J Anal Res Clin Med, 2016, 4(4), 221-7.
doi: 10.15171/jarcm.2016.037, *http://journals.tbzmed.ac.ir/JARCM*

Original Article

Comparison of citalopram and fluoxetine sexual side-effects in male patients referred to psychiatric clinic

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Article info
Article History:
Received: 24 Jul 2016
Accepted: 15 Oct 2016
ePublished: 24 Dec 2016

Keywords:
Sexual Side-Effects,
Fluoxetine,
Citalopram,
International Index of Erectile Function (IIEF) Questionnaire

Abstract
Introduction: Selective serotonin reuptake inhibitors (SSRIs) are among the selected medication to treat depression, panic disorder and many other psychiatric disorders. The most common undesirable effects of SSRIs are sexual dysfunctions that may lead to discontinuation of treatment in some patients. This study was conducted to compare sexual side-effects of two common drugs, citalopram and fluoxetine in male patients.
Methods: This cross-sectional study was carried out on 60 male patients referred to the psychiatric clinics of Tabriz University of Medical Sciences, Iran, in 2013. They were candidates for SSRIs treatment and the clinic physicians prescribed citalopram or fluoxetine for them. The patients were examined in two groups after taking written informed consent and initial completion of the International Index of Erectile Function (IIEF) questionnaire and no history of sexual dysfunction, considering the inclusion and exclusion criteria. Both citalopram and fluoxetine groups completed IIEF questionnaire again at the end of the first and second months after treatment and statistical analysis was done using SPSS.
Results: Sexual dysfunction was observed in both groups in the all sexual function indices and its components. Although there was no significant difference in terms of sexual function components between the two groups, general sexual dysfunction was significantly higher in the fluoxetine group. In both groups, age was inversely related to the general sexual function index.
Conclusion: Unlike many other studies suggesting no difference on SSRI sexual side-effects, the present study showed a reduction in sexual function of men taking citalopram and fluoxetine and the reduction was more prominent with fluoxetine.

Citation: Herizchi S, Mogaddam A. **Comparison of citalopram and fluoxetine sexual side-effects in male patients referred to psychiatric clinic.** J Anal Res Clin Med 2016; 4(4): 221-7. Doi: 10.15171/jarcm.2016.037

Introduction

Sexual relationship is among the essential elements in marital relationship that offers the individual the sense of physical and psychological and social desirability. Normal sexual function of men requires interaction of vascular, neurologic, hormonal and physiological systems. The first necessary step for sexual activity in men is starting and maintaining the erection of the penis which is the first vascular event and its three main factors are arisen by neurological signals.

The main three forms of male sexual dysfunction include erectile dysfunction, decreased libido, and ejaculation dysfunction.[1]

Mechanisms responsible for sexual dysfunction in men include:

1. Decreased libido which can be related to reduced androgen,[2] depression and taking certain medications.[3]

2. Erectile dysfunction which may reflect inadequate arterial blood flow (failure to fill) or accelerated venous drainage caused by lack of storage in corpora cavernous of the penis.

3. Ejaculation disorders. Sexual disorders in men and women may be the result of physiological and psychological factors, hormonal abnormalities, autonomic

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neuropathy, vascular disease or drug side-effects. It is reported that among the drugs, serotonin reuptake inhibitors (SSRIs) reduce libido in men and women and lead to orgasm disorders in women and ejaculation delay in men.[4-7]

It is estimated that more than 50% of individuals taking fluoxetine develop sexual dysfunction.[8] The prevalence of adverse effects on sexual function with other SSRIs is not so clear, however, based on clinical experience, all SSRIs tend to cause sexual side-effects.[9]

Both autonomic nerves are involved in male sexual stages: the parasympathetic nervous system in erection and the sympathetic nervous system in the ejaculation.[10]

SSRIs h inhibit specific selective serotonin reuptake by common presynaptic neurons and have relatively little effect on the reuptake of norepinephrine and are almost ineffective in the reabsorption of dopamine. SSRIs are selected drugs to treat depression, obsessive-compulsive disorder and panic disorder and many other disorders. The most famous of these drugs is fluoxetine introduced in 1988 and since then it has been the most common antidepressants prescribed worldwide. Subsequently, sertraline, paroxetine, fluvoxamine and citalopram have been used. Although the drugs were initially used to treat depressive disorder, they have been effective on a broad spectrum of eating disorders, panic disorder and other anxiety disorders, borderline personal disorder and obsessive-compulsive disorder.[11] However, some unwanted side-effects of this group include gastrointestinal adverse effects such as constipation, nausea, weight gain, headaches, insomnia or drowsiness and sexual dysfunction. The most common unpleasant effect of SSRIs is sexual dysfunction and its incidence is 50 to 80 percent, all SSRIs seem to be associated with the risk of developing sexual dysfunction. Inhibition of orgasm and decreased libido are the most common complaints that are dose-dependent. Unlike most undesirable effects of SSRIs, sexual dysfunction does not subside in the first few weeks of taking drugs, and usually continues. The treatment of sexual dysfunction caused by SSRIs include reducing the dose, switching to bupropion or nefazodone, which provides less sexual dysfunction.[11]

Since sexual relation is one of the necessities in human relationships, these side-effects may lead to discontinuation of therapy and treatment in some patients.

Citalopram and fluoxetine are two of the most commonly used drugs in Iran. In the present study, the researchers have attempted to evaluate and compare the incidence of sexual side-effects of these drugs.

Methods

This cross-sectional study was carried out on 60 male patients referred to Razi psychiatric clinics and Sheykh Al Raeis clinic, Tabriz, Iran, to treat the underlying depressive disorder in 2013. They were candidates for SSRIs treatment and the clinic physicians prescribed citalopram or fluoxetine for them.

Inclusion criteria were as follows: age between 18-60, married and having sexual intercourse at least once a week, having sex satisfaction for the time being.

Exclusion criteria were as follows: history of severe illness such as kidney, liver or heart failure, systemic and neurological disorders such as multiple sclerosis, history of sexual dysfunction before the study, severe mental disorders, addiction or drug abuse or any psychiatric drugs such as antidepressants, amphetamine, alcoholic or alcohol abuse and a history of infectious or anatomic genital disease.

All patients underwent psychiatric interview and physical examination at the beginning of the study and laboratory tests were done, if necessary. The patients were studied in two groups after obtaining written informed consent and completing the initial International Index of Erectile Function (IIEF) questionnaire,

1. The first group treated with fluoxetine 20 mg dose
2. The second group treated with citalopram 20 mg dose

Table 1. Age of participants

	Group	Mean ± SD	Max	Min	Numbers
Age (year)	Fluoxetine	35.73 ± 9.07	50	20	30
	Citalopram	34.67 ± 7.99	47	22	30

SD: Standard deviation

During the two months in which patients were studied, they filled questionnaires at the first and second months and sexual side-effects in this study were defined two months after starting the treatment.

IIEF questionnaire

The test is designed to evaluate erectile function; however, it is also used to assess other dysfunctions due to its comprehensiveness. The tool is used to evaluate ejaculation through a few items that actually examine orgasm function. Brevity, reliability and validity are some characteristics of the tool. It has15 questions that examine five domains of male sexual functions including erectile function, orgasm, sexual desire, intercourse satisfaction and generally sexual satisfaction. The questionnaire was approved by FDA for clinical trials as an alternative in situations where overwhelming and interventional tools are required to measure the stiffness of the penis. In addition, Rosen et al.[8] showed that in the study of male sexual dysfunction, IIEF questionnaire is a sensitive and specific tool and its validity has been confirmed in several languages and is the most widely used of its kind.[12]

Descriptive statistics, chi-square and paired t-test were used for data analysis using SPSS (version 20, SPSS Inc., Chicago, IL, USA). Mean values are reported based on the mean ± standard deviation (SD) and $P < 0.05$ is considered significant.

Results

Age Descriptive Indicators: based on table 1, age was calculated by mean, median, SD, variance, minimum and maximum.

Kolmogorov-Smirnov test was used to study the normal score distribution of variables. Based on the results, sexual function variables and sexual function changes were normally distributed ($P < 0.050$). However, sexual function components were not normally distributed ($P > 0.050$).

1. Hypothesis 1: treatment with citalopram does not cause sexual dysfunction in men.

Paired t-test was used to test this hypothesis. Mean sexual function before and after treatment were 19.43 and 15.70 respectively and the difference was significant ($P = 0.001$). As a result, sexual function was significantly decreased after treatment. This means that citalopram caused sexual dysfunction in men (Table 2).

Wilcoxon test was used to study the effects of citalopram treatment on sexual function components. Wilcoxon test results showed that the erection, satisfaction, libido and ejaculation significantly decreased after treatment ($P = 0.050$ and Z is negative) (Table 3).

2. Hypothesis 2: treatment with fluoxetine does not cause sexual dysfunction in men.

Paired t-test was used to test this hypothesis. Mean sexual function before and after treatment were 19.73 and 13.03 respectively and the difference was significant ($P < 0.001$). This means that fluoxetine caused sexual dysfunction in men (Table 4).

Wilcoxon test was used to study the effects of fluoxetine treatment on sexual

Table 2. The results of paired t-test to compare sexual function before and after treatment in the citalopram treatment group

Variable	Time	Number	Mean ± SD	t	df	P
Sexual function	Before treatment	30	19.43 ± 1.75	15.916	29	0.001
	After treatment	30	15.70 ± 1.82			

SD: Standard deviation; df: Degree of freedom

Table 3. Results of the Wilcoxon test to compare the components of sexual function before and after treatment in the citalopram treatment group

Components of sexual function	Rank	N	Mean	Sum of ranks	Z	P
Erectile function	Positive rank	0	0	0	-3.742	< 0.001
	Negative rank	14	7.50	105		
	Ties	16				
Intercourse satisfaction	Positive rank	0	0	0	-4.244	< 0.001
	Negative rank	22	11.50	253		
	Ties	8				
Sexual desire	Positive rank	0	0	0	-4.669	< 0.001
	Negative rank	24	12.50	300		
	Ties	6				
Orgasm	Positive rank	0	0	0	-4.532	< 0.001
	Negative rank	25	13.00	325		
	Ties	5		-		

function components. Wilcoxon test results showed that the erection, satisfaction, libido and ejaculation significantly decreased after treatment (P = 0.050 and Z is negative) (Table 5).

3. Hypothesis 3. The effect of fluoxetine and citalopram on male sexual behavior is the same.

Independent t-test was used to test this hypothesis.

The mean of sexual function changes in citalopram and fluoxetine groups were -3.73 and -6.7 respectively and P = 0.001. Thus it could be concluded the decline in sexual function in the fluoxetine treatment group was significantly higher than citalopram treatment group (Table 6).

Mann-Whitney test was used to study the effects of fluoxetine and citalopram on sexual function components. Mann-Whitney test results showed that changes in sexual function components in the citalopram and fluoxetine treatment group were not significantly different (P > 0.050) (Table 7).

4. Examining the relationship between age and sexual function

Pearson correlation test was used to examine the relationship between age and sexual function. Pearson correlation coefficient was -0.546 and P = 0.001. This means that there was a significant inverse relationship between age and sexual function in men and sexual function decreases with aging (Table 8).

Table 4. The results of paired t-test to compare sexual function before and after treatment in the fluoxetine treatment group

Variable	Time	Number	Mean ± SD	t	df	P
Sexual function	Before treatment	30	19.73 ± 1.68	22.927	29	< 0.001
	After treatment	30	13.03 ± 2.59			

SD: Standard deviation; df: Degree of freedom

Table 5. Results of the Wilcoxon test to compare the components of sexual function before and after treatment in the fluoxetine treatment group

Components of sexual function	Rank	N	Mean of rank	Sum of ranks	Z	P
Erectile function	Positive rank	3	10.50	31.50	-3.644	< 0.001
	Negative rank	21	12.79	268.50		
	Ties	6				
Intercourse satisfaction	Positive rank	0	0	0	-4.485	< 0.001
	Negative rank	24	12.50	300.00		
	Ties	6				
Sexual desire	Positive rank	0	0	0	-4.354	< 0.001
	Negative rank	22	11.50	253.00		
	Ties	8				
Orgasm	Positive rank	0	0	0	-4.416	< 0.001
	Negative rank	23	12.00	276.00		
	Ties	7				

Table 6. Independent t-test to compare sexual function before and after treatment in the citalopram and fluoxetine treatment groups

Dependent variable	Group	N	Mean ± SD	t	df	P
Sexual function changes	Citalopram	30	-3.73 ± 1.28	7.917	58	< 0.001
	Fluoxetine	30	-6.70 ± 1.60			

SD: Standard deviation; df: Degree of freedom

Table 7. The results of Mann-Whitney test to compare sexual function before and after treatment in the fluoxetine and citalopram treatment groups

Changes in Components of sexual function	Group	N	Mean of rank	Sum of ranks	Mann-Whitney	Z	P
Changes in erectile function	Citalopram	30	34.13	1024.00	341.0	-1.788	0.074
	Fluoxetine	30	26.87	806.00			
Changes in intercourse satisfaction	Citalopram	30	30.62	918.50	446.5	-0.056	0.955
	Fluoxetine	30	30.38	911.50			
Changes in sexual desire	Citalopram	30	30.40	912.00	447.0	-0.052	0.959
	Fluoxetine	30	30.60	918.00			
Changes in orgasm	Citalopram	30	28.60	858.00	393.0	-0.933	0.351
	Fluoxetine	30	32.40	972.00			

Table 8. Comparing Global rate of sexual function side effects in the fluoxetine and citalopram

Sexual function	Citalopram (%)	Fluoxetine (%)
Decrease in total Sexual function	66	80
Decrease in Erectile function	83	70
Decrease in intercourse satisfaction	73	80
Decrease in sexual desire	80	73
Decrease in orgasm	83	76

Discussion

Sixty patients with depression were enrolled in this study, 30 were treated with fluoxetine (20 mg) and 30 with. In this section, we compare the results with similar studies conducted by different researchers and published in authoritative psychiatry sources and journals.

In their study, Safa et al. reported 71% decline in sexual function in the citalopram group and 100% in fluoxetine group.[13]

In another study conducted by Arias et al. on sexual dysfunction in patients using SSRIs, it was reported that about 62.6 percent of patients had major sexual dysfunction (such as libido, orgasm, arousal), of which 39% pertained to fluoxetine and 28.9% pertained to citalopram.[14]

In another study conducted by Lee et al. sexual dysfunction in SSRIs recipients was as follow: citalopram 60.0%, venlafaxine 54.5%, paroxetine 54.2%, fluoxetine 46.2%.[15] Gregorian et al. reviewed 200 articles in English on the sexual dysfunction in users of anti-depressions such as fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, venlafaxine, nefazodone, bupropion, mirtazapine in published between 1986 and 2000, and reported that sexual dysfunction was a common side-effect of antidepressant treatment. Studies showed that 31% to 65% of patients treated with SSRIs believed that some forms of major sexual dysfunctions were due to the treatment.[16]

Montejo-Gonzalez et al. indicated that of the total population under only one SSRI treatment 36%-46% (both male and female) had sexual dysfunction and SSRI treatment caused sexual dysfunction 4 to 6 times more compared to patients treated by bupropion.[9]

In a systematic review on SSRIs as the first line treatment, Anderson and Edwards reported no difference in sexual dysfunction in the patients taking citalopram, fluoxetine, fluvoxamine and sertraline.[17]

In our study, sexual function significantly decreased after treatment with citalopram. Also the results showed that erection, satisfaction, libido and ejaculation decreased significantly after treatment with citalopram.

In our study sexual function significantly decreased after treatment with fluoxetine. Also erection, satisfaction, libido and

ejaculation decreased significantly after treatment with fluoxetine.

Conclusion

The results of our study indicated that in general, fluoxetine can cause sexual dysfunction more than citalopram. However, no significant difference was seen in the sexual function components (erection, satisfaction, libido and ejaculation) between fluoxetine and citalopram (Pearson correlation coefficient = -0.546 and P = 0.001).

Recommendations

Given the role of sexual function in individual life, satisfaction and self-confidence and the effect of SSRIs (fluoxetine and citalopram) in reducing sexual function, it is recommended to use citalopram that has less effect on sexual function decrease, in case SSRIs are selected for treatment.

Due to great differences in the results of various studies on the effect of SSRIs on sexual function decline, case studies and also studies with more patients in the long run are recommended.

Acknowledgments

Authors appreciate participants for their kind cooperation.

Authors' Contribution

Sepideh Herizchi, supervised, designed the research, and wrote the article and Akbar Mogaddam, gathered and analyzed the data as a thesis for MD. degree.

Funding

In this Research, there was not any financial support.

Conflict of Interest

Authors have no conflict of interest.

Ethic Approval

As there was not any intervention by researcher and drugs were prescribed by the clinicians own selves, only informed consent by the patients was considered.

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