



RANDOMIZED CLINICAL TRIALS (RCTs) STUDY; EFFICACY OF FLUOXETINE IN TREATMENT OF POSTMENOPAUSAL HOT FLASHES

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ABSTRACT

Hot flash is a common problem of women in menopause and post menopause (climacteric). Despite the fact that hormonal treatments are considered as the most effective therapies, they are not used for the treatment of hot flashes, because they may increase the risk of breast cancer and cardiac diseases. Therefore, we aimed the efficacy of Fluoxetine in treatment of postmenopausal hot flashes

A randomized clinical controlled trial was conducted at obstetrics and Gynecology clinic at Razi medical and educational center, Ahvaz, Iran during year 2011. A total of 120 menopause women were participated in this study for 8 weeks follow-up. The subjects were divided into two groups. 60 subjects were selected to treat with fluoxetine (20 mg as one capsule per day), and 60 subject got placebo as control group. Frequency of hot flashes was evaluated during one week, two weeks, four weeks and eight weeks. Data was analyzed using SPSS, version 16. The mean number and severity of hot flashes in fluoxetine group was less than placebo, and showed meaningful difference. The rate of side effects was equal in both groups. Fluoxetine was effective in treatment of hot flashes. It is a cheap and accessible drug, and does not cause the incidence of breast cancer and cardiovascular disease.

Key Words: Fluoxetine, menopause, hot flashes, Iran

INTRODUCTION

Hot flashes are known as symptoms of menopause and are the most prevalent complaints of menopausal women. The most prevalent cause of referring to the therapeutic clinics is postmenopausal hot flashes. About 95-100 percent of women who remove their ovaries due to some causes, 75-80 percent of women who became menopause naturally and 40 percent of women experience hot flashes in the years before menopause. 30% of them report more than ten attacks per day.^{1,2} Waking up of night sleep is usually accompanied by changes in body temperature which cause excitability, fatigue, depression, memorial changes and decrease in concentration, that eventually decrease the ability and disorder the social and personal function¹⁻³. The mechanism of hot flash is not totally known, but neuroendocrine and estrogen play significant role in affecting the central cores of thermoregulation in hypothalamus, and in some studies the absence of balance in cerebral serotonin may affect the incidence of hot flashes.^{1,3,4}

According to some studies, the mean age of menopause in 51.3% years, and regarding the increase of life expectancy women suffer from the menopausal side effects for a considerable duration. Hot flashes in most women may last one to two years.⁵ However, 25% of cases may last up to 5 years.⁴

One of the most prevalent therapies for hot flash is estrogen that treats more than 95% of hot flash attacks. The long duration of hot flashes which may even last for 15 years in 10%, the risk of long term treatment is significant.⁷

Considering the potential side effects of estrogen and restricted usage of hormones in some women such as women with tumor, sensitive to estrogen, function disorders of liver, risk bag, increased blood coagulation, hyperlipidemia, migraine, spasm or acute vascular thrombosis,³ and regarding the fact that estrogen may increase the risk of breast cancer,^{9,10} using alternative treatments is necessary. One of

the alternatives for SSRL (selective serotonin reuptake inhibitors) is fluoxetine. Many studies have been performed regarding the use of this drug on patients with breast cancer.^{11,12}

In a great study, a combined diet consisting of conjugated estrogen and medroxy progesterone acetate were compared with placebo. It was indicated that the combined diet increased the risk of coronary disease, breast cancer, cerebral apoplexy and venous thromboembolism. So, they concluded that it was necessary to find a non-hormonal drug.¹³

In Finland study¹⁴ in 2005 has investigated that there were no statistically significant differences between the groups (citalopram, fluoxetine and placebo) to number of hot flashes.

In the present study, considering the effect of neurotransmitters in the incidence of hot flashes, we examine the efficacy of fluoxetine in the treatment of hot flashes. Some of the factors affecting the selection of this drug are low side effects, accessibility and cheapness.

MATERIALS AND METHODS

A randomized clinical controlled trial was conducted at obstetrics and Gynecology clinic at Razi medical and educational center, Ahvaz, Iran during year 2011. The study was approved by Ahvaz Jundishapur University of Medical Sciences, and Ethics Committee (ε/3-308 -2011). A total of 120 menopause women were participated in this study for 8 weeks follow-up. The subjects were divided into two groups. 60 subjects were selected to treat with fluoxetine (20 mg as one capsule per day), and 60 subject got placebo as control group. Frequency of hot flashes was evaluated during one week, two weeks, four weeks and eight weeks. The standards for entering the study were as follow: consent to participate in the study, menstrual interruption since 6 months ago or more and proved menopause with testing, receiving no hormonal or antidepressant drug blocking calcium canal since two weeks ago, no record of renal and diabetic disease,

affecting hot flashes more than twice a day. From all subjects request to record the number and duration of hot flashes attacks per day.

Hot flashes were categories as below:

- Consider slight hot flashes as 2-3 times a day
- Consider median hot flashes as 4-9 times a day
- Consider severe hot flashes as 9 times

The study was double blinded. Fluoxetine and placebo were coded by a resident, and then they were delivered to the patients by another resident who did not know the drugs. After two weeks, the information about the severity and number of hot flashes were collected and recorded, and it was repeated after four and eight weeks.

Table 1: Mean and standard deviations of demographic groups

	Placebo group	Fluoxetine group	p-value
BMI	29.20 + 3.1	28.99 + 3.4	0.62
Age	52.61 + 3.2	51.06 + 3.4	0.16
Age at menopause	49.33 ±	48 + 2.98	0.49

Table 2: The frequency of hot flashes in postmenopausal women before treatment

	Placebo group	Fluoxetine group
Slight 2-3times per day	15%	14%
Mid 4-5 times per day	38%	35.50%
Sever ≥10 times per day	47%	50.50%

Table 3: The frequency of hot flashes in postmenopausal women after treatment

	Placebo group	Fluoxetine group	p-value
Slight 2-3times per day	10%	12%	0.12
Mid 4-5 times per day	52%	23.50%	0.009
Sever <10 times per day	38%	28.00%	0.039
without hot flash	0	37%	<0.0001

RESULTS:

The personal characteristics of the research units have been indicated in table 1.

In Placebo group, the mean duration of hot flash in the day before treatment was 82% and in fluoxetine group was 80% between 2 - 4 min/day.

Regarding the severity of hot flashes, there was a meaningful difference between two groups, (P=0.000).

In drug group, the severity of hot flashes decreased in 15 cases after two weeks, in 45 cases did not show any change, and after 8 weeks it showed decrease in 20 cases and in 40 cases no change was observed.

In fluoxetine group, the severity of hot flash decreased in 40 cases after two weeks, in 47 cases it decreased significantly after 8 weeks, 5 cases showed less decrease in hot flashes, and 8 patients showed no change.

Considering the incidence of side effects, headache was reported by 20% of fluoxetine group, and in placebo group 48% anxiety was reported.

DISCUSSION

This study showed that of 20 mg fluoxetine is effective in treating hot flashes of menopausal women. Since the difference was significant after two months, most previous studies in this regard was performed on breast cancer survivors who had restricted usage of estrogen. ^{11,15,16} Loprinzi et al. in their study on breast cancer patients have attained similar results. ^{11,17,18}

Albertazzi et al. consider serotonergic modulation as an alternative for hormone therapy in the treatment of vasomotor symptoms in menopausal women. ^{19,20}

The mechanism of fluoxetine function is not known totally. It seems that this drug and other drugs of this group do not affect hot flashes as hormones operation, but probably they have central effect. ¹¹

According to different studies, these drugs show their therapeutic effects after the first and the second week. After the third week (SSRI) the effect of drug on hot flash reaches

to a fixed level, so the fourth week is more appropriate for concluding. ¹¹ In a study has shown that, effect of citalopram, which belongs to fluoxetine group, on hot flash was evaluated, and 63% clinical response was recorded. ²¹ Also, in another study, they has found, the effect of fluoxetine in treating hot flashes in breast cancer patients was evaluated, and 50% positive clinical response was reported. ¹¹

In other studies, the effect of different drugs such as clonidine, gabapentin, fluoxetine and paroxetine in treating hot flashes showed positive clinical responses (38%, 52%, 6% and 56.1% respectively). ^{22,23} Also a study in 2003 treated 92 menopausal women with more than three times hot flashes using fluoxetine for eight weeks. The hot flashes of 52% of patients were treated with fluoxetine, and 32% decreased with placebo. ²⁴ Those studies were conformed to our study on efficacy of fluoxetine to reduce the hot flashes and this finding was as two more study in Iran. ^{25,26}

Beside hormonal or non-hormonal therapies there are other factors that help menopausal women improve their lives and quality of life and decrease osteoporosis and cardiac diseases. Some of these factors are quitting smoking, weight control, systematic practice, eating little of greasy foods and controlling diet. ²⁷

CONCLUSION

The success percentage of fluoxetine in treating hot flashes is greatly higher than placebo. Regarding the low side effects, cheapness and accessibility of fluoxetine, it can be used as a replacement for hormone therapy.

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