

Salvage Use of Citalopram for Treatment of Fluoxetine-Resistant Premature Ejaculation in Recently Married Men

A Prospective Clinical Trial

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Introduction: A wide variety of therapeutic modalities have been tried for treatment of premature ejaculation. Selective serotonin reuptake inhibitors are from the latest and most effective medical agents. Among these drugs, fluoxetine hydrochloride has been used for some years in our institutions with considerable drug untoward effects and significant failure rates. We tried to salvage treatment process by using citalopram in fluoxetine-resistant patients.

Materials and Methods: In a prospective clinical trial, we used citalopram hydrobromide as a salvage agent in 16 newly married men with premature ejaculation who experienced a history of unsuccessful treatment with fluoxetine hydrochloride. Intravaginal ejaculation latency time (IVELT) was recorded by a stopwatch before and after the treatment, and a 5-stage visual scale was designed and used to compare patients' sexual satisfaction levels during the 1-month treatment period.

Results: The IVELT and sexual satisfaction levels both significantly improved after citalopram prescription. The mean measured IVELT was 0.388 ± 0.212 minutes before the treatment, which increased to 4.313 ± 2.886 minutes after the treatment. The reported drug untoward effects were mild. Citalopram was ineffective only in 1 patient, which was discontinued after 4 weeks.

Conclusion: Our study showed that citalopram is effective and safe in the treatment of premature ejaculation in newly married men after failed treatment with fluoxetine.

Keywords: ejaculation, serotonin uptake inhibitors, sexual dysfunction, male

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INTRODUCTION

Premature ejaculation (PE) has been defined as "ejaculation before or very soon after the beginning of intercourse."⁽¹⁾ Others have stated an ejaculation time of 2 minutes after vaginal intromission as a definition of normal intravaginal ejaculation latency time (IVELT).⁽²⁾ Premature ejaculation in recently married men has been reported

by many authors. Lack of sexual experience and performance stress have been presumed as the contributing factors of temporary PE in newly married men.⁽³⁾ Probably due to cultural differences and earlier sexual activity, PE in newly married men may be less frequent in western countries.⁽⁴⁾ During the past decades and based on different theories, multiple

therapeutic modalities have been used to treat this annoying disorder, including pharmacologic therapy and intercourse maneuvers like “stop-start method.”^(5,6) During the recent years, new detailed studies on the pathophysiology of PE have been carried out,⁽³⁾ and a more precise treatment strategy based on a better defined neurohormonal explanation has been introduced to lengthen the IVELT through affecting cerebral serotonin reuptake system.⁽⁷⁾

A relatively common drug in selective serotonin reuptake inhibitors (SSRIs) family, fluoxetine hydrochloride, has been used for a decade by urologists with a remarkable efficacy and of course a relatively severe side effects profile.⁽⁸⁾ Considering the relatively high incidence of PE in recently married men in our region and considerable failure rate and drug untoward effects of fluoxetine treatment in these patients, more research is warranted to evaluate alternative therapeutic agents with better safety margin and/or more efficacy.

Citalopram hydrobromide, another agent of the SSRIs family, has been introduced as an antidepressant, which has proved its efficacy during clinical use as an ejaculation retarder agent. Also, due to less drug untoward effects and better tolerance of citalopram in patients with depression,^(9,10) we hypothesized that it could be a better tolerated drug for treatment of PE, as well. Thus, we designed a prospective clinical trial on citalopram as a salvage agent in newly married men with a history of PE who failed to respond to fluoxetine hydrochloride. We evaluated the drug in terms of alterations in IVELT, sexual satisfaction rate, and adverse effects.

MATERIALS AND METHODS

During a 2-year period from December 2006 till October 2008, we selected a total of 16 newly married potent men being married for less than 1 year through direct clinical interviews. They all had a chief complaint of primary PE and a history of failed treatment with fluoxetine hydrochloride. Our inclusion and exclusion criteria are shown in Table 1.

All of the patients underwent a full medical

Table 1. Inclusion and Exclusion Criteria

Patient Selection Criteria	
Inclusion	
	Age between 20 and 35 years
	Married for the first time for less than 1 year
	History of primary premature ejaculation
	Intravaginal ejaculation latency time less than 1 minute
	History of fluoxetine use for premature ejaculation for at least 1 month with a dose of at least 10 mg, twice a day, with unsatisfactory results
	History of no prescribed drug use for at least 1 month
Exclusion	
	Past history of psychological problems
	Any past history of long-term medical treatment
	History of diabetes mellitus or smoking
	Drug noncompliance
	History of impotency
	History of marital conflicts
	Past history of pelvic or central nervous system trauma, fracture, or operations

interview and physical examination. After filling a detailed informed consent form, they were enrolled in the study. Primarily, the mean IVELT was recorded by the patients using a stopwatch technique after detailed training during a 2-week period with at least 3 consecutive sexual intercourse sessions. In addition, a 5-stage analogue scale was designed to check and record the level of sexual satisfaction after each intercourse (Table 2). Furthermore, the patients were asked to record their sexual satisfaction level precisely before and after drug administration. An IVELT of less than 1 minute after at least a 4-week period of treatment with fluoxetine hydrochloride was presumed as an unsatisfying result and fluoxetine failure.

Citalopram hydrobromide (Pharma Chemie Co, Tehran, Iran) was prescribed for all of the patients with a primary dosage of 20 mg every night. Then, the patients were asked to write down their IVELT and sexual satisfaction level after each sexual encounter. All of the patients were

Table 2. Sexual Satisfaction Analogue Visual Scale

Score	Condition
4	Very satisfied with present sexual activities
3	Moderately satisfied with present sexual activities
2	Sexual satisfaction is not good
1	Often unsatisfied with present level of sexual activity
0	Unsatisfied at all

visited by the researchers 2 weeks later and the changes in the IVELT, sexual satisfaction level, and drug complications were recorded. A second visit of the patients was planned for 2 weeks later, and treatment continued for at least 6 months by the same dose if it was reported as successful by the patients. In 3 patients, we doubled the primary dose due to unsatisfactory results and in 1, we discontinued it after 4 weeks due to ineffectiveness. The latter patient later reported severe interpersonal and marital problems with his partner.

The final results after 4 weeks of treatment were recorded and analyzed using the SPSS software (Statistical Package for the Social Sciences, version 14.0, SPSS Inc, Chicago, Illinois, USA). We used the nonparametric Wilcoxon signed rank test to compare IVELTs and sexual satisfaction scores of each patient before and after the treatment. *P* values less than .05 were considered significant.

RESULTS

The measured IVELT and sexual satisfaction level results before and after the 1-month treatment with citalopram hydrobromide in newly married patients with PE and fluoxetine resistance are listed in Table 3.

The median age of the patients was 28.5 years and the mean calculated IVELT was 0.388 ± 0.212

minutes before the treatment, which increased to 4.313 ± 2.886 minutes after the treatment. The mean calculated primary sexual satisfaction level was 0.63 ± 0.81 which rose to a mean of 3.75 ± 1.44 after treatment, both of these findings were statistically significant (*P* = .001). The observed adverse effects were dizziness, dry mouth, and lowered libido which were reported in 7 patients (43%), but they did not lead to discontinuation of treatment in none of the patients. One of the participants reported no satisfaction with citalopram and his IVELT remained unchanged after 4 weeks of drug administration. We considered him a case of drug failure and discontinued the drug. On the final assessment after 4 weeks of treatment, 15 patients (93.75%) were treated successfully with citalopram after fluoxetine failure.

DISCUSSION

Premature ejaculation is a worldwide sexual disorder that may be seen by every urologist in a daily basis. It has a strong negative impact on patients' self-esteem, sexual satisfaction, and libido and may be a major factor in marital sex conflicts.⁽⁸⁾ Some theories have been proposed to define the cause of PE; two more widely accepted theories which may explain the occurrence of fast uncontrolled ejaculation are penile hypersensitivity and 5-hydroxytryptamine

Table 3. Characteristics of Patients With Premature Ejaculation, Outcome of Treatment With Citalopram, and Complications

Patient	Age, y	Intravaginal Ejaculation Latency Time		Drug dose, mg	Sexual Satisfaction Score		Complications
		Before Treatment	After Treatment		Before Treatment	After Treatment	
1	28	0.3 to 0.5	5 to 6	20	1	5	Dizziness
2	25	0.5	4	20	0	5	No
3	32	0.3	4	20	1	4	No
4	20	0.1	7 to 8	20	1	5	No
5	22	0.5	4	20	1	4	Dizziness
6	27	0.1	2 to 5	40	0	4	Dizziness
7	29	< 0.1	2 to 5	40	0	5	No
8	32	< 0.1	10	20	0	4	Dry mouth
9	35	0.6	0.5	20	2	1	No
10	30	0.6	> 10	20	2	5	No
11	27	0.3 to 0.5	1 to 2	20	2	3	Dizziness
12	29	< 0.1	5 to 10	20	0	3	Low libido
13	32	0.5	4	40	0	4	No
14	31	0.6	0.5	40	0	0	Dry mouth
15	23	0.6	5	20	0	4	No
16	24	0.5 to 0.6	5	20	0	4	No

receptor sensitivity.⁽⁷⁾ The first theory proposes that men with PE have a hypersensitive penis,⁽¹¹⁾ lower penile vibration perception threshold, and shorter somatosensory evoked potential latency times in the glans and penile shaft.⁽¹²⁾ The second theory proposes that disorders in 5-hydroxytryptamine type c receptors in the hypothalamus and brain medulla will facilitate ejaculation and may directly lead to PE, and pharmaceutical agents with potent effects on these receptors may be able to affect ejaculation latency time.⁽¹³⁾

A vast array of different therapeutic modalities has been used for treatment of PE. Psychological/behavioral treatment has been advocated by Masters and Johnson and used for years by psychologists and sex therapists with varying results.⁽⁶⁾ Other therapeutic means such as extracorporeal functional magnetic stimulation have been discussed by Morales and coworkers in 2009 which showed to be as efficacious as SSRIs.⁽¹⁰⁾ Injection of hyaluronic acid in the penis glans by Kwak and colleagues in 2008 showed also a moderate long-term positive effect,⁽¹⁴⁾ and also, acupuncture was reported by Chen in 2009 to be of variable effects.⁽¹⁵⁾ In another study, Shi and associates performed selective dorsal penile nerve resection in 2008 to control PE and introduced it as a safe and effective measure.⁽¹⁶⁾

Pharmacotherapy for PE has also a long history. In the recent years and after better understanding of erection and ejaculation physiology, pharmacologic agents have been selected as the first treatment modalities.⁽¹⁷⁾ Among pharmaceutical agents which have been suggested to treat this disorder, the SSRIs family which includes fluoxetine, fluvoxamine, paroxetine, sertraline, and citalopram, have been used in many clinical studies during the past decade and proved their propensity to delay ejaculation.⁽¹⁸⁾ This drug family, being used as antidepressants, can activate 5-hydroxytryptamine type c receptors, adjust ejaculatory threshold set point, and delay ejaculation.⁽¹⁹⁾ As their prototype, fluoxetine has been used extensively by urologists to treat PE in the recent years. Unfortunately, some drug reactions such as intolerable fatigue or dizziness have been reported by many patients

as reasons to discontinue treatment. Drug ineffectiveness has also been reported by other patients which had the therapists search for better tolerable and more effective therapeutic agents.⁽²⁰⁾ Another member of the SSRIs family, citalopram, has shown less frequent adverse effects and more considerable ejaculation retarding ability,⁽⁹⁾ and has been used as an effective agent in men with PE. Another agent in the SSRIs family, dapoxetine, which has a short acting time and less untoward effects, has been introduced recently by Hellstrom.⁽²¹⁾ Dapoxetine showed a good ejaculation retardation activity. In addition, it can be used in an as-needed manner and is awaiting more detailed studies now.

In our study, we tried citalopram as a salvage agent in young newly married men resistant to fluoxetine, and according to the results, we achieved a statistically significant therapeutic effect in this difficult group of patients. The stopwatch time measurement of the IVELT recorded a considerable ejaculation retardation effect, a mean improvement of more than 4 minutes. Sexual satisfaction level also increased with a mean increase of 3 units. In addition, we did not detect any significant clinical adverse effects with this drug regimen. In another placebo-controlled study by Safarinejad and Hosseini in 2006, beneficial effects of citalopram and little side effects were reported.⁽²²⁾ In a study carried out by Atmaca and colleagues, similar results were acquired.⁽²³⁾ All these studies were conducted in potent middle-aged men and all showed an increase in sexual satisfaction and performance after drug administration. In our literature search, we could not find any studies on the use of citalopram after a failed treatment with fluoxetine, and it seems that this drug can be used as a salvage agent in this group of men.

CONCLUSION

In this prospective clinical trial, we used citalopram as a salvage agent to treat PE in newly married men with a history of fluoxetine resistance. According to our results, after 4 weeks of continuous drug administration, IVELT and sexual satisfaction both improved significantly. Citalopram had some mild untoward effects,

and nearly all patients were satisfied with this treatment. Therefore, it seems that this agent can be used as a powerful choice to treat patients with PE, especially in newly married men in whom other medical therapies have failed.

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CONFLICT OF INTEREST

None declared.

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