Iranian Journal of Reproductive Medicine Vol.8. No.2. pp: 55-59, Spring 2010

Efficacy of selective serotonin reuptake inhibitor (SSRI) in patient with premature ejaculation

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Received: 24 June2009; accepted: 17 November 2009

Abstract

Background: Premature ejaculation (PE) is the most common sexual dysfunction compliant in about 35-40% of men younger than 40 years; therefore a study for survey and diagnosis of this disorder is very important.

Objective: In this study, the efficacy of 2 drugs (fluoxetine and citalopram) for treatment of patients suffering from PE is compared. We studied the effectiveness of both drugs in PE with different protocols to find out the most effective drug with least side effects.

Materials and Methods: In total 77 patients referred to the Urology Clinic of Emam Reza Hospital, Tehran from 2006 to 2008 for the treatment of PE, including 25 patients with anxiety disorder, were randomly divided into 2 study groups. Patients belonging to first group (N= 43) received 40 mg (2 capsules of 20 mg) fluoxetine daily for 4 weeks and patients of the group II (N=34) received 40 mg citalopram daily for 4 weeks.

Results: The mean Intra Vaginal Ejaculation Latency Time (IVELT) before treatment in patients of group I was 58.26±41.83 seconds while after treatment it raised to 466.2±10.85 seconds. In group II, the mean IVELT before treatment was 51.76±34.39 seconds while after treatment it elevated to 403.8±7.58 seconds.

Conclusion: Difference was significant in mean IVELT before and after treatment with fluoxetine and citalopram (each drug separately). In this study, both drugs improved ejaculation duration while difference between 2 drugs was not significant (p>0.05)

***Key words**: Citalopram, Fluoxetine, Impotency, Premature ejaculation.*

Introduction

Premature ejaculation (PE) is the most prevalent sexual disorders in men. This disorder is the main complain of 35-40% of those men treating because of sexual disorders (1). PE is a frequent male sexual complaint that is mediated mainly by disturbances of serotonergic neurotransmission and certain serotonin (5-HT) receptors and, to a lesser extent, oxytocinergic neurotransmission in the central nervous system (2).

The sympathetic, parasympathetic and somatic spinal centers under the influence of sensory genital and cerebral stimuli integrate and process at the spinal cord level, act in synergy to command physiological events occurring during ejaculation. Experimental evidences indicate that serotonin (5-hydroxytryptamine, 5-HT) throughout brain descending pathways, exerts an inhibitory role on ejaculation (3). Serotonin is important at the level of the central nervous system in the complex regulatory mechanisms involved in ejaculation (4). Selective serotonin reuptake inhibitor (SSRI) antidepressants (paroxetine, fluoxetine and sertraline) and the tricyclic antidepressant clomipramine improve ejaculatory control and delay ejaculation in men suffering from PE, suggesting that pharmacological intervention might be useful for PE (4). The Diagnostic Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) criteria for premature ejaculation is

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multifactorial and has low positive predictive value, suggesting that PE diagnosis should be based solely on Intra Vaginal Ejaculation Latency Time (IVELT) (5), while new classification of PE has been proposed for the pending DSM-V; distinguishing four PE categories; lifelong PE, acquired PE, natural variable PE and premature-like ejaculatory dysfunction (6). Selective serotonin reuptake inhibitors (SSRIs) are known to induce delayed orgasm and delayed ejaculation (7). Emerging clinical evidence indicates chronic and on-demand dosing of SSRIs has a beneficial effect for the treatment of men with PE (2). On-demand dapoxetine, and SSRI with a short half-life, recently has been shown to significantly increase IVELT and improve PE patient-related outcomes (8).

Citalopram, a potent and highly selective SSRI antidepressant, is used to treat patients with premature ejaculation and has been effective significantly (compared to placebo) in terms of IVELT and intercourse satisfaction (9). Fluoxetine, an antidepressant, which selectively inhibits uptake of 5-HT has shown to delay the onset of ejaculation in patients and is effective in cases of PE (10).

In a study by Montejo *et al*, fluoxetine increased IVELT to 199.35 sec. This meaningful result occurred in 68% of cases (11). In another study done by Hackett *et al* the effect of topical lidocain-perlikain in PE was studied which increased the time of ejaculation (12). While Atmaca *et al* examined citaloperam effect on treatment of PE and showed that it increased the time of ejaculation (13). Strassberg *et al* showed that using clomiperamine 4-6 hours before sexual activity increased the time of ejaculation in patients suffering from PE (14). In addition Hellstrom *et al* examined dapoxetin effect (which is short effect halter) on treatment of PE and showed that it increased the time of ejaculation (16).

We compared the efficacy and side effects of fluoxetine and citalopram for patients suffering from PE without evident organic causes. Until present time most of the studies were about the efficacy of drugs in treatment of different sexual dysfunction specifically PE, but to our knowledge there was no comparison between the efficacy of fluoxetine and citalopram. In this study, we tried to find out which of these drugs are better and more effective in the treatment of PE.

Materials and methods

This study was a randomized clinical trial on 110 patients referring to the Urology Clinic of Emam Reza Hospital, Tehran from 2006 to 2008 for the treatment of PE. Out of these, 33 patients were excluded from the study on different grounds: 5 patients were excluded from the study due to drug side effects like headache, dizziness, insomnia and diarrhea. The remaining 28 patients were excluded from the study because of their unwillingness to continue the treatment or on the basis of our exclusion criteria like suffering from erection impotency, urogenital infection, systemic or neurological disorders, psychological problems, alcoholism, and drug abuse. Though anxiety is a psychological disorder but because it can be the basis and a causing agent for PE, therefore we did not exclude these cases from our study. At last, the study continued with 77 patients. According to the information collected from the questionnaire filled by each patient, all patients were married and had intercourse only with their wives. They were asked to have at least one intercourse in a week. A consent form was filled by each patient. Except 25 patients with anxiety disorder no patient had psychological problems.

Patients´ age ranged from 18 to 60 years with the mean of 33.8 years. The patients were randomly divided into 2 study groups. Care was taken to match the patients of the 2 groups by age and clinical criteria. On the basis of information obtained from health forum-GHQ-28, twenty five patients suffered anxiety disorder and were divided into both study groups. 15 patients were placed in group I (treated with fluoxetine) and 10 were placed in group II (treated with citalopram).

The ejaculation time for every patient was measured before treatment thrice by stopwatch by the patients´ sexual partner. An instruction to use the stopwatch was given by our coworker working in the Urology Clinic to the patients´ wife.

Patients belonging to group I (N=43) received 2 capsules of 20 mg fluoxetine daily for 4 weeks (morning and night). Patients of the group II (N=34) received 40 mg citalopram daily for 4 weeks. Ejaculation latency time was again measured as before after treatment was over.

Statistical analysis

Statistical differences between treatment groups were determined with the analysis of variance test using the computerized statistical analysis of SPSS 14.

The experimental model was completely randomized design (CRD) experiment ($Y_{ij} = \mu + T_i + e_{ij}$). Where differences were observed between treatments, the means were compared using paired sample T Test for time of ejaculation before and after treatments and also between of two groups.

Results

Table I shows the number of intercourses in week in 2 study groups. Mean number of intercourses in week in group I was 1.53 and in group II, it was 1.70. As it is clear from Table 2, the mean age of the 77 patients was 33.8 years. PE was more common in young men of up to the age of 30 (>20-29) years (37/77), while men older than 50 years face this problem to lesser extent (7/77).

Table I. Number of intercourses in week in 2 study groups.

	N	Min	Max	Mean	S.D.
Group II	34	1	4	1.71	0.906
Group I	43	1	4	1.53	0.735

S.D. = Std. Deviation

Table II. Age and grouping of the study cases.

Age	No. in each group	No. in treatment groups	
		Group I	Group II
<20-29	37	21	16
30-39	22	12	10
40-49	11	8	3
>50-59	7	2	5
Total	77	43	34

The mean age of 43 patients belonging to group I was 33.21±9.66 years. The mean ejaculation time before treatment in normal patients of group I was 58.26±41.83 (10-120) seconds while after treatment it raised to 466.2±10.85 seconds. Among 15 patients with anxiety disorder, the mean ejaculation time before treatment was calculated separately to be 49.33±40.12 seconds. Their IVELT recorded after 4 weeks of treatment was 379.8±6.45 seconds. In group II, the mean age of 34 patients was calculated to be 34.56±10.94 years. The mean ejaculation time before treatment in these patients was 51.76±34.39 seconds while after treatment it raised to 403.8±7.58 seconds in normal patients. The mean ejaculation time before treatment for patients with anxiety disorder was 65±41.96 seconds and after treatment this raised to 480±6.71 seconds (Table III).

Table III. Ejaculation time before and after treatment in 2 study groups.

Mean ejaculation time (Seconds)	Group I (Fluoxetine)	Group II (Citalopram)
Before Treatment		
Patients without anxiety	58.26±41.83	51.76±34.39
Patients with anxiety	49.33±40.12	65±41.96
After Treatment		
Patients without anxiety	466.2±10.85	403.8±7.58
Patients with anxiety	379.8±6.45	480±6.71

Discussion

PE is the most common male sexual dysfunction (15). Sexual disorder is a source of severe marital and family discord. PE is estimated to be present in at least 25% of clinical cases (16). To date, three 5-HT receptor subtypes (5-HT1A, 5-HT1B, and 5-HT2C) have been postulated to mediate 5-HT's modulating activity on ejaculation (17). In the present study, statistical analysis indicates that there is significant difference in ejaculation time before and after treatment using fluoxetine ($p<0.01$) and citalopram ($p<0.01$) while difference between 2 drugs was not significant ($p>0.05$). Sexual dysfunction was positively correlated with dose (9). Madeo *et al* used 20 mg/day fluoxetine as well as citalopram for the first week and increased the dose to 40 mg/day for more 3 weeks. He measured Masturbation Ejaculatory Latency Time (MELT) during visual erotic stimulation and self filled questionnaires (7). In our study we used 40 mg citalopram and fluoxetine/ day /4 weeks but the treatment duration was the same.

Madeo *et al* reported dysfunction disappeared completely in only 5.8% of his patients within 6 months and 81.4% showed no improvement at all by the end of this period (7). In addition, they reported a delay in ejaculation time both during citalopram and fluoxetine treatment when compared with placebo, reaching a statistical significance only with citalopram (7). Safarinejad *et al* in a similar study used 20 mg/oral/ daily / 12 weeks (9). Waldinger *et al* assessed putative differences between the major SSRIs (fluoxetine, fluvoxamine, paroxetine, and sertraline) with regard to their ejaculation-delaying effect. They used fluoxetine 20 mg/day for men with lifelong rapid ejaculation for 6 weeks. We advised both fluoxetine and citalopram to different patients 40 mg/ day for only 4 weeks (18).

The present study indicated that increasing drug dose leads to shorter treatment duration. According

to Madeo *et al* the treatment with citalopram or with fluoxetine was confirmed to delay ejaculation, but was significant only for citalopram. He stated that citalopram and fluoxetine did not affect sexual desire. According to him, citalopram and fluoxetine did not directly affect penile erection as objectively assessed by RigiScan, although an impairment in the subjective assessment of erectile function was observed, but was significant only for citalopram, and it was thought to be a possible consequence of the delayed ejaculation perceived as a trouble (7). Waldinger *et al* also reported significant difference ($p<0.001$) in the evolution of IVELT delay due to fluoxetine in his patients compared to placebo (18).

Rama Raju *et al* prescribed one capsule of fluoxetine (20mg) in the morning for 4 weeks for management of PE. He stated that all his patients reported marked subjective improvement of time from penetration to ejaculation for two to four minutes (10). Comparing our findings with Rama Raju´s results, we observed elevation of ejaculation time to 2-4 minutes while in our patients the ejaculation time was quite higher. So on the basis of our findings it is better to use higher doses of drugs than what has been conventionally used till now to treat PE. Some patients in our study were excluded because of drug side effects. In a similar study, Rama Raju *et al* also observed mild and transient side effects like glossitis, lack of concentration and vague headache due to fluoxetine (20 mg/4 weeks) taken in the morning for management of PE (10).

Our findings indicate that fluoxetine and citalopram efficacies on PE are highly effective and it is advised to increase the dose to fasten the treatment and leads to quicker mental remedy for patients. Waldinger *et al* demonstrated similar efficacies for daily treatment with the serotonergic antidepressants such as paroxetine hemihydrate, clomipramine, sertraline and fluoxetine, which paroxetine hemihydrate exerting the strongest effect on ejaculation. They suggested that on-demand SSRI treatment will not lead to similarly impressive delays in ejaculation as has been observed with daily SSRI treatment (2). Waldinger stated that on-demand treatment with SSRIs generally exert much less ejaculation delay than daily SSRIs treatment (19).

We also used daily SSRIs treatment for treating these patients. Mattus *et al* also reported significant difference in the IVELT delay due to flouxetine compared to tadalafil (20).

Acknowledgement

The authors thank faculty and members of Urology Department of Emam Reza Hospital and all those who helped us is a way to complete this project.

References

1. Rezakhaniha B, Safarinejad MA. A survey of prevalence of sexual disorders and risk factors in patient who Reffered in Urology ward in 501 Army Medical center 1383- 84, *JAMA* 2008; 4: 1041-1045.
2. Waldinger MD. Premature ejaculation: definition and drug treatment. *Drugs* 2007; 67: 547-568.
3. Giuliano F, Clément P. Serotonin and premature ejaculation: from physiology to patient management. *Eur Urol* 2006; 50: 454-566.
4. Giuliano F, Hellstrom WJ. The pharmacological treatment of premature ejaculation. *BJU Int* 2008; 102: 668-675.
5. Shabsigh R, Rowland D. The Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision as an appropriate diagnostic for premature ejaculation. *J Sex Med* 2007; 4: 1468-1478.
6. Waldinger MD. Recent advances in the classification, neurobiology and treatment of premature ejaculation. *Adv Psychosom Med* 2008; 29: 50-69.
7. Madeo B, Bettica P, Milleri S, Balestrieri A, Granata AR, Carani C, et al. The effects of citalopram and fluoxetine on sexual behavior in healthy men: evidence of delayed ejaculation and unaffected sexual desire. A randomized, placebo-controlled, double-blind, double-dummy, parallel group study. *J Sex Med* 2008; 5: 2431-2441.
8. Hellstrom WJ. Emerging treatments for premature ejaculation: focus on dapoxetin. *Neuropsychiatr Dis Treat* 2009; 5: 32-46.
9. 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; 18:164-169.
10. Rama Raju GA, Usha Rani P, Naidu MUR, Ramesh T, Schobha JC. Evaluation of fluoxetine in premature ejaculation. *Indian Journal of Pharmacology* 1997; 29: 204-205.
11. Montejo-González AL, Llorca G, Izquierdo JA, Ledesma A, Bousoño M, Calcedo A, et al. SSRI-induced sexual dysfunction: fluoxetine, paroxetine, sertraline, and fluvoxamine in a prospective, multicenter, and descriptive clinical study of 344 patients. *J Sex Marital Ther* 1997; 23:176-194.
12. Dinsmore WW, Hackett G, Goldmeier D, Waldinger M, Dean J, Wright P, et al. Topical eutectic mixture for premature ejaculation (TEMPE); A novel aerosol delivery from of lidocaine-prilocain for treating premature ejaculation. *BJU int* 2007; 99: 369-375.
13. Atmaca M, Kuioglu M. The efficacy of citalopram in the treatment of premature ejaculation; a placebo-control study. *Int J Impot Res* 2002; 14:502-505.
14. Sterassberg D, Roland D, Colmipramine in the treatment of rapid premature ejaculation. *J Sex Marital Ther* 1999; 25:89-101.
15. Porest H. Premature ejaculation. *J Urologe A* 2009; 48: 663,664.
16. McMahon CG, Althof SE, Waldinger MD, Porst H, Dean J, Sharlip ID, et al. An evidence-based definition of

lifelong premature ejaculation: report of the International Society for Sexual Medicine (ISSM) ad hoc committee for the definition of premature ejaculation. *J Sex Med* 2008; 5: 1590-1606.
17. Clement P, Giuliano F. Serotonin and premature ejaculation: from physiology to patient management. *Eur Urol* 2006; 50:454-466.
18. 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: 274-281.
19. Waldinger MD. Premature ejaculation: state of the art. *Urol Clin North Am* 2007; 34:591-599.
20. Mattos RM, Marmo lucan A, Srougi M.Tadalafil and fluoxetine in premature ejaculation: prospective, randomized, double-blind, placebo-controlled study. *Urol Int* 2008; 80: 162-165.