Huysal, Hakan Demirci, Erkan Karadağ, Muhammet Güzelsoy, Soner Çoban, Analysis or Interpretation: Yasemin Üstündağ Budak, Hakan Demirci, Literature Search: Yasemin Üstündağ Budak, Hakan Demirci, Writing: Yasemin Üstündağ Budak, Hakan Demirci.

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