Discontinuation of Dapoxetine Treatment in Patients With Premature Ejaculation: A 2-Year Prospective Observational Study

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ABSTRACT

Introduction: Although dapoxetine is the only oral pharmacologic agent approved for the treatment of premature ejaculation (PE) and is very effective, the discontinuation rate is high.

Aim: To assess the discontinuation rate of patients with PE and the reasons for discontinuation in real-world practice.

Methods: In total, 182 consecutive patients were enrolled. Type of PE, self-estimated intravaginal ejaculation latency time, and medical history were evaluated in all patients who also completed the erectile function domain of the International Index of Erectile Function (IIEF). Visits were scheduled 1, 3, 6, 12, and 24 months after initiation of therapy; treatment status and the reasons for discontinuation in those who did discontinue were checked. The relations of discontinuation rates were compared with various parameters and the time to discontinuation after treatment commencement.

Results: Of all patients, 9.9% continued treatment to 2 years. The cumulative discontinuation rates at 1, 3, 6, 12, and 24 months were 26.4%, 61.6%, 79.1%, 87.3%, and 90.1%, respectively. Moreover, 79.1% of all patients discontinued treatment within 6 months. After 12 months, the discontinuation rate decreased sharply. The reasons for discontinuation were cost (29.9%), disappointment that PE was not curable and that dapoxetine was required every time sexual intercourse was contemplated (25%), side effects (11.6%), perceived poor efficacy (9.8%), a search for other treatment options (5.5%), and unknown (18.3%). Patients with acquired PE (vs lifelong PE), with intravaginal ejaculation latency time longer than 2 minutes before treatment, on phosphodiesterase type 5 inhibitors, and with IIEF erectile function scores lower than 26 tended to discontinue early and thus exhibited high dropout rates.

Conclusion: The treatment discontinuation rate of dapoxetine was very high. The main reasons for discontinuation were the cost and disappointment that treatment was required every time adequate sexual function was required. **Park HJ, Park NC, Kim TN, et al. Discontinuation of Dapoxetine Treatment in Patients With Premature Ejaculation: A 2-Year Prospective Observational Study. Sex Med 2017;X:XXX–XXX.**

Key Words: Premature Ejaculation; Serotonin Uptake Inhibitors; Compliance

INTRODUCTION

Premature ejaculation (PE) is one of the most common male sexual dysfunctions. PE decreases sexual satisfaction and the quality of life of patients and their partners.[1] Recently, the International Society for Sexual Medicine defined PE is a "male sexual dysfunction characterized by ejaculation that always or nearly always occurs prior to or within 1 min of vaginal penetration from the time of the first sexual experience (lifelong PE), or a clinically significant reduction in latency time, often to about 3 minutes or less (acquired PE)."[2] Currently, several treatments for PE are available. Psychological-behavioral pharmacologic therapies, including selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, tramadol, phosphodiesterase type 5 (PDE5) inhibitors, and α_1-andreoreceptor antagonists; topical anesthetics; and even surgery have been used to treat PE in real-world practice.[3] Dapoxetine is the first oral pharmacologic agent developed to treat PE and is the only SSRI approved for such treatment in more than 60 countries.[4] The introduction of dapoxetine was associated with high expectations, given the optimal efficacy-safety profiles evident in phase 3 trials.[5]

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However, although several clinical studies have confirmed drug efficacy in increasing the intravaginal ejaculation latency time (IELT) and safety, the rate of discontinuation is as high as when taking off-label SSRIs.[4,5] The discontinuation rate is high compared with those of PDE5 inhibitors in patients with erectile dysfunction (ED).[4,6]

To date, dapoxetine is the only approved medical treatment for PE; no second-line therapy is available in those who do not respond or who refuse to take dapoxetine. Thus, a comprehensive evaluation of factors leading to dropout was needed, especially in a real-practice setting. Therefore, we assessed dapoxetine discontinuation by patients with PE in a clinical setting, and the reasons for such discontinuation, over a follow-up period of 2 years.

METHODS

Study Design

This was a 2-year prospective observational study conducted in a single clinical center in accordance with Good Clinical Practice and in conformity with the ethical principles of the Declaration of Helsinki. The local ethics committee approved the study protocol and all patients signed informed consent forms.

At baseline, all patients were asked to self-estimate their IELT using a stopwatch, completed the International Index of Erectile Function erectile function domain (IIEF-EFD), and gave a medical history. The IELT was defined as the time from the start of vaginal intromission to commencement of intravaginal ejaculation.[7] According to the new definition of the International Society of Sexual Medicine,[2] lifelong PE was defined as ejaculation that always or nearly always occurred before or within approximately 1 minute of vaginal penetration, commencing at the first sexual experience, and acquired PE was defined as a clinically significant and bothersome decrease in latency time, often to no longer than 3 minutes. The two types of PE have been associated with an inability to delay ejaculation after all or nearly all vaginal penetrations and associated with negative personal consequences, including distress, worry, frustration, and/or avoidance of sexual intimacy.

Subjects

In total, 182 consecutive patients seeking medical treatment for PE were enrolled. The inclusion criteria were male sex, no history of dapoxetine treatment, age older than 19 years, and involvement in a stable monogamous relationship with a female sexual partner.

Men with the following conditions were excluded: any anatomic penile deformity; spinal cord injury; prior radical prostatectomy; pelvic organ surgery; diagnosis of any sexual disorder other than ED; any uncontrolled psychiatric disorder; any history of a major hematologic, renal, or hepatic abnormality; a history of alcoholism or substance abuse; and/or an organic illness limiting the ability to take SSRIs. Patients did not receive any financial incentive to participate in this observational survey. Concomitant use of any other PE treatment was prohibited during the study period.

Outcome Measurements

After a 4-week run-in period, patients took dapoxetine 30 mg 1 to 3 hours before planned sexual intercourse. Dose escalation to 60 mg was allowed after 1 month if the 30-mg dose was inadequate. Patients were re-evaluated 1, 3, 6, 12, and 24 months after initiating therapy for treatment status and the reason for discontinuation if they had discontinued. If a patient missed any visit, then he was contacted by telephone or mail to collect the required data. The primary end points were the discontinuation rates and the reasons for discontinuation. We compared the discontinuation rates with various parameters and the interval from commencement to discontinuation.

Statistical Analyses

We undertook a prospective cohort study. We compared the baseline characteristics of patients continuing and discontinuing treatment using the χ^2 test to evaluate categorical variables. A P value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc, Chicago, IL, USA).

RESULTS

We consecutively enrolled 182 patients from October 1, 2011 through September 30, 2013. The mean age of all patients was 38.2 years (range = 19−63) and the mean baseline IELT was 61.2 ± 23.4 seconds. Of all patients, 9.9% continued treatment to 2 years. The cumulative discontinuation rates at 1, 3, 6, 12, and 24 months were 26.4%, 61.6%, 79.1%, 87.3%, and 90.1%, respectively. Moreover, 79.1% of all patients discontinued treatment within 6 months. After 12 months, the discontinuation rate decreased sharply (Figure 1). Patients with acquired PE (vs lifelong PE), with IELTs longer than 2 minutes before treatment, on PDE5 inhibitors, and with IIEF-EFD scores lower than 26 tended to exhibit high dropout rates at the end of the study (Table 1). The reasons for discontinuation were cost (29.9%), disappointment that PE was not curable and that dapoxetine was needed whenever sex was planned (25%), side effects (11.6%), perceived inefficacy (9.8%), a search for other treatment options (5.5%), and unknown (18.3%; Table 2). The most common side effects included yawning, nausea, dizziness, and headache. No severe side effects, such as self-harming or aggressive behavior, serotonin syndrome, postural hypotension, or syncope, were reported.

DISCUSSION

Before the introduction of dapoxetine, off-label SSRIs, topical anesthetics, and the narcotic analgesic tramadol were the only medical agents used to treat PE. The discontinuation rates in patients with PE were very high.[7,8] Salonia et al[7] found that up