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Analysis of orthostatic intolerance symptoms in patients with premature ejaculation

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Abstract. – OBJECTIVE: The autonomic nervous system (ANS) plays an important role in maintaining physiological regulation. It regulates the body's response to many variable situations. Orthostatic intolerance (OI) is one of the most important signs of autonomic dysfunction. Autonomic dysfunction is known to cause premature ejaculation (PE) by disturbing the balance in erection and ejaculation cycles. Considering that OI may develop due to autonomic dysfunction in patients with PE, we hypothesized that OI symptoms would increase in these patients. The aim of our study was to investigate the relationship between orthostatic intolerance and PE.

PATIENTS AND METHODS: This case-control study included a total of 39 patients with PE and 47 volunteers without PE. All subjects were assessed using the self-reported Orthostatic Grading Scale (OGS). In addition, the validated five-item Turkish version of the Premature Ejaculation Diagnostic Tool (PEDT) was used to evaluate PE. The PE group included patients with a PEDT score ≥ 11.

RESULTS: The mean ages of the PE and control groups were 38.2 ± 7.8 and 40.5 ± 9.1 years, respectively ($p = 0.137$). The mean PEDT scores of the PE and control groups were 13.9 ± 3.6 and 6.6 ± 2.9, respectively ($p < 0.0001$), and their mean OGS scores were 5.6 ± 2.4 and 1.6 ± 1.3, respectively ($p < 0.0001$). A statistically significant correlation was found between the PEDT and OGS scores (r: 0.686, $p < 0.0001$).

CONCLUSIONS: The orthostatic intolerance symptoms of patients with PE were higher than those of the control group. There was a correlation between the severity of PE and the severity of orthostatic intolerance. This is the first study in the literature to reveal a relationship between orthostatic intolerance and PE.

Key Words:
Orthostatic intolerance, Premature ejaculation, Autonomic nervous system, Cardiovascular autonomic dysfunction, Ejaculation, Orthostatic symptoms.

Introduction

The autonomic nervous system (ANS) plays an important role in maintaining physiological regulation[1]. ANS influences the function of almost every organ in the body, innervating most of the muscles and glands. It is a system that controls all tissues and organs, except for skeletal muscles[2]. It consists of the parasympathetic and sympathetic nervous systems, which have peripheral and central nervous system components[3]. It controls vital functions, such as arterial blood pressure and body temperature[4]. ANS regulates the body's response to many variable situations. Examples of these responses include cardiovascular responses during exercise, the transition from supine to upright posture, an inflammatory response, and sexual intercourse[2].

Disorders in the ANS form the basis of many diseases[2]. An imbalance in the modulation of the sympathetic and parasympathetic systems causes cardiovascular autonomic dysfunction[5]. ANS dysfunction, also called autonomic dysfunction, is involved in the pathophysiology of various diseases, such as diabetes mellitus, hypertension, and orthostatic hypotension (OH). Clinical signs of cardiovascular autonomic dysfunction include bradycardia, tachycardia, hypertension, orthostatic intolerance (OI), and OH[6]. Diagnosis of cardiovascular autonomic dysfunction is difficult because compensatory mechanisms mask symptoms. However, a careful medical history and assessment of the blood pressure response to standing up can be helpful for diagnosis[7].

Orthostatic intolerance is one of the most important signs of autonomic dysfunction. OI symptoms may include near syncope or syncope, lightheadedness, dizziness, headache, fatigue, exercise intolerance, and cognitive impairment[6]. These symptoms may be the first clue to autonomic dysfunction[4]. OI may occur without OH[7].

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Premature ejaculation (PE) is one of the most commonly reported male sexual disorders[8]. The sympathetic system controls ejaculation. However, the exact pathogenesis of PE remains unclear. It has been reported[9] that autonomic dysfunction disrupts the balance in the erection and ejaculation cycles, causing PE. Studies in the literature evaluating the association between the ANS and PE are insufficient. Considering that OI may develop due to autonomic dysfunction in patients with PE, we hypothesized that OI symptoms would increase in these patients. To our knowledge, there is no study investigating the association between OI and PE in the literature. The aim of the current study was to investigate this relationship.

Patients and Methods

Study Design

This study was designed as a case-control study. The institutional Ethics Committee approved the study, and all participants provided written consent. The patients older than 18 years of age with a diagnosis of PE who presented to the urology outpatient clinic were included in the study. A total of 39 patients with PE and 47 volunteers without PE constituted the sample. All participants were evaluated by urology and cardiology specialists.

Selection of Patients and Volunteers

All participants were sexually active men who had been in a stable sexual relationship with a single partner for the last six months. The control group without PE included age-matched volunteers. Patients who were taking phosphodiesterase inhibitors, selective serotonin reuptake inhibitors, alpha-blockers, anticholinergics, antipsychotics, or tricyclic antidepressants were excluded.

Data Collection

The subjects' demographic characteristics were noted, including age, body mass index (BMI), smoking history, alcohol use, and partner age. Comorbidities such as hypertension, diabetes mellitus, and coronary artery disease were recorded. Intercourse characteristics were also noted, such as the frequency of intercourse and the duration of sexual partnership. All subjects were assessed using the self-reported Orthostatic Grading Scale (OGS) developed by Schrezenmaier et al[10] in 2005.

During the physical examination of the subjects, systolic blood pressure (BP) was measured in the supine position. Then, the patients were asked to stand up, and their standing first-minute systolic BP values were measured to calculate the decrease in systolic BP while standing.

The validated five-item Turkish version of the Premature Ejaculation Diagnostic Tool (PEDT) was used to evaluate PE[11]. All subjects were given a thorough explanation of the PEDT by a urologist and the OGS by a cardiologist. Then, the subjects answered the questions on the scales. The PE group included patients with a PEDT score ≥ 11. Each patient calculated the intravaginal ejaculatory latency time (IELT) using the stopwatch-measured technique[12].

Statistical Analysis

Statistical analysis was performed using the SPSS 24 (IBM Corp., Armonk, NY, USA) statistical package program. The normality of the data distribution was analyzed with the Kolmogorov-Smirnov test. Mean and standard deviation values were used for normally distributed variables, while median and interquartile range values were employed for non-normally distributed variables. Comparisons between the two groups were undertaken using the independent-samples *t*-test for normally distributed variables, and the Mann-Whitney U test for non-normally distributed variables. The Chi-squared test was performed to compare categorical variables between the two groups. The correlation analysis was performed using Pearson's test. A p-value < 0.05 was considered statistically significant.

Results

Premature Ejaculation vs. Control Group

The mean ages of the PE and control groups were 38.2 ± 7.8 and 40.5 ± 9.1 years, respectively ($p = 0.137$). There was no statistically significant difference between the two groups in terms of partner age ($p = 0.468$), duration of partnership ($p = 0.395$), frequency of intercourse ($p = 0.293$), BMI ($p = 0.524$), smoking status ($p = 0.272$), alcohol use ($p = 0.641$), or the presence of comorbidities ($p = 0.102$). The demographic features of the patients with PE and the control group are indicated in Table I.

The mean IELT values of the PE and control groups were 31.3 ± 16.2 and 488.6 ± 307.8 seconds, respectively ($p < 0.0001$). The mean PEDT scores of the PE and control groups were 13.9 ± 3.6 and 6.6 ± 2.9, respectively ($p < 0.0001$).

Table I. Comparison of the demographic and clinical characteristics of the study groups.

	PE group (n = 39)	Control group (n = 47)	p
Age (years), mean ± SD	38.2 ± 7.8	40.5 ± 9.1	0.137[a]
Partner age (years), mean ± SD	34.2 ± 6.8	37.4 ± 7.8	0.468[a]
Duration of partnership (years), median (interquartile range)	11 (2-13)	12 (4-15)	0.395[b]
Frequency of intercourse (month), mean ± SD	7.6 ± 4.1	8.1 ± 5.2	0.293[a]
BMI (kg/m^2), mean ± SD	27.8 ± 4.7	26.9 ± 4.4	0.524[a]
Smoker, n (%)	28 (71.7)	30 (63.8)	0.272[c]
Alcohol use, n (%)	11 (28.2)	15 (31.9)	0.641[c]
Presence of comorbidities	10 (25.6)	6 (12.7)	0.102[c]
IELT (seconds), mean ± SD	**31.3 ± 16.2**	**488.6 ± 307.8**	**< 0.0001[a]**
PEDT score, mean ± SD	**13.9 ± 3.6**	**6.6 ± 2.9**	**< 0.0001[a]**
Standing first-minute systolic BP decrease (mm Hg), mean ± SD	**9.8 ± 6.7**	**4.3 ± 3.8**	**< 0.0001[a]**
Orthostatic symptom score, mean ± SD	**5.6 ± 2.4**	**1.6 ± 1.3**	**< 0.0001[a]**

[a]Independent-samples *t*-test; [b]Mann-Whitney U test; [c]Chi-squared test. SD: standard deviation; IELT: intravaginal ejaculatory latency time; PEDT: Premature Ejaculation Diagnostic Tool; PE: premature ejaculation (PEDT score ≥ 11); BMI: body mass index; BP: blood pressure.

The mean standing first-minute systolic BP decrease was 9.8 ± 6.7 mmHg for the patients with PE and 4.3 ± 3.8 mmHg for the controls ($p < 0.0001$). The mean OGS scores of the PE and control groups were 5.6 ± 2.4 and 1.6 ± 1.3, respectively ($p < 0.0001$) (Table I).

A correlation analysis was performed using the data of all participants. A statistically significant inverse correlation was found between the IELT and the OGS scores (r: -0.553, $p < 0.0001$). There was also a statistically significant correlation between the PEDT and OGS scores (r: 0.686, $p < 0.0001$).

Life-long Premature Ejaculation vs. Secondary Premature Ejaculation Patients

The mean age of the patients with lifelong PE was 34.1 ± 4.6 years, and that of the patients with secondary PE was 40.4 ± 8.3 years ($p = 0.030$). There was a statistically significant difference between the patients with lifelong PE and those with secondary PE in terms of the IELT values ($p = 0.037$), partner age ($p = 0.018$), duration of partnership ($p = 0.008$), and smoking status ($p = 0.024$). However, no statistically significant difference was observed between these two groups in terms of the frequency of intercourse ($p = 0.146$), BMI ($p = 0.487$), alcohol use ($p = 0.714$), presence of comorbidities ($p = 0.359$), PEDT score ($p = 0.624$), standing first-minute systolic BP decrease ($p = 0.567$), or OGS score ($p = 0.321$) (Table II).

The correlation analysis performed revealed no statistically significant correlation between the IELT values and the OGS scores in the PE patients (r: 0.136, $p = 0.416$). However, a statistically significant correlation was detected between the PEDT and OGS scores in the PE patients (r: 0.408, $p = 0.011$).

Discussion

In this study, the mean OGS score of the patients with PE was higher than that of the control group. Additionally, there was a correlation between the PEDT and OGS scores in the whole sample. This study showed that OI symptoms developed more frequently in patients with PE. The severity of PE and the severity of autonomic dysfunction were parallel. To the best of our knowledge, this is the first study in the literature to indicate a relationship between OI and PE.

Autonomic dysfunction is an important condition involving the whole body. It can cause various cardiovascular events[13,14]. It usually shows its effect on the cardiovascular system as increased sympathetic and decreased parasympathetic activity[15]. It is reported[16] that autonomic dysfunction significantly affects the cardiovascular system. An imbalance between the parasympathetic and sympathetic systems may also affect ejaculation time. An uncontrolled increase in sympathetic activity may result in the shortening of the emission phase and subsequent premature ejaculation[9]. Various studies[17] have shown increased sympathetic activity in patients with PE. Various tests[18] are available in the autonomic laboratory to diagnose autonomic dysfunction. An important advantage of the current study is the use of a self-report questionnaire,

Table II. Comparison of patient characteristics according to the form of PE.

	Lifelong PE (n = 13)	Secondary PE (n = 26)	p
Age (years), mean ± SD	**34.1 ± 4.6**	**40.4 ± 8.3**	**0.030[a]**
Partner age (years), mean ± SD	**30.2 ± 5.9**	**36.3 ± 7.1**	**0.018[a]**
Duration of partnership (years), median (interquartile range)	**8 (2-9)**	**12.5 (3-15)**	**0.008[b]**
Frequency of intercourse (month), mean ± SD	7.8 ± 3.7	7.5 ± 4.3	0.146[a]
BMI (kg/m^2)	27.3 ± 4.9	28.1 ± 5.2	0.487[a]
Smoker, n (%)	**6 (46.1)**	**22 (84.6)**	**0.024[c]**
Alcohol use, n (%)	4 (30.7)	7 (26.9)	0.714[c]
Presence of comorbidities	2 (15.4)	8 (30.7)	0.359[c]
IELT	**26.4 ± 8.7**	**34.2 ± 12.1**	**0.037[a]**
PEDT	14.3 ± 3.7	13.7 ± 3.8	0.624[a]
Standing first-minute systolic BP decrease (mm Hg), mean ± SD	9.3 ± 6.9	10.1 ± 6.3	0.567[a]
Orthostatic symptom score, mean ± SD	5.4 ± 2.1	5.7 ± 2.3	0.321[a]

[a]Independent-samples *t*-test; [b]Mann-Whitney U test; [c]Chi-squared test. SD: standard deviation; IELT: intravaginal ejaculatory latency time; PEDT: Premature Ejaculation Diagnostic Tool; PE: premature ejaculation (PEDT score ≥ 11); BMI: body mass index; BP: blood pressure.

which is more practical than other tests in terms of allowing the evaluation of more patients in a shorter time. Furthermore, although previous studies in the literature have investigated autonomic dysfunction in patients with PE, they have not evaluated its effects on clinical symptoms.

In our study, two five-item questionnaires were applied to patients with PE and a control group. The first questionnaire was the PEDT, and the second was the self-reported OGS[10,11]. The five questions on the OGS address the frequency and severity of orthostatic symptoms, the relationship of symptoms to orthostatic stressors, and the impact of symptoms on activities of daily living and standing time. According to the results of these two simple questionnaires, the assessment of PE and OI was consistent. In a previous study[15] investigating PE and heart rate variability, it was found that heart rate variability decreased in the PE group. These results support the relationship between PE and autonomic dysfunction.

One of the first signs of autonomic dysfunction is OI. Coordination of the cardiovascular system and ANS is necessary for a healthy hemodynamic response to changes in posture[19]. One of the important functions of the ANS is to regulate BP according to body position. In patients with autonomic dysfunction, orthostatic symptoms may occur due to the inability to increase cardiac output and systemic vascular resistance[20]. In our study, an orthostatic symptom score questionnaire was utilized to investigate OI. According to the results of the OGS, OI symptoms were more frequent among patients with PE. The standing first-minute systolic BP decrease was also higher in this group than in the control group. In addition, orthostatic BP variability was higher in the PE group. OI has been reported[21] to have many causes. We consider that PE may be one of the factors resulting in OI symptoms.

The effects of PE on the ANS are complex and multivariable[17]. Current evidence[9,22] suggests that the ANS is involved in the pathophysiology of PE. Disruption of the balance in sympathetic and parasympathetic system activity causes PE[23]. Rowland[24] investigated the effect of erotic stimulation on both penile response and heart rate in patients with PE. In another study[15], it was reported that both penile response and heart rate were affected following an erectile stimulus in patients with PE. Another study by Majzoub et al[25] determined that PE was higher in patients with diabetes mellitus than in healthy individuals due to autonomic dysfunction. These results suggest that autonomic dysfunction can exhibit both cardiovascular and sexual effects.

Various questionnaires[12] have been created to detect the presence of PE. We used the PEDT, which can successfully distinguish PE. The PEDT score and the IELT are easy and frequently used parameters for the diagnosis and follow-up of PE[26]. In our study, the OGS and PEDT scores were found to have a strong correlation. According to our results, the PEDT and OGS are useful and credible tools for the evaluation of PE and OI.

Lifelong PE is a form of PE that begins when a male becomes sexually active, while secondary PE begins later in sexual life. Autonomic

dysfunction is important in both forms[27]. In our study, patients with lifelong PE were younger than those with secondary PE. However, there was no significant difference between these two PE groups in terms of orthostatic symptom scores. This suggests that autonomic function is affected in patients with PE, regardless of the etiology.

Limitations

This study has several limitations. First, it had a case-control and single-center design, which may have limited the generalizability of the results. Second, the sample size was relatively small. Third, blood pressure values were measured only once in all participants since the primary focus was on OI symptoms. Lastly, the number of patients with PE was small. Despite these limitations, the preliminary results presented are valuable in terms of confirming our hypothesis.

Conclusions

Patients with PE had a higher level of OI symptoms than the control group. There was a correlation between the severity of PE and the severity of OI. More extensive cohort studies are needed to confirm our preliminary results.

Authors' Contributions

All authors contributed to: (1) substantial contributions to the conception and design, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be published.

Informed Consent

All patients signed an informed consent.

Availability of Data and Materials

Data are available. The data that support the findings of this study are available upon request from the corresponding author.

Ethics Approval

This study was approved by the Ethics Committee of Ankara City Hospital, Turkey (ID: E2-23-4774), and conducted according to the Helsinki Declaration on Human Rights.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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