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The efficacy of citalopram in the treatment of premature ejaculation: A placebo-controlled study

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Background: Despite the limited number of available study comparing of their efficacy, selective serotonin re-uptake inhibitors (SSRI) have been thought to have beneficial effects for the patients with premature ejaculation. In the present study, we decided to examine the efficacy of citalopram, an SSRI, in the treatment of premature ejaculation.

Method: The study was consisted of 26 married patients diagnosed with premature ejaculation according to Diagnostic and Statistical Manual of Mental Disorders Third Revised Version (DSM-III-R). The patients were randomly assigned to two groups, citalopram (group I) and placebo (group II), each consisting of 13 patients. The effects of drug on the ejaculatory function were assessed by the intravaginal ejaculation latency time. Additionally, all patients were screened by using Clinical Global Impression-Improvement Scale (CGI-I) and Yonsei Sexual Function Inventory-II (YSFI-II).

Results: The increase in the intravaginal ejaculation latency time in the citalopram group was statistically significant than that of placebo group. In addition, with respect to the subscales of the YSFI-II scale, similar overall significant improvements were seen in the patients given citalopram compared to those given placebo. Of group I patients, five (38.5%) were considered as 'very much improved' and four (30.8%) 'much improved' by CGI-I and only one of group II patients (7.7%) showed 'much improved'.

Conclusion: The patients treated with citalopram showed significantly greater improvement compared to the patients receiving placebo.

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Keywords: SSRI; citalopram; placebo; premature ejaculation

Introduction

Premature ejaculation has been defined as uncontrolled ejaculation whose essential feature is the recurrent or persistent orgasm with minimal sexual stimulation before, on, or after penetration and before the person desires it. The majority of men experienced premature ejaculation can have delay ejaculation and orgasm during self-masturbation for a considerably longer time compared to during coitus.[1] Different treatment approaches have been used for the treatment of premature ejaculation including local anaesthetic sprays, vascular surgery, propranolol and serotonin reuptake inhibitors.

Sexual side effects, eg decreased libido, orgasm inhibition, erectile dysfunction and priapismus, related to use of antidepressant drugs **have been reported**. Sexual dysfunction is a common side effect reported by most of the available antidepressant drugs. Studies that were not specifically designed to determine antidepressant-associated sexual side effects reported 5–10% sexual dysfunction in the patients using **tricyclic antidepressants** (TCAs), while this rate was 10–30% in those using SSRI.[2–4] On the other hand, despite the limited number of available study comparing of their efficacy, SSRIs; fluoxetine, paroxetine have been thought to have beneficial effects for the patients with premature ejaculation.[5–7] In the patients with depression, sertraline has been reported to cause retarded ejaculation.[8] However, to the best of our knowledge, so far, citalopram, an SSRI, has not been systematically

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studied for the treatment of the premature ejaculation. Citalopram shows an effective antidepressant activity without an important cardiotoxic, anticholinergic and sedating effects.[9]

In the present study, we decided to examine the efficacy of citalopram in the treatment of premature ejaculation and hypothesized that it might have beneficial effects on this condition.

Method

Twenty six married male patients (aged 24–46 y) were studied. They applied to Firat University School of Medicine Departments of Psychiatry and Urology and were diagnosed with premature ejaculation according to DSM-III-R[10] and met the study admission criteria. After complete description of the study to the subjects, the written informed consent was obtained from each patient. The study was approved by Local Ethics Committee of the Firat University School of Medicine. Each patient underwent diagnostic evaluation by one trained psychiatrist by using Structured Clinical Interview for DSM-III-R outpatient form (SCID-OP).[11] According to SCID-OP, one patient was diagnosed with comorbid major depressive disorder **(MDD)** and one with obsessive compulsive disorder (OCD). To be able to exclude the organic sexual dysfunctions, the fasting glucose level, urine analysis, complete blood count, sex hormones and prolactin levels were obtained. Exclusion criteria included the presence of erectile dysfunction and inhibited male orgasm, a severe physical illness, the history of alcohol and any substance abuse or dependence, the presence of any endocrinological state and treatment with any psychotropic medication within last 2 weeks. All patients were heterosexual.

The patients were randomly assigned to either citalopram (group I) ($n=13$) or placebo (group II) ($n=13$) treatment in the double-blind design. The drugs were taken after breakfast. In group I, the patients initially received 20 mg citalopram per day. Titration up to 60 mg per day was permitted according to the patient's tolerability and clinical response, with increase of one tablet within the period of two weeks. In group II, the patients received initially identical one placebo tablet per day and placebo was titrated to three capsules according to the clinical response, with increase of one tablet in two weeks' period. The use of concomitant medications was prohibited, with the exception of benzodiazepine. However, no patient required additional drug throughout the study including benzodiazepine. The intravaginal ejaculation latency time was defined as the duration between vaginal intromission and ejaculation.[12] The subjects were asked to determine the average intravaginal ejaculation latency time for three consecutive episodes of coitus verified by both patients and their wives via a chronometer. The patients and their wives were encouraged to engage in coitus twice a week and record intravaginal ejaculation latency time. All patients and their partners were individually interviewed at the beginning of the study and at week 2, 4, 8. All patients were screened by using Clinical Global Impression-Improvement Scale (CGI-I).[13] Additionally, changes in general sexual function were examined by using Yonsei Sexual Function Inventory-II (YSFI-II).[14] This scale is the self-rating of 7-item 100 mm visual analogue scale which demonstrates performance anxiety for the rapid ejaculation, sexual desire, satisfaction with ejaculation and overall sexual functions. The score ranged from 0 (not at all) to 100 (most ever). On the other hand, in one patient with major depression and one patient with OCD, the psychopathology at each interview was screened by Hamilton Depression Rating Scale (HDRS)[15] and Yale-Brown Obsession Compulsion Scale (Y-BOCS)[16] respectively. Statistical analysis was performed by using chi-square, Student's t and repeated measures ANOVA tests.

Results

All patients completed the study. The mean age, age of wives and duration of illness in group I were 32.74 ± 10.54, 30.34 ± 11.26 and 8.84 ± 5.11 y, respectively whereas those in group II were 31.51 ± 9.88, 28.94 ± 10.12 and 9.08 ± 4.78 y, respectively ($P > 0.05$). At the end of the study, among group I patients, nine (69.2%) were receiving 20 mg/day, two (15.4%) 40 mg/day, and two (15.4%) 60 mg/day of citalopram. In group II patients, one (7.7%) was receiving two tablets/day, day, and 12 (92.3%) three tablets/day at the end of the study.

At the baseline, the mean intravaginal latency time was 33.46 ± 17.96 in group I and 30.38 ± 14.64 seconds in group II. The difference was not statistically significant ($P > 0.05$). The mean time at last assessment was 283.85 ± 80.50 in group I and 35.77 ± 13.52 seconds in group II ($P < 0.001$). **The intravaginal ejaculation latency time considerably increased after 8 weeks of treatment in group I ($P < 0.001$) but not in group II ($P > 0.05$).** The difference in the mean intravaginal latency time between groups arrived a statistical significance at the evaluation of week 2 ($P < 0.001$). This separation continued until the end of the trial (Table 1).

With respect to the subscales of the YSFI-II scale, greater significant improvements were seen in group I compared to group II. The mean changes

Table 1 Intravaginal ejaculation latency time (sec) and the mean CGI-I scores

	Intravaginal ejaculation latency time (sec)				*CGI-I*			
Week	**Citalopram** *(n = 13)*	*Placebo (n = 13)*	t*	P*	**Citalopram** *(n = 13)*	*Placebo (n = 13)*	t*	P*
0	33.46 ± 17.96	30.38 ± 14.64	0.48	0.64	–	–	–	–
2	119.23 ± 42.71	32.69 ± 12.52	7.01	<0.001	4.00 ± 0.71	4.77 ± 1.09	−2.13	<0.05
4	233.46 ± 42.20	35.00 ± 12.08	16.30	<0.001	2.08 ± 0.64	4.46 ± 0.77	−8.54	<0.001
8	283.85 ± 80.50	35.77 ± 13.52	10.96	<0.001	1.38 ± 0.51	4.08 ± 1.04	−8.41	<0.001
0–2**	50.57, <0.001	2.96, 0.11			–	–		
2–4**	162.95, <0.001	3.60, 0.08			105.00, <0.001	3.08, 0.104		
4–8**	10.51, <0.01	0.11, 0.75			15.68, <0.01	4.55, 0.054		

*, Used Student *t*-test.
**, Used repeated measures ANOVA test (given *F* and *P* values, respectively).

from the baseline to the last assessment in group I were significantly higher compared to group II in all subscales: the sexual desire (19.5 mm for citalopram group and 2.8 mm for placebo group; $P < 0.001$); the quality of erection (21.4 mm for citalopram group and 4.2 mm for placebo group; $P < 0.001$); anxiety for rapid ejaculation (−28.3 mm for citalopram group and −5.23 mm for placebo group; $P < 0.001$); the satisfaction with ejaculation (21.4 mm for citalopram group and 6.1 mm for placebo group; $P < 0.01$); the partner's satisfaction with ejaculation (35.8 mm for citalopram group and 8.3 mm for placebo group; $P < 0.001$); the overall sexual satisfaction (29.3 mm for citalopram group and 7.4 mm for placebo group; $P < 0.001$) and the partner's overall satisfaction (31.2 mm for citalopram group and 9.1 mm for placebo group; $P < 0.01$).

At the evaluation of week 2, CGI-I scores were 4.00 ± 0.71 and 4.77 ± 1.09 points in group I and II, compared with 1.38 ± 0.51 and 4.08 ± 1.04 points at the last assessment in group I and II, respectively. Group I separated from group II at the evaluation of week 2 on the CGI-I scale ($P < 0.05$). According to CGI-I, of group I patients, five (38.5%) were considered as very much improved and four (30.8) much improved. Only one of group II patients (7.7%) showed much improved by CGI-I. There was a statistically significant difference between the treatment groups with respect to the treatment response, as determining by CGI-I ($P < 0.0001$) (Table 1).

One patient with MDD and one patient with OCD were randomly assigned to group I. The HDRS score of depressive patient was 30 at the baseline, 28 at the week 2 evaluation. 26 at the week 4 evaluation and 18 at the last assessment. The Y-BOCS score of the patient with OCD was 29 at the baseline, 27 at the week 2 evaluation, 18 at the week 4 evaluation and 12 at the last assessment.

Three patients from group I complained from headache and nausea and one patient from group II experienced sweating. It is worth noting that no patient withdrew from each treatment group because of adverse events.

Discussion

The main findings of our study are as follows: (1) Citalopram is more efficacious than placebo in the treatment of premature ejaculation, (2) the onset of the therapeutic effect seems to occur with citalopram by week 2, (3) citalopram provides also significant improvements on the overall sexual functions of the patients with the premature ejaculation, as determining by YSFI-II scale.

The inhibitory effect of serotonin on libido, ejaculation and orgasm has been attributed to serotonin-induced decrease in dopamine (a neurotransmitter enhancing sexual function) level in central nervous system.[17,18] Methylene-dioxymetamphetamine induces serotonin and dopamin release with the central action, and causes increase in libido and sexual satisfaction by dopamin release, while causes delay and prominent inhibition in the ejaculation and orgasm by serotonin activation.[19] Actually, the effect of serotonin in the development of premature ejaculation and other sexual dysfunctions was hypothesized based on the observations that imipramine had more significant sexual dysfunctions compared to the desipramine, and antidepressant-induced orgasm inhibition could be reversed by a non-selective serotonin antagonist, cyproheptadine.[12,20]

Selective or non-selective serotonin reuptake inhibitors have been demonstrated to be effective for the treatment of premature ejaculation.[5–7,21] Girgis *et al*[21] reported that clomipramine, a non-selective serotonin reuptake inhibitor, in low doses was effective in the treatment of premature ejaculation, though high doses could limit its use because of adverse events. In addition, the efficacy of fluoxetine[6] and paroxetine,[5] SSRIs, has been shown in the patients with the premature ejaculation. **In the present study, the intravaginal ejaculation latency time changed considerably in 69.3% of 13 patients in citalopram treated group, as also supported by CGI-I. Another important finding of**

the present study is that significant improvements in all subscales of YSFI-II scale have been seen in group I compared to group II, suggesting that the overall sexual functions of patients with the premature ejaculation including sexual desire and partner's satisfaction have improved. In two patients with comorbid MDD and OCD, the significant improvement in the intravaginal ejaculation latency time, despite not in depressive and obsessive-compulsive symptoms, within two weeks of the treatment is considered that this situation may be associated with the direct effect of the central serotonin reuptake blockage of citalopram, the most selective reuptake inhibitor among all SSRIs.[9] Although the clinical improvement in MDD and OCD generally results in the improvement of related sexual dysfunctions, this generally appears within after at least three or four weeks of treatment with SSRIs. On the other hand, one can speculate that less dose of citalopram might be enough to postpone ejaculation since more than two third of the patients given citalopram was receiving 20 mg daily at the last assessment.

In summary, our results suggest that citalopram may be effective in treatment of the premature ejaculation with mild side effects. However, further investigations with large sample in which long-term effectivity of this drug is taken into consideration are required.

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