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Comparison Between Tadalafil Plus Paroxetine and Paroxetine Alone in the Treatment of Premature Ejaculation

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Abstract

Background: Several recent studies have investigated the therapeutic role of phosphodiesterase type 5 (PDE5) inhibitors in premature ejaculation (PE) used in the treatment of erectile dysfunction.
Objectives: In the present research, the efficacy of paroxetine alone and paroxetine plus tadalafil was compared in patients referred because of premature ejaculation.
Patients and Methods: This quasi-experimental study was performed on 100 consecutive 17 to 49-year-old potent men with premature ejaculation and without any clear organic disease. All patients had lifelong PE with an intravaginal ejaculation latency time (IELT) shorter than 1.5 minutes. Informed consent was obtained from all patients who were randomly divided into two groups using a computer-generated random tabulation list. In group A, patients received 10 mg paroxetine daily, in addition to four hours before planned sexual activity. In group B, 10 mg paroxetine was taken daily, plus 10 mg tadalafil one hour before planned sexual activity. The duration of the intervention was six months and patients were evaluated for IELT three and six months after the beginning of therapy.
Results: The mean age of patients in groups A and B were 33 ± 9.6 and 31.2 ± 9.3 years, respectively (P = 0.368). The mean number of intercourses were 1.08 ± 0.6 and 1.12 ± 0.6 per week in groups A and B, respectively (P = 0.791). Mean IELT at the 3-month follow up in groups A and B was 4.5 ± 1.5 and 5 ± 2.4 minutes, respectively (P = 0.285) and at the 6-month follow up was 4.8 ± 1 and 5.3 ± 2 minutes, respectively (P = 0.278).
Conclusions: The results of the study show that tadalafil can increase the mean IELT and can be used for treatment of premature ejaculation in combination with paroxetine.

Keywords: Premature Ejaculation, Serotonin Uptake Inhibitors, Paroxetine Tadalafil Plus Paroxetine and Paroxetine

1. Background

Premature ejaculation (PE) is defined as ejaculation that occurs with minimal stimulation, and which happens before or shortly after penetration, resulting in harassment and anxiety. The patient has very little or no voluntary control of PE (1).

PE is the most common sexual dysfunction in men younger than 40 years old, affecting approximately 30% of men. However, PE is more common in blacks, Hispanic males and Muslims (2, 3). There are two types of premature ejaculation, lifelong or primary, and acquired or secondary (4).

PE is identified and categorized based on sexual and medical history. Primary, or lifelong, premature ejaculation is defined as PE that has been a problem since initially beginning coitus. In secondary, or acquired, premature ejaculation the patient has previously had desirable intercourse with subsequent development of PE. Measuring the time of ejaculation, usually defined as intravaginal ejaculation latency time (IELT) is very important (5). Self-estimated IELT is enough to practice. Self-estimated and stopwatch-measured IELT accurately determine PE status with 80% sensitivity and 80% specificity and are interchangeable (6). In addition, the primary method of evaluation of men with PE is physical examination to diagnose the underlying medical problems, which can be related to PE or other sexual dysfunctions such as chronic disease, endocrinopathy, autonomic neuropathy, Peyronie's disease, urethritis and prostatitis. Without specific findings from a history or physical examination, conducting laboratory tests or physiological testing are not commonly recommended (7). The most common treatments for PE are pharmacologic and behavior therapy.

Sometimes the most effective treatment method is medication combined with non-medication treatment (8). There are several behavior therapies, such as the squeezing and start-stop methods, but many couples find these cumbersome. Pharmacologic therapy may include selective serotonin reuptake inhibitor (SSRI) therapy (citalopram,

sertraline, fluoxetine, dapoxetine or paroxetine), phosphodiesterase type 5 (PDE5) inhibitor therapy (tadalafil or sildenafil), topical desensitizing agents (prilocaine or lidocaine) and other agents (tramadol or pindolol). Nowadays, the first choice of treatment for PE is SSRIs (9).

It is worth mentioning that an increase of IELT may begin a few days after initiation of daily SSRI intake, and the maximum delay is not observed until after a 1 - 2-week course (10). The therapeutic effect of daily SSRIs on PE is supported by many double-blind, placebo-controlled and well-designed trials (11, 12).

Paroxetine is better than fluoxetine, clomipramine and sertraline in the treatment of PE. Fluoxetine is inferior to sertraline, while the effect of clomipramine does not significantly differ from fluoxetine and sertraline. Doses of paroxetine, sertraline, fluoxetine and clomipramine were 20 - 40 mg, 25 - 200 mg, 10 - 60 mg and 25 - 50 mg, respectively. No significant relationship was found between dose and response of different drugs. There is little evidence to show that citalopram is less effective than other SSRIs and that fluvoxamine is not effective (13, 14). A few days after drug intake, ejaculation delay may occur, but 1 - 2 weeks later, the effect is more obvious because the receptor desensitization takes time (15). Diarrhea, fatigue, yawning, perspiration, nausea, dry mouth, drowsiness and vomiting are the usual side effects of SSRIs. At first, these side effects are usually mild, and they gradually decline after two to three weeks (15). The increase of IELT commonly occurs within a week after beginning treatment. The medication enhances the increase of IELT 6 - 20 times more than before treatment. Although the males are satisfied with the treatment, many of them interrupt it within a year (16).

2. Objectives

The aim of this study was to compare the efficacy of paroxetine alone and paroxetine plus tadalafil in patients complaining of premature ejaculation.

3. Patients and Methods

In 2014, this quasi-experimental study was performed on 100 consecutive 17 to 49-year-old potent men with premature ejaculation and without any clear organic disease. All married patients with lifelong PE and IELT shorter than 1.5 minutes were included in the study. Patients with a past history of psychiatric problems and medications were not included. Additional exclusion criteria included patients with erectile dysfunction (ED), prostatitis, severe drug complications and poor control over ejaculation. The study participants were equally classified into two groups, A and B, using a computer-generated random tabulation list. This research was approved by the ethical committee of Babol University of Medical Sciences and informed consent was obtained from all patients.

The assessment before treatment contained a history, physical examination, U/C and Stamey test to exclude genital tract infection. All patients self-completed the international index of erectile function (IIEF) questionnaire.

Group A included 50 patients who received 10 mg daily doses of paroxetine four hours before planned sexual activity for 30 days, and if it was needed the dose was increased to 20 mg. Group B included 50 patients who received daily doses of 10 mg tadalafil one hour before intercourse, plus 10 mg paroxetine four hours before planned sexual activity for 30 days. If it was needed, the dose was increased to 20 mg. The medication was continued for up to six months in both groups. This study was open and only the outcome assessor was blinded. The primary outcome was IELT and secondary outcomes were intercourse satisfaction in men and drug side effects. Other variables, such as age and number of intercourses per week, were recorded for all patients.

Patients were followed-up with at three and six months after beginning therapy to assess primary and secondary outcomes. The data were analyzed using SPSS Version 15 statistical software, and the independent t-test with intention to treat method was used. A value of $P < 0.05$ was considered as significant.

4. Results

The mean age and number of intercourses per week in both groups are shown in Table 1. Mean ejaculatory latency time at the 3-month follow up in groups A and B were 4.5 ± 1.5 and 5 ± 2.4 minutes, respectively ($P = 0.285$), and at the 6-month follow up were, 4.8 ± 1 and 5.3 ± 2 minutes, respectively ($P = 0.278$) (Figure 1).

The 3-month and 6-month mean intercourse satisfaction domain values of the IIEF were 9, 11 and 11, and 9, 11 and 14 in groups A and B, respectively. There was no significant difference between groups A and B regarding intercourse satisfaction ($P > 0.05$). The side effects in group A included gastrointestinal upset and/or nausea in 5 (10%) patients, headache in 4 (8%) patients, decreased libido in 2 (4%) patients and delayed ejaculation in 1 (2%) patient. The side effects in group B included headache in 11 (22%) patients, flushing in 8 (16%) patients and gastrointestinal upset and/or nausea in 4 (8%) patients. Flushing episodes were more significant in group B ($P = 0.000$) than in group A. Other side effects did not show a significant difference between the two groups.

Table 1. The Mean Age and Number of Intercourses Per Week in Both Groups[a]

	Paroxetine	Paroxetine + Tadalafil	P Value
Age, y	33 ± 9.6	31.2 ± 9.3	0.368
Number of intercourses per week	1.08 ± 0.6	1.12 ± 0.6	0.791

[a]Values are expressed as mean ± SD.

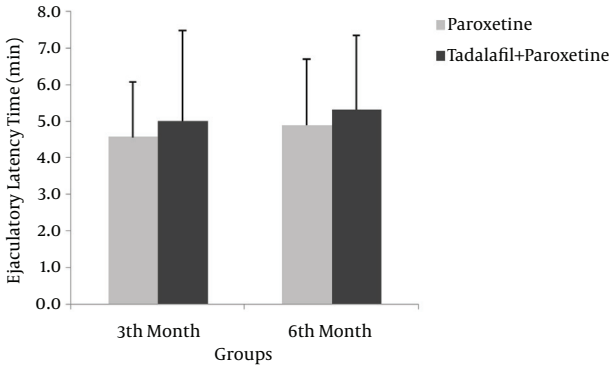

Figure 1. Mean Ejaculatory Latency Time at 3-Month and 6-Month Follow Up in Groups A and B

5. Discussion

Recently, some studies have investigated the therapeutic role of phosphodiesterase 5 (PDE5) inhibitors in PE. PDE5s may decrease performance anxiety because of improved erections and may downregulate the erectile limen to a lower state of arousal, so that greater arousal is necessary to reach the ejaculation limen; however, many of the mechanisms involved are speculative (17-19). Therefore, the aim of this study was to compare the efficacy of paroxetine alone and paroxetine combined with tadalafil in patients complaining of premature ejaculation. The results of the present study show that IELT at the 3-month and 6-month follow up, in the group with combination therapy of paroxetine and tadalafil, was higher than that of the paroxetine group, but this difference was not significant.

Previously, sildenafil was compared with placebo in a well-designed, randomized, double-blind, placebo-controlled study (20). In this study, sildenafil enhanced the perception of ejaculatory control, overall sexual satisfaction and confidence, reduced anxiety and the demand time to reach a second erection after ejaculation, though IELT was not significantly increased. In another randomized, double-blind, placebo-controlled study, the combination of sildenafil (50 mg before intercourse) with lidocaine or prilocaine had the same effect, but showed no superiority to placebo (IELT was not considered) (21). One double-blind randomized study showed that sildenafil improved IELT and satisfaction and reduced anxiety in comparison with several SSRIs and the pause-squeeze technique. Sildenafil, clomipramine, sertraline, paroxetine and the pause-squeeze technique improved the baseline IELT from 1 minute to 15 minutes, 4 minutes, 3 minutes, 4 minutes and 3 minutes, respectively (22). Various open-label studies have indicated that sildenafil combined with an SSRI is superior to SSRI monotherapy. In contrast to paroxetine alone, sildenafil plus paroxetine improved IELT and satisfaction (23). Sildenafil plus sertraline, in comparison to sertraline alone, significantly improved IELT and satisfaction (24). The combination of sildenafil with paroxetine and psychological and behavioral counseling in patients who had failed with other treatments considerably improved IELT and satisfaction (25). Finally, behavioral therapy alone compared to sildenafil plus behavioral therapy was significantly inferior in the improvement of IELT and satisfaction (26). Other PDE5 inhibitors (tadalafil and vardenafil) have limited data on their effect in PE (19, 27). In the current study, PE was treated by paroxetine alone and in combination with tadalafil and showed that IELT increases with combination therapy.

In summary, the role of PDE5 inhibitors is not established in PE patients without ED, and there are few double-blind placebo controlled studies. Paroxetine is more effective than sertraline, clomipramine and fluoxetine (13, 14). The current study is limited because it was not blind and this could affect the result. Nevertheless, the results show that paroxetine plus tadalafil provides better results in terms of IELT and intercourse satisfaction, versus paroxetine alone in potent patients with premature ejaculation; however, combined treatment mildly increases drug side effects.

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Footnote

Authors' Contribution: Emadouddin Moudi and Ali Akbar Kasaeeyan performed the surgery and collected the patient information. The initial draft was written and revised by Emadouddin Moudi and Ali Akbar Kasaeeyan. All authors read and approved the final manuscript for publication.

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