EFFECT OF FLUOXETINE ON WEIGHT REDUCTION IN OBESE PATIENTS

Afkhami-Ardekani M and Sedghi H

Diabetes Research Center of Yazd, Shahid Sadoughi University of Medical Science, Jomhoori, Blvd, Yazd,
PO Box : 89175-316, I.R.IRAN

ABSTRACT

Obesity is one of the most important health problems, which many people suffer from it. As a chronic disease, it is a precipitating factor for many medical conditions like hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, sleep apnea syndrome and some malignancies (breast, uterus, prostate and colon carcinoma). With attention to this fact that obesity is an independent risk factor associated with significant increase in morbidity and mortality, treatment of overweight individuals is very important. One of the medications for short-term weight loss is fluoxetine. In this clinical trial study, fluoxetin effect on weight loss induction during 8 weeks was investigated. 201 cases with BMI between 25-42 were selected randomly (113 female and 88 male) and all received fluoxetine (40 mg daily) for 8 weeks. Measurement was carried out after the 4th and 8th week of administration and 4 weeks after end of treatment. Management of 9 cases (4 due to weight gain and 5 due to headache) were discontinued after 4 weeks of treatment. Data assessments were performed using t-test and SPSS program. Mean body weight at first visit was 89.32 ± 13.30 kg. At the 4th, 8th week of treatment and 4 weeks after study, the mean body weight of cases reached 86.09 ± 13.27 ($p=0.00$), 82.69 ± 11.31 ($p=0.00$) and 81.97 ± 13.26 ($p=0.00$) respectively. Mean BMI at first visit was 34.90 ± 5.20 kg/m². At 4th, 8th weeks of treatment it was 33.72 ± 5.20 kg/m² and 32.40 ± 5.18 kg/m² respectively. Mean weight loss at 4th and 8th weeks of treatment was 3.24 kg and 6.67 kg respectively without any weight gain at the end of the 4th week after discontinuation of the drug. Fluoxetine is an effective, well-tolerated and relatively safe drug for short-term treatment of obesity.

KEY WORDS

Fluoxetine, Obesity, Treatment.

INTRODUCTION

Obesity is one of the most important health problems which many people suffer from it (1). Prevalence obesity is reported 10.3% in Iran and 9.1% in Yazd province (2). Obesity is a risk factor for several chronic diseases including hypertension, dyslipidemia, diabetes, cardiovascular disease, sleep apnea, osteoarthritis and some cancers (breast, uterus, prostate and colon carcinoma)(3).

Obesity now affects 15% of the population, and is an underlying factor in many diseases, yet surprisingly, it has recently attracted little medical or scientific interest. The epidemic of obesity is probably as a result of increasingly sedentary lifestyles combined with easy availability of palatable, high fat foods. However, not everyone exposed to this environment becomes obese,

and there is a good evidence that the tendency to develop obesity is inherited in the vast majority of cases as a complex polygenic trait with a few rare cases of external obesity being due to single gene defects (4).

An estimated 97 million U.S adults are overweight, 22 percent of those are classified as obese. Obesity is growing at such an alarming rate that it's being called the epidemic of the New World (5). The prevalence of obesity is increasing a lot in young adult aged 18 to 29 years with some college education and in Hispanics. An estimated 6.8 percent of healthcare costs in the United States; (more than 100 billion a year), are caused by obesity. Obesity is directly related to about 325,000 preventable deaths each year (6). The etiology of obesity includes both genetic and environmental factors. Obesity may also be induced by certain drugs (for example, high dose glucocorticoids) or be secondary to a variety of neuroendocrine disorders such as Cushing's syndrome and polycystic ovary syndrome (7-8).

With attention to this fact that obesity is an independent risk factor for increasing in morbidity and mortality, treatment of overweight individuals is very important (9). One of the medical methods for short-term weight

Author for Correspondence

Afkhami-Ardekani M

Diabetes Research Center of Yazd, Shahid Sadoughi University of Medical science, Jomhoori, Blvd, Yazd, PO Box : 89175-316, I.R.IRAN
E-Mail: Afkhamiam@yahoo.com

loss is fluoxetine administration (10-11).

Fluoxetine is an oral antidepressant (12). It is the prototype of the selective serotonin reuptake inhibitors (SSRIs) and has the longest half-life of all the SSRIs. The SSRIs are structurally distinct from the other classes of antidepressants (12-13). Fluoxetine effect on appetite centers in hypothalamus reduces appetite and decreased calorie intake (12).

METHODS

In this clinical trial (before and after), fluoxetine's effect on weight reduction during 8 weeks was investigated among 201 cases (113 female and 88 male) with BMI between 25 and 42 kg/m². These cases were selected randomly from obese patients referred to Yazd endocrine clinic, after rule out secondary obesity such as Cushing's syndrome, hypothyroidism etc. The age of patients was between 20 to 48 years.

According to pilot study and side effects of 60mg fluoxetine, we decided to administer 40mg fluoxetine daily for 8 weeks for these cases. Measurement was carried out after 4 and 8 weeks of administration, and 4 weeks after end of treatment.

Weights of the patients were assessed at each visit. Management of 9 cases was discontinued after 4 weeks of treatment due to complications (4 due to weight gain and 5 due to headache). Data assessments were done using t-test and SPSS program.

RESULTS

Mean body weight of patients at the first visit was 89.32

± 13.30 kg. Mean age of cases was 33.6 ± 5.6 years (Minimum 20 and Maximum 48 years). Mean body weight of the cases after 4 and 8 weeks of treatment reached to 86.09± 13.27 (p=0.01) and 82.69 ± 11.31 kg, respectively. Mean body weight of patients was 81.97±13.26 kg 4 weeks after discontinuation of drug (p=0.001) (Table 1). Mean BMI of patients at first visit was 34.90± 5.20kg/m² but it was 33.72 ± 5.20kg/m² and 32.40 ±5.18 kg/m² at 4 and 8 weeks of treatment respectively (P =0.001) (Table 2). Mean weight loss at 4 and 8 weeks of treatment was 3.24 kg and 6.67 kg without any weight gain at 4 weeks after end of treatment (Table 3). At 4 weeks after discontinuation of fluoxetine, mean weight loss was 0.71kg. None of the patients gained weight.

DISCUSSION

Weight loss may have an effect on cardiovascular risk ≥ 5% factors such as dyslipidemia, hypertension (14-15). In this study we found that fluoxetine (40mg/day) produced significant weight loss over the 8 weeks of treatment (p =0.001). In addition to weight loss during treatment with fluoxetine; 4 weeks after discontinuation of it, mean weight loss was about 0.71kg and none of patients gained weight. Fernandez ML et al studied 42 obese women (BMI 35±5.3 kg/m²) that were randomized to start treatment with 60mg/day fluoxetine (group A) or placebo (group B) for 3 months. There was no significant difference in weight loss between Two groups(13). This difference between these two studies was due to several factors such as difference in number of patients and gender of patients.

In double blind study in England, 12 non depressed obese female subjects (BMI>30 kg/m²) were

Table 1. Mean Weight parameters of patients (male & female) at each stage of study

Sex	Number	1 st Visit		2 nd Visit		3 rd Visit		4 th Visit	
		Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
Female	105	88.25	11.91	85.16	12.60	82.5	12.5	81.2	12.33
male	87	90.62	14.56	87.22	14.55	83.46	14.21	82.9	14.32
Sum	192	89.32	13.30	86.09	13.27	82.69	11.31	81.97	13.26

Table 2. BMI Parameters of patients (male & female) at each stage of study

Sex	Number	1 st visit		2 nd visit		3 rd visit		4 th visit	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Female	105	35.66	5.05	34.52	4.99	33.31	4.97	32.88	5.02
Male	87	33.93	5.25	32.69	5.30	31.28	5.25	31.08	5.34
Sum	192	34.90	5.20	33.72	5.20	32.40	5.18	32.07	5.23

Table 3. Comparisons of mean weight of patients at each visit

Visit1	Visit2	Mean difference	S.E	P-Value	95%Confidence interval for Difference	
month	month				Max	Min
1	2	3.24	17%	INSIGNIFICANT	3.58	2.91
1	3	6.67	213%		7.1	6.25
1	4	7.39	25%		7.88	6.89
2	3	3.43	17%		3.77	3.09
3	4	4.14	22%		4.58	3.70

randomized into 2 groups (treatment with fluoxetine 60mg/dl or placebo). This study showed treatment with fluoxetine produced a significant weight loss of 1.97kg over 2 weeks of treatment compared a weight loss of only 0.04kg on placebo(16) that is similar to our study, because we found 3.24kg weight loss during 4 weeks of treatment (approximately 1.62 kg during 2 weeks).

Goldstein et al treated 458 obese outpatients with fluoxetine (60mg/day) in 52 week double blind randomized study . Maximum mean weight loss occurred at week 20th. Mean weight loss was not significantly different at week 20th and 52th, but studjects with higher baseline BMI (>40kg/m²) attained and maintained a greater weight loss than subjects with lower baseline BMI (<40kg/m²) in same condition(17), But In our study, there was no significant correlation between weight loss and baseline BMI because most of our patients had BMI <40kg/m² and we studied patients for a shorter period .

O'Kane et al treated 19 obese diabetic patients with fluoxetine (60mg/day) for 12 months. Mean weight loss was 3.8 kg after 3 months; 6.5 kg after 6 months ;7.1kg after 9 months and 5.8kg after 12 months(18) but in our study, weight loss was 6.67 kg after 2 months treatment with fluoxetin (40mg/day) that this difference between 2 studies can be due to different condition of patients ,different nutritional habits and age of patients and different fluoxetin dosage .

In our study , after 1 month wash out period, mean weight loss was 0.71 kg and none of patients gained weight. This fact shows that effect of fluoxetin in weight loss is persistant.

In none of previous studies, patients did not follow up after end of treatment and there was no report about weight gain after end of treatment. In this study except 9 patients that had drug side effects; other patients tolerated fluoxetine without any side effect. Other studies did not report any complication of fluoxetin side

effects. According to the rare complications of fluoxetin, it can be a safe drug for treatment of obesity.

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