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 initial 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, paroxetine).

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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).

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

|                      | Paroxetine | Paroxetine + Tadalafil | P Value |
|----------------------|------------|------------------------|---------|
| Age, y               | 31 ± 9.6   | 31.2 ± 9.3             | 0.368   |
| Number of intercourses per week | 1.08 ± 0.6 | 1.12 ± 0.6             | 0.791   |

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 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.
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, combination treatment mildly increases drug side effects.

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Footnote

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References

1. McMahon CG, Abdo C, Incrocci L, Perelman M, Rowland D, Waldinger M, et al. Disorders of orgasm and ejaculation in men. J Sex Med. 2004;1(1):58–65. doi: 10.1111/j.1743-6109.2004.00109.x. [PubMed: 14622984]
2. Richardson D, Goldmeier D. Premature ejaculation—does country of origin tell us anything about etiology? J Sex Med. 2005;2(4):508–12. doi: 10.1111/j.1743-6109.2005.00074.x. [PubMed: 16422845]
3. Carson C, Gunn K. Premature ejaculation: definition and prevalence. Int J Impot Res. 2006;18 Suppl 1:55–11. doi: 10.1038/sj.ijir.3901507. [PubMed: 16953247]
4. Godpodinoff ML. Premature ejaculation: clinical subgroups and etiology. J Sex Marital Ther. 1989;15(3):330–4. doi: 10.1080/00926238908403817. [PubMed: 2769774]
5. Balon R, Segraves RT, Clayton A. Issues for DSM-V: sexual dysfunction, disorder, or variation along normal distribution: toward rethinking DSM criteria of sexual dysfunctions. Am J Psychiatry. 2007;164(2):198–200. doi: 10.1176/ajp.2007.164.2.198. [PubMed: 1726777]
6. Rosen RC, McMahon CG, Niederberger C, Broderick GA, Jamie.son C, Gagnon DD. Correlates to the clinical diagnosis of premature ejaculation: results from a large observational study of men and their partners. J Urol. 2007;177(3):1059–64. doi: 10.1016/j.juro.2006.10.044. [PubMed: 17269441]
7. Shabsigh R. Diagnosing premature ejaculation: a review. J Sex Med. 2006;3 Suppl 4:318–23. doi: 10.1111/j.1743-6109.2006.00307.x. [PubMed: 16939476]
diesterase type 5 inhibitors in the management of premature ejaculation: a critical analysis of basic science and clinical data. Eur Urol. 2005;52(3):333-9. doi: 10.1016/j.eururo.2007.08.005. [PubMed: 17728050]

19. Wang WF, Minhas S, Ralph DJ. Phosphodiesterase 5 inhibitors in the treatment of premature ejaculation. Int J Androl. 2006;29(5):503-9. doi: 10.1111/j.1365-2605.2006.00689.x. [PubMed: 16571707]

20. McMahon CG, Stucky BG, Andersen M, Purvis K, Koppiker N, Haugheie S, et al. Efficacy of sildenafil citrate (Viagra) in men with premature ejaculation. J Sex Med. 2005;2(3):368-75. doi: 10.1111/j.1743-6109.2005.00197.x. [PubMed: 15931533]

21. Althof SE, Abdou CH, Dean J, Hackett G, McCabe M, McMahon CG, et al. International Society for Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation. J Sex Med. 2010;7(9):2947-69. doi: 10.1111/j.1743-6109.2010.01975.x. [PubMed: 21050914]

22. Hatzimouratidis K, Amar E, Eardley I, Giuliano F, Hatzichristou D, Montorsi F, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. Eur Urol. 2010;57(5):804-14. doi: 10.1016/j.eururo.2010.02.020. [PubMed: 2089712]

23. Waldinger MD, Zwinderman AH, Olivier B. SSRI and ejaculation: a double-blind, randomized, fixed-dose study with paroxetine and citalopram. J Clin Psychopharmacol. 2001;21(6):556-60. [PubMed: 11763001]

24. Waldinger MD, Hengeveld MW, Zwinderman AH, Olivier B. Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine, and sertraline. J Clin Psychopharmacol. 1998;18(4):274-81. [PubMed: 9690692]

25. Waldinger MD. Premature ejaculation: definition and drug treatment. Drugs. 2007;67(4):547-68. [PubMed: 17352514]

26. Althof SE. Treatment of rapid ejaculation: Psychotherapy, pharmacotherapy, and combined therapy. In: Leiblum SR, editor. Principles and practice of sex therapy. 4th ed. NY: Guilford; 2007. pp. 212-40.

27. Shabsigh R, Patrick DI, Rowland DL, Franklin M, Apgar K, Takedo U. Comparison of efficacy of sildenafil-only, sildenafil plus topical EMLA cream, and topical EMLA-cream-only in treatment of premature ejaculation. Urology. 2006;67(2):388-91. doi: 10.1016/j.urology.2005.09.002. [PubMed: 16460999]

28. Abdel-Hamid IA, El Naggar EA, El Gilany AH. Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation. Int J Impot Res. 2001;13(1):41-5. doi: 10.1038/sj.ijir.3900630. [PubMed: 11313839]

29. Salonia A, Maga T, Colombo R, Scattoni V, Briganti A, Cestari A, et al. A prospective study comparing paroxetine alone versus paroxetine plus sildenafil in patients with premature ejaculation. The Journal of urology. 2002;168(6):2486-9. [PubMed: 12441946]

30. Zhang XS, Wang YY, Huang XY, Leng J, Li Z, Han YF. Comparison between sildenafil plus sertraline and sertraline alone in the treatment of premature ejaculation. Zhonghua Nan Ke Xue. 2005;41(7):520-2. [PubMed: 16078671]

31. Chen J, Mabjeesh NJ, Matzkin H, Greenstein A. Efficacy of sildenafil as adjuvant therapy to selective serotonin reuptake inhibitor in alleviating premature ejaculation. Urol. 2003;61(1):297-200. doi: 10.1016/S0090-4295(02)02075-7. [PubMed: 12559295]

32. Yang W, Ma L, Zhao L, Liu Y, Chen Z. Clinical efficacy of Viagra with behavior therapy against premature ejaculation. Zhonghua Nan Ke Xue. 2006;40(5):536-7. [PubMed: 15908831]