Comparison of Sertraline and Citalopram for Treatment of Premature Ejaculation

Turgay Akgül, Tolga Karakan, Ali Ayyıldız, Cankon Germiyanoğlu

Introduction: We evaluated the efficacy of citalopram and sertraline in the treatment of premature ejaculation (PE).

Materials and Methods: Of 101 married men with PE, 80 were eligible and consented to participate in this randomized controlled trial. Erectile dysfunction and administration of drugs for the treatment of PE were the exclusion criteria. The patients were evaluated using index of premature ejaculation (IPE) questionnaire and were randomly assigned into groups 1 (sertraline) and 2 (citalopram). They received one of these drugs for 8 weeks and then were re-evaluated by the IPE. Pretreatment and posttreatment results were compared within and between the study groups.

Results: A total of 80 patients entered and completed the study. The mean age of the patients was 38.4 ± 7.7 in group 1 and 37.5 ± 6.9 in group 2 ($P = .60$). The mean pretreatment IPE scores were 21.4 ± 1.8 and 20.9 ± 1.3 in the patients of groups 1 and 2, respectively ($P = .23$). After 8 weeks, significant improvement was seen in both groups in terms of the IPE questionnaire results (39.8 ± 1.4; $P < .001$ and 39.5 ± 2.9; $P < .001$, respectively). However, the treatment response was not different between the 2 groups ($P = .50$). No serious adverse effects were detected in any of the patients and both drugs were tolerated well.

Conclusion: Citalopram and sertraline are safe and effective in patients with PE. Additionally, we failed to find any difference between the effects of these two drugs in the treatment of this condition.

Keywords: premature ejaculation, selective serotonin reuptake inhibitors, citalopram, sertraline

Urol J. 2008;5:41-5.
www.uj.unrc.ir

INTRODUCTION

Premature ejaculation (PE) is defined as "stressful recurrent ejaculation with minimal sexual stimulation and before the subject wish it" which is associated with "marked distress or interpersonal difficulty.[1]" It has been reported as the most common sexual problem in men with prevalence rates ranging from 9% to 31%.[2] It has been shown that the prevalence of PE in patients younger than 40 and older than 70 years is higher than 40% and less than 10%, respectively.[3] Moreover, the association between PE and sexual function and satisfaction emphasizes clinical importance of this symptom.[4]

The etiology of PE is unknown in most cases; however, a combination of organic and psychogenic

Department of Urology, Ankara Training and Research Hospital, Ankara, Turkey

Corresponding Author:
Turgay Akgül, MD
No 11, Sokak 18/406500, Bahçelievler, Ankara, Turkey
Tel: +90 505 229 3859
Fax: +90 312 240 2966
E-mail: turgayakgul@gmail.com

Received November 2007
Accepted January 2008

factors is the most probable cause. Although the basic treatment has been short-term directive sex therapy for a long time, PE is increasingly treated pharmacologically with a variety of different medications.[5] Different treatment modalities including local anesthetic creams, selective serotonin reuptake inhibitors (SSRIs), clomipramine, posphodiesterase type 5 inhibitors, adrenergic α1-antagonists, and a centrally acting analgesic (tramadol) have been used for treatment of PE.[6] Nowadays, a combined treatment protocol with drugs and psychotherapy is becoming the treatment of choice.[7]

After studies evaluating clomipramine and paroxetine for the treatment of PE, the effectiveness of SSRIs in the treatment of PE has been established in numerous studies.[8,9] Sertraline has also been found effective in the treatment of PE.[10,11] Citalopram, another SSRI, shows an effective antidepressant activity without important cardiotoxic, anticholinergic, and sedating effects and has been found effective in PE treatment.[12] In the present study, we aimed to evaluate and compare the efficacy of citalopram and sertraline in the treatment of premature ejaculation.

MATERIALS AND METHODS

Patients and Treatment

Between June 2006 and February 2007, we recruited 101 married men who referred to our clinics for PE. Men experiencing ejaculation within 2 minutes of penetration in 75% of their sexual intercourse attempts or more were considered to have PE. All patients were interviewed individually and a comprehensive history including marriage relation status and the partner's obstetric features was taken.

Patients were included if they had a score of 22 or more on the erectile function domain of the international index of erectile function (IIEF).[13] Patients with erectile dysfunction were excluded from the study. Additionally, those with a history of vascular disease and those under treatment of PE by drugs such as organic nitrates or cytochrome P450 inhibitors were excluded. The eligible patients were given medical information about the treatment protocol. After providing oral consent, 80 patients were evaluated with the index of premature ejaculation (IPE) questionnaire[14] and were randomly assigned into groups 1 and 2. Patients in group 1 received citalopram (Relaxol, Biofarma, Istanbul, Turkey), 20 mg/d, and those in group 2 received sertraline hydrochloride (Lustral, Pfizer, Surrey, UK), 50 mg/d. At the end of the 8th week of treatment, the patients were re-evaluated using the IPE score by another clinician who was blind to the study protocol and the results were compared with the pretreatment values.

Index of Premature Ejaculation

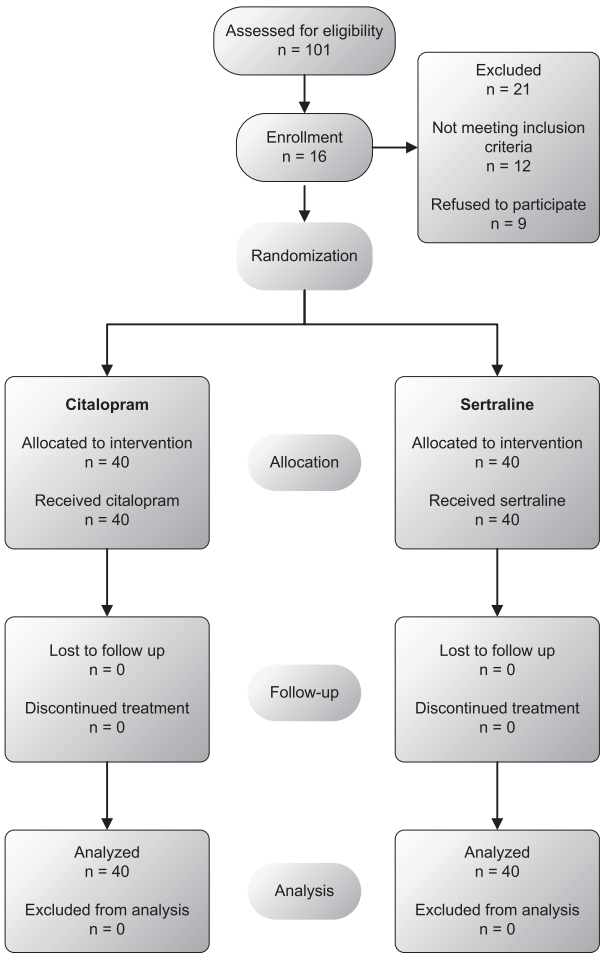
The previously validated IPE questionnaire[14] included 10 questions on sexual libido, frequency of erection enough for sexual intercourse, frequency of maintaining erection to complete sexual intercourse, intravaginal ejaculatory latency (IELT), difficulty in prolonged sexual intercourse, sexual satisfaction, partner's sexual satisfaction, frequency of reaching orgasm in the partner, confidence in completing sexual activity, and frequency of feeling anxious, depressed, or stressed during sexual activity. Each questionnaire was scored from 1 (never/almost never) to 5 (always/almost always).

Statistical Analyses

The collected data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 13.5, SPSS Inc, Chicago, Ill, USA). Differences in numerical values before and after the treatment were analyzed by the t test and paired *t* test. *P* values less than .05 were considered significant.

RESULTS

A total of 80 patients entered and complete the study (Figure). The mean age of the patients was 38.4 ± 7.7 in group 1 and 37.5 ± 6.9 in group 2 (Table 1). The mean pretreatment IPE scores were 21.4 ± 1.8 and 20.9 ± 1.3 in the patients of groups 1 and 2, respectively ($P = .23$). After 8 weeks, significant improvement was seen in both groups in terms of the IPE questionnaire results (Table 2). However, the treatment response was not



The Consolidated Standards of Reporting Trials (CONSORT) flowchart of the randomized study is shown.[15]

different between the 2 groups ($P = .50$).

No serious adverse effects were detected in any of the patients. Three patients (7.5%) in group 1 and 2 (5.0%) in group 2 had mild nausea at the beginning of the treatment. However, they could tolerate well and continued their treatment until the end of the study period.

DISCUSSION

The most studied neurotransmitter in the physiology of ejaculation is 5-hydroxytryptamine (5-HT),[16] which is an inhibitor of ejaculation acting via decreasing serotonin-induced dopamine. The SSRIs inhibit presynaptic reuptake of 5-HT in the central nervous system.[12] The effect of sertraline, a well-known SSRI, on PE has been demonstrated in previous studies.[17] Arafa and Shamloul investigated the effect of sertraline, 50 mg daily, in a placebo-controlled study using an Arabic translation of the IPE scoring system and confirmed the usefulness of sertraline for improvement of ejaculation time.[11] They also reported that treatment with sertraline had no negative impact on erectile function and libido, which is completely in accordance with our results.

Citalopram has also been previously investigated for the treatment of PE. This drug is different from other SSRIs because it does not inhibit any cytochrome P450 isoform and shows linear kinetics throughout the duration of the treatment.[18] It has also been stated that absorption of citalopram is not affected by food, and steady-state concentrations are reached within 1 to 2 weeks with once-daily dosage.[19,20] However, there are few studies in the literature about the efficacy of citalopram in PE. Atmaca and colleagues investigated the efficacy of citalopram in PE and stated that it was more efficacious than placebo.[12] Safarinejad

Table 1. Demographic and Clinical Features of Patients With Premature Ejaculation Who Received Either Citalopram or Sertraline*

Features	Group 1 Citalopram	Group 2 Sertraline	*P*
Mean age, y	38.4 ± 7.7 (23 to 53)	37.5 ± 6.9 (27 to 52)	.60
Mean deliveries of partners	1.9 ± 1.6 (0 to 7)	1.8 ± 1.32 (0 to 5)	.73
Mean number of marriages	1.1 ± 0.3 (1 to 2)	1.2 ± 0.4 (1 to 2)	.99

*Values are demonstrated as mean ± standard deviation (range).

Table 2. Pretreatment and Posttreatment Scores of IPE in Patients on Citalopram and Sertraline*

Patient Groups	Baseline IPE	Posttreatment IPE	*P*
Group 1 (citalopram)	21.4 ± 1.8 (18 to 26)	39.8 ± 1.4 (36 to 42)	< .001
Group 2 (sertraline)	20.9 ± 1.3 (18 to 23)	39.5 ± 2.9 (31 to 44)	< .001

*Values are demonstrated as mean ± standard deviation (range). IPE indicates index of premature ejaculation.

and Hosseini reported similar results with citalopram and showed improvement in the overall sexual satisfaction with citalopram which is in accordance with our findings.[20] In our study, citalopram was found to be effective according to the IPE questionnaire. However, we did not separately evaluate the effect of citalopram on sexual function.

Dosage is one of the important points in the treatment of PE. The SSRIs taken daily significantly delay ejaculation.[21,22] With daily administration of antidepressants, the delay of ejaculation usually occurs within 5 to 10 days.[23] Although some authors have reported a 4-fold to 11-fold increase in ejaculation latency,[24,25] others have reported only a 1.3-fold increase when paroxetine, 20 mg, was taken as on-demand dosing 3-4 hours before intercourse.[26] Daily treatment appears to be associated with better ejaculatory control than on-demand dosing; however, it leads to considerable drug exposure for events that usually do not occur everyday. By contrast, daily dosing removes the need to anticipate the occurrence of sexual intercourse 4 or 6 hours before it is likely to occur, which may put excessive pressure on the couple.[27] However, it has been hypothesized that long-term treatment with SSRIs leads to higher synaptic 5-HT levels than episodic treatment.[27] Although there are still arguments about this subject, we prefer to administer daily dosage of SSRIs in the treatment of PE and, in our opinion, this regimen is more practical for evaluating the effectiveness of drugs.

Side effects are the major issues concerning daily treatment with SSRIs in depressive patients. Their adverse effects include psychiatric, anticholinergic, and dermatologic reactions; changes in body weight; and cognitive impairment.[27] In the present study, we did not observe any clinically important side effect causing drug withdrawal. Only 5 patients from both groups experienced mild nausea at the beginning of the treatment.

The most widely used assessment guideline on PE is IELT.[28,29] It is important to consider that nearly half of the adult women suffer from sexual dysfunction and patients with PE may also have other sexual disturbances, which complicate the relationship between the partners more than before.[30] Besides, many clinicians consider the stopwatch IELT measurement to be impractical in clinical use.[3] Similarly, we think that IELT measurement method is not practical especially in conservative societies and can give misleading results due to reasons described before. Therefore, we used the IPE scoring system that was firstly introduced by Yuan and associates.[31]

The lack of a control group that has not received any treatment or a placebo-control group is the limitation of our study. However, because the effectiveness of SSRIs in PE is already known, this condition cannot limit the importance of our results significantly. Nevertheless, we believe that placebo-controlled studies with greater sample sizes are needed.

CONCLUSION

Using a validated questionnaire, we confirmed that citalopram and sertraline administered on a long-term daily basis are safe and effective in the patients with PE. However, we failed to find any significant difference between the effects of these two drugs in PE treatment.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM IV). 4th ed. Washington, DC: American Psychiatric Association; 1994. p. 509-11.
2. Lewis RW, Fugl-Meyer KS, Bosch R, et al. Definitions, classifications and epidemiology of sexual dysfunction. In: Lue TF, Basson R, Rosen R, Giuliano F, Khoury S, Montorsi F, editors. Sexual medicine. Sexual dysfunctions in men and women. Oxford (UK): Health Publication; 2004. p. 37-72.
3. Jannini EA, Lenzi A. Epidemiology of premature ejaculation. Curr Opin Urol. 2005;15:399-403.
4. Rowland D, Perelman M, Althof S, et al. Self-reported premature ejaculation and aspects of sexual functioning and satisfaction. J Sex Med. 2004;1:225-32.
5. Lue TF, Giuliano F, Montorsi F, et al. Summary of the recommendations on sexual dysfunctions in men. J Sex Med. 2004;1:6-23.
6. Gurkan L, Oommen M, Hellstrom WJ. Premature ejaculation: current and future treatments. Asian J Androl. 2008;10:102-9.
7. Perelman MA. A new combination treatment for

premature ejaculation: a sex therapist's perspective. J Sex Med. 2006;3:1004-12.

8. Goodman RE. The management of premature ejaculation. J Int Med Res. 1977;5:78-9.
9. Waldinger MD, Hengeveld MW, Zwinderman AH. Paroxetine treatment of premature ejaculation: a double-blind, randomized, placebo-controlled study. Am J Psychiatry. 1994;151:1377-9.
10. Murat Başar M, Atan A, Yildiz M, Baykam M, Aydogănli L. Comparison of sertraline to fluoxetine with regard to their efficacy and side effects in the treatment of premature ejaculation. Arch Esp Urol. 1999;52:1008-11.
11. Arafa M, Shamloul R. Efficacy of sertraline hydrochloride in treatment of premature ejaculation: a placebo-controlled study using a validated questionnaire. Int J Impot Res. 2006;18:534-8.
12. Atmaca M, Kuloglu M, Tezcan E, Semercioz A. The efficacy of citalopram in the treatment of premature ejaculation: a placebo-controlled study. Int J Impot Res. 2002;14:502-5.
13. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology. 1997;49:822-30.
14. Althof S, Rosen R, Symonds T, Mundayat R, May K, Abraham L. Development and validation of a new questionnaire to assess sexual satisfaction, control, and distress associated with premature ejaculation. J Sex Med. 2006;3:465-75.
15. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet. 2001;357:1191-4.
16. Wolters JP, Hellstrom WJ. Current concepts in ejaculatory dysfunction. Rev Urol. 2006;8:S18-25.
17. Waldinger MD, Zwinderman AH, Schweitzer DH, Olivier B. Relevance of methodological design for the interpretation of efficacy of drug treatment of premature ejaculation: a systematic review and meta-analysis. Int J Impot Res. 2004;16:369-81.
18. Hyttel J. Citalopram--pharmacological profile of a specific serotonin uptake inhibitor with antidepressant activity. Prog Neuropsychopharmacol Biol Psychiatry. 1982;6:277-95.
19. Barton DL, Loprinzi CL, Novotny P, et al. Pilot evaluation of citalopram for the relief of hot flashes. J Support Oncol. 2003;1:47-51.
20. Safarinejad MR, Hosseini SY. Safety and efficacy of citalopram in the treatment of premature ejaculation: a double-blind placebo-controlled, fixed dose, randomized study. Int J Impot Res. 2006;18:164-9.
21. 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;18:274-81.
22. Waldinger MD, Schweitzer DH, Olivier B. On-demand SSRI treatment of premature ejaculation: pharmacodynamic limitations for relevant ejaculation delay and consequent solutions. J Sex Med. 2005;2:121-31.
23. Giuliano F, Clément P. Serotonin and premature ejaculation: from physiology to patient management. Eur Urol. 2006;50:454-66.
24. 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;13:41-5.
25. McMahon CG, Touma K. Treatment of premature ejaculation with paroxetine hydrochloride as needed: 2 single-blind placebo controlled crossover studies. J Urol. 1999;161:1826-30.
26. Waldinger MD, Zwinderman AH, Olivier B. On-demand treatment of premature ejaculation with clomipramine and paroxetine: a randomized, double-blind fixed-dose study with stopwatch assessment. Eur Urol. 2004;46:510-5.
27. Riley A, Segraves RT. Treatment of premature ejaculation. Int J Clin Pract. 2006;60:694-7.
28. Rowland DL, Strassberg DS, de Gouveia Brazao CA, Slob AK. Ejaculatory latency and control in men with premature ejaculation: an analysis across sexual activities using multiple sources of information. J Psychosom Res. 2000;48:69-77.
29. Choi HK, Jung GW, Moon KH, et al. Clinical study of SS-cream in patients with lifelong premature ejaculation. Urology. 2000;55:257-61.
30. Moynihan R. The making of a disease: female sexual dysfunction. BMJ. 2003;326:45-7.
31. Yuan YM, Xin ZC, Jiang H, et al. Sexual function of premature ejaculation patients assayed with Chinese Index of Premature Ejaculation. Asian J Androl. 2004;6:121-6.