ORIGINAL RESEARCH—EJACULATORY DISORDERS

The Sympathetic Skin Response Located in the Penis as a Predictor of the Response to Sertraline Treatment in Patients with Primary Premature Ejaculation

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ABSTRACT

Introduction. The pathologic mechanisms of primary premature ejaculation (PPE) are complex and multifactorial, and hyperactivity of the sympathetic nervous system is one of the mechanisms.

Aim. To examine the effects of sertraline on sympathetic nervous system activity and assess the predictive value of the sympathetic skin response located in the penis (PSSR) on the response to sertraline treatment in PPE patients.

Methods. Sixty-one patients with PPE were recruited. Each received 50 mg sertraline daily for 8 weeks. Before and after the experiment, the patients were evaluated for PSSR tests and sexual performance parameters. Additionally, based on the latency of PSSR, we divided the patients into a normal PSSR group and an abnormal PSSR group, and compared the sertraline treatment efficacy between the two groups.

Main Outcome Measures. Changes in intravaginal ejaculation latency time (IELT) and the Chinese premature ejaculation index-5 (CIPE-5), and the latencies and amplitudes of PSSR after sertraline treatment.

Results. Overall, 58 (95.1%) patients completed the entire study and were analyzed. After the 8-week sertraline treatment, compared with those of pretreatment, IELT and CIPE-5 scores were significantly increased (both $P < 0.001$), and the amplitudes and latencies of PSSR in the PPE patients were remarkably decreased and prolonged, respectively (both $P < 0.001$). In addition, the changes of the latencies of PSSR were positively correlated with the increment of IELT ($r = 0.375$, $P = 0.004$). The treatment outcome was better in patients with a baseline abnormal PSSR than in those with a baseline normal PSSR ($P = 0.021$).

Conclusions. These results suggest that clinical improvement in response to sertraline in the PPE patients, at least in part, is mediated through reducing sympathetic nervous system activity indexed by PSSR. Measurement of the PSSR appears to provide useful information for predicting treatment responses in the PPE patients. **Xia J, Chen T, Chen J, Han Y, Xu Z, Zhou L, Chen Y, and Dai Y. The sympathetic skin response located in the penis as a predictor of the response to sertraline treatment in patients with primary premature ejaculation. J Sex Med 2014;11:2801–2808.**

Key Words. Medical Management of Premature Ejaculation; Autonomic Nervous System; Sympathetic Skin Response; Sertraline

Introduction

Premature ejaculation (PE) is the most common male sexual dysfunction, affecting 20–30% of men worldwide [1]. It could have profound effects on the psychosexual relationship of couples; in its most severe form, it could lead to secondary impotence and male infertility [2]. Although there are multiple definitions of PE crafted by various professional organizations or

individuals, three common characteristics underlie most definitions: (i) a short ejaculatory latency; (ii) a lack of perceived self-efficacy or control about the timing of ejaculation; and (iii) distress and interpersonal difficulty, which are related to the ejaculatory dysfunction [3]. Clinically, PE has been classified as either primary PE (PPE), which is present at nearly every intercourse from the first sexual encounter onward, or secondary PE (SPE), meaning that a male develops the condition after an interval of normal sexual function [4]. In 2008, International Society for Sexual Medicine (ISSM) developed the first contemporary multivariate evidence-based definition of PPE, which states that PPE is a male sexual dysfunction that is characterized by ejaculation, which occurs or nearly always occurs prior to or within about a minute of vaginal penetration, and the inability to delay ejaculation on all or nearly all vaginal penetrations and includes negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy [5].

While great progress has been made in the etiology of PE, the exact mechanism of PE is still not well known. In general, SPE is usually considered to be associated with opioid substance withdrawal, chronic prostatitis, and specific endocrinopathies, including diabetes mellitus and hyperthyroidism [6]. In the circumstances, SPE can often be reversed with the underlying disorder treated [7,8]. Meanwhile, PPE has been claimed to be caused by somatic disorders and/or neurobiological imbalances, such as penile hypersensitivity, hyperarousability, and genetic predisposition [6]. More recently, our study, in which sympathetic skin response located in the penis (PSSR) tests were used, indicated that hyperactivity of the sympathetic nervous system may be another factor involved in the pathological mechanisms of PPE [9]. The results are in agreement with a recent study reporting the sympathetic overactivity in PPE patients through measuring 24-hour heart rate variability (HRV) in the men with PPE [10]. It is well known that HRV and rhythm are largely mediated via the autonomic nervous system (ANS), and the degree of HRV depends on the influence of sympathetic and parasympathetic activity on the sinus node [11], therefore, HRV reflects the status of ANS, and is associated with the balance between sympathetic and parasympathetic activities.

Until now, several forms of pharmacotherapy have been used to treat PE. They include topical local anesthetics, selective serotonin reuptake inhibitors (SSRIs), phosphodiesterase-5 inhibitors, alpha adrenergic blockers, and selective oxytocin receptor antagonists [12–16]. Sertraline, a highly potent SSRI, has been demonstrated to have a marked increase in ejaculatory latency after 4 weeks therapy in PPE patients [17–19]. On the other hand, some studies have found sertraline could decrease the sympathetic activity apparently [20,21]. Therefore, it is interesting to explore whether or not the PSSR is a trait marker related to the responses of PPE patients to sertraline treatment.

We hypothesized that the PSSR test can be used to predict the response to sertraline treatment in the PPE patients. To the best of our knowledge, there has been no study to have examined the effects of sertraline on sympathetic nervous system activity and assess the predictive value of PSSR in the PPE patients, which is the purpose of this present study.

Methods and Materials

Subjects

Between September 2011 and June 2013, we recruited 61 PPE patients from the Department of Andrology of our hospital. The diagnostic criteria were based on the guidelines of ISSM [5]. PPE was defined as the uncontrolled occurrence of ejaculation since the beginning of sexual life, with the stopwatch intravaginal ejaculation latency time (IELT) less than 1 minute. In addition, the PPE patients should be in a stable, heterosexual relationship with the sexually active partner for at least 1 year. IELT was measured with the stopwatch for the 4-week baseline period during which patients were asked to have sexual intercourse at least four times. The exclusion criteria were as follows: (i) secondary PE; (ii) abnormal routine physical and neurological examination; (iii) obvious psychological problems requiring psychiatric support; (iv) any condition that could affect the status of sympathetic activity, such as cardiac arrhythmia, hypertension, diabetes, or taking drugs that disrupt the sympathetic activity; (v) any organic cause, including genitourinary tract infection and hyperthyroidism; (vi) any treatment that has been applied before this visit; and (vii) erectile dysfunction. All the participants gave their informed consent to the experimental procedures, which were approved by the institutional review boards of Nanjing Drum Tower Hospital and conducted in accordance with regulations laid down in the Declaration of Helsinki.