Relation between Fluoxetine and Menstrual Cycle Disorders

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Abstract

Objective: To investigate the effect of fluoxetine as an SSRI on menstrual disorders.

Materials and methods: In this cross-sectional study 200 women referring to the Islamic Azad University affiliated hospitals during March 2011- March 2010 were divided into 4 groups. All included patients in this study had the chief complaint of mood disorders in peri- menstrual period. All patients received daily vitamin B6 tablets as primitive treatment. In groups A, B and C patients also received daily doses of 10 mg, 20 mg and 40 mg of fluoxetine respectively for 6 months and in group D as the control group fluoxetine was not given. Data were analyzed by spss18 statistical software. Significant difference was set at $p<0.05$.

Results: In the groups receiving fluoxetine (groups A - C) 34 patients and in control group 5 patients showed irregular menstruation started during fluoxetine administration and following 3 months. Significant difference with $p<0.05$ was found regarding the incidence of menstrual irregularity between groups with and without fluoxetine prescription.

Conclusion: Fluoxetine consumption leads to increased incidence of menstrual irregularity compared to the control group. The incidence increases with increasing dosage of the drug.

Keywords: Fluoxetine, SSRI, Menstrual Cycle disorders

Introduction

Fluoxetine is an anti-depressant of the selective serotonin reuptake inhibitor (SSRI) class and Propylamin cyclic derivatives. As a drug used in treating obsession, bulimia, stressand depression, often limited side effects and high tolerability, have been reported by most studies (1). Anti-depressant activity of this drug is gained through inhibiting the uptake of serotonin (5HT) in neurons of the central nervous system (1). In addition, the drug has a weak effect on the uptake of norepinephrine and dopamine (2-4). Due to limited cases of fluoxetine contraindications mostly it is highly regarded as treatment of choice for relating complaints in clinical researches (5). It is also used in treatment of

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premenstrual syndrome (PMS), premenstrual mood disorders and depression in women during the menstrual cycles (4, 5). Studies also suggest that it is a good alternative for the treatment of hot flashes and symptoms of climacteric period in women who do not want to use hormone therapy (6). Based on studies comparing fluoxetine side effects with tricyclic antidepressants (TCA) the drug has relatively low complications (6, 7). Fluoxetine is an antidepressant that is approved for use in children (8). However, some studies have shown that taking the fluoxetine with impact on cytochrome P450 and related enzymes can lead to changes in the serum levels of estrogen and may cause menstrual abnormalities. Generally a regular menstrual period results of regular hormonal feedback of the hypothalamus, pituitary, ovary and endometrial target. Hormonal changes can disturb the regular menstrual cycle and may lead to menstrual disorders (9). It is shown that the menstrual cycles have the highest regularity in women aged 20 to 40 (8, 9). In previous studies most mentioned disorders included oligomenorrhea, polymenorrhea and menorrhagia (7-10). The differential diagnosis of these disorders, depends on several indices including the patient's age and therefore may need different therapies. Menstrual disorders for women at different stages of life creates different problems and may affect their performance, mood, memory, sleep and general abilities (9, 10). In some cases it may prevent patients from presence in public places and reduces their job capabilities, satisfaction and quality of life. Considering the importance and the few studies performed in this field in Iran, the aim of this study is evaluation of relation between fluoxetine and menstrual disorders.

Materials and methods

This study was a cross-sectional study with random sampling performed on 200 women with the chief complaint of mood disorders in peri- menstrual period referred to the Islamic Azad University affiliated hospitals including Boo-Ali, Javaheri and Amir-al-Momenin in Tehran, Iran from March 2010 to March 2011. The study was approved in the research committee of Azad University. For data collection, a questionnaire was used. In the questionnaire, patients' characteristics including personal and demographic information such as menstrual changes during the past 6 months (dysmenorrhea, timing and duration of bleeding and spotting), age, marital status, weight, height and education level, were asked (Table 1).

Exclusion criteria included pregnancy, menopause, lactation, hypothyroidism or hyperthyroidism, use of oral contraceptives or injection of depo-provera in past 6 months, prolactin disorder over the recent 6 months, polycystic ovary syndrome confirmed by ultrasonography, diabetes, blood dyscrasia, any other endocrine disorders and kidney or liver failure.

Questionnaires were collected during three consecutive months. From 254 distributed questionnaires 250 were completed. Of these 31 patients did not have inclusion criteria. Nineteen people also were not willing to cooperate in the study. Finally 200 women were consisted in the study and written consent was taken from them for participation in the study. Subjects were examined in four groups of 50 persons. All patients received daily vitamin B6 tablets as primitive treatment. In case groups (A, B and C) patients received doses of 10, 20, 40 mg of fluoxetine respectively for 6 months and group D were controls and did not receive fluoxetine. All women were examined by a gynecologist at beginning of the study. Information about changes in the volume of menstrual bleeding, days of bleeding and other menstrual disorders were recorded. Women with any possible complications arising from the use of fluoxetine were planned to be excluded from

Table 1: Definitions of menstrual disorders

	Distance between the menstrual cycles	The duration of menstrual cycle	The amount of menstrual blood
Menorrhagia	Regular	Long	High
Metrorrhagia	Irregular	Long	Normal
Menometrorrhagia	Irregular	Long	High
Oligomenorrhea	Irregular	Variable	Low
Polymenorrhea	Regular	low	Normal
hypomenorrhea	Regular	Normal or low	Low
Hypermenorrhea	Regular	Normal	High

further participation, but in this study no significant complications were reported by women. Statistical analysis was done using t-test and multi variate regression in SPSS version 18. Significant difference was set at $p<0.05$.

Results

The average age of studied women was 32.8 ± 4.2 years. The average of age in fluoxetine group was 31.2 ± 2.8 years and in control group was 33.4 ± 3.2 years. Studied women reported an age for menarche ranging from 9 to16 years and the average age of menarche was 12.6 ± 1.25 years (table 2).

Totally 35.2% of fluxetine consumers reported improvement, 59% reported no difference and 5.8 reported worsening of their mood situation during or after treatment. In control group 74% reported no difference, 26% reported improvement and nobody reported worsening of mood in the same duration.

Menstrual disorders were reported in 19.3 % of cases and 10% of controls. The most common menstrual regularity disorder in experimental groups was oligomenorrhea (12 %) and in control group was polymenorrhea (4 %). Totally 74.8% of subjects reported mild to severe abdominal pain before and during their menstrual cycle. The average length of cycle in fluoxetine group before entering the study was 28.4 ± 0.32 days and after using the drug was 27.86 ± 0.49 days. The menstrual indices and their frequency are shown in table 3. There was significant association between menstrual cycle length and use of fluoxetine (p= 0.03). Minimum and maximum frequency of menstrual disorders after using fluoxetine were related to 16 years and 13 years of age respectively.

Table 2. Some characteristics of studied women

		Treatment group n (%)	Control group n (%)
Marital Status	Married	118 (78.7)	38 (76)
	Single	23 (15)	8 (16)
	Divorced	5 (3.3)	2 (4)
	Widow	4 (3)	2 (4)
Education	Under Graduates	40 (26.6)	12 (24)
	High school diploma	51 (34)	16 (32)
	University educated	59 (39)	22 (44)
BMI	20 or less	62 (41)	21 (42)
	21 to 25	35 (23)	11 (22)
	26 to 30	46 (30.5)	16 (32)
	31 or more	7(4.6)	2 (4)
Age of menarch	13 years and blow	59 (39)	19 (37)
	14 years to 17 years	89 (59.5)	31 (63)
	18 years and above	2 (1.3)	0

Discussion

Totally 35.2% of fluxetine consumers reported improvement in symptoms of PMS during or after treatment. Miners study in 2002 Showed that the used of 90 mg of fluoxetine can reduce symptoms of PMS (Premenstrual syndrome). Breasley in his study in 2000 observed that 65% of women with PMS respond to treatment with fluoxetine. In addition to the therapeutic effects it also has side effects. The results of this study showed that used fluoxetine had significant relationship with increased menstrual

Table 3. Distribution of Menstrual Cycle Disorders

		group A n (%)	group B n (%)	group C n (%)	P value	Total(A+B+C) n(%)	group D n (%)	P value
Duration of menstrual shedding before starting the study	1 days or below	0(0)	0(0)	0(0)	1	0 (0)	1(2)	0.83
	2 days to 7 days	50 (100)	48(96)	50(100)	0.68	148 (98.6)	49(98)	0.78
	8 days or above	0(0)	2(4)	0(0)	0.72	2 (1.3)	0(0)	0.66
Duration of menstrual shedding after the study.	1 days or below	0 (0)	1(2)	3 (6)	0.34	4 (2.6)	1(2)	0.35
	2 days to 7 days	50 (100)	45 (90)	45 (90)	0. 09	140 (93)	49(98)	0.23
	8 days or above	0 (0)	4 (8)	2 (4)	0.05	6 (12)	0(0)	0.04
Menstrual disorders	Oligomenorrhea	2 (4)	3 (6)	6 (12)	0.03*	11 (7.3)	2 (4)	0.04*
	polymenorrhea	1 (2)	3 (6)	3 (6)	0.05	7 (4.6)	2 (4)	0.07
	Hypomenorrhea	0 (0)	1(2)	1 (2)	0.05	2 (1.3)	0 (0)	0.02*
	Hypermenorrhea	0 (0)	1(2)	3 (6)	0.04*	4 (2.6)	1(2)	0.42
	Menorrhagia	0 (0)	2(4)	1(2)	0.12	3 (2)	0 (0)	0.03*
	Metrorrhagia	0 (0)	1(2)	1(2)	0.18	2 (1.3)	0 (0)	0.04*

*: significant

cycle disorders. According to the findings of this study, the number of days of bleeding is increased in the fluoxetine group. Brambilla observed in a study in 2005 that disorders such as irritability, sleep disorders, agitation, tremor and gastrointestinal disorders such as nausea, vomiting and weight loss on fluoxetine consumers are more frequent than consumers of other SSRI drugs. Few studies are done regarding the effect of fluoxetine on menstrual disorders.The research conducted by Thompson in 2003 Showed that consuming at least 5weeks of fluoxetine resulted in effects on cytochrome P450 and the disorders 16-Alpha-hydroxyestrone : 2-hydroxyestrone and in this way lead to hormonal disorders that can disturb the regularity of menstrual cycle (11,12). In present study also it was shown that irregular menstrual cycles in the fluoxetine group was significantly more than control group. It has been determined that the dosage of fluoxetine is associated with the frequency of irregular menstrual (13). In present study also disruption of menstrual cycles in group A was reported by 3 of 50, in group B by 11 of 50 and in group C by 15 of 50 patients (p= 0.04). Steiner et al in 1997 showed the effect of fluoxetine on menstrual disorders, that use of fluoxetine lead to increased incidence of irregular menstrual cycle in women and it is directly associated with fluoxetine dosage (14). He showed the incidence of irregular menstruation to be 6% in consumers of fluoxetine 20 mg daily and 15% in consumers of 60 mg daily. These results are consistent with the findings of present study.

Conclusions

Considering the findings of this study Fluoxetine consumption leads to increased incidence of menstrual cycle disorders in women compared with the control group. Its incidence increases with increasing dosage of the drug. Further studies on larger groups with longer follow up duration are recommended in order to make more reliable conclusions.

Acknowledgement

There is no conflict of interest to declare.

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