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Title: Efficacy of Fluoxetine, Fluvoxamine, and Sertraline in Treating Anxiety, Depression, and Obsessive-Compulsive Disorder

Running Title: Efficacy of Three SSRIs for Anxiety, Depression, and OCD

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Abstract

Objective: This study aims to compare the efficacy of three common Selective Serotonin Reuptake Inhibitors (SSRIs)—fluoxetine, fluvoxamine, and sertraline—in treating anxiety disorders, major depressive disorder, and obsessive-compulsive disorder (OCD).

Methods: This eight-week randomized controlled clinical trial included 90 participants who were randomly assigned to receive either fluoxetine (20 mg), fluvoxamine (150 mg), or sertraline (100 mg). Symptom severity was assessed at baseline and after treatment using the Beck Anxiety Inventory (BAI), Beck Depression Inventory-II (BDI-II), and the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).

Results: The results indicated that all three medications significantly reduced symptoms of anxiety, depression, and OCD ($p < 0.05$). However, a one-way ANOVA showed no statistically significant difference among the efficacies of the three drugs in reducing scores on any of the assessment scales.

Conclusions: While fluoxetine, fluvoxamine, and sertraline were all effective, none demonstrated superior efficacy over the others. The choice of medication should therefore be based on considerations such as side effect profiles, drug interactions, cost, and patient-specific characteristics.

Keywords: SSRIs, Fluoxetine, Fluvoxamine, Sertraline, OCD, Depression, Anxiety

Introduction

Anxiety disorders, major depressive disorder, and obsessive-compulsive disorder (OCD) **are** among the most prevalent and debilitating psychiatric disorders worldwide, imposing a significant burden on **individuals and public health** (Sharma et al., 2021). These disorders not only **lead** to considerable mental distress, functional impairment in various life domains, and reduced quality of life, but also **increase** the risk of other health problems. For example, they **raise** the risk of suicide by increasing suicidal ideation. Comorbidity among these disorders **is also common**, with many individuals with OCD experiencing episodes of major depression.

Pharmacological treatments, particularly selective serotonin reuptake inhibitors (SSRIs), **are considered** first-line therapy for these disorders (Bandelow et al., 2012). These drugs **work by increasing** the concentration of serotonin, a key neurotransmitter **that regulates** mood, anxiety, and obsessive thoughts in the synaptic cleft. Fluoxetine, fluvoxamine, and sertraline **are** three well-known and widely used drugs from the SSRI family. Their **efficacy has been demonstrated** in numerous studies for the treatment of each of these three disorders individually (Bloch, McGuire, Landeros-Weisenberger, Leckman, & Pittenger, 2010; Geddes et al., 1996; Jakubovski, Johnson, Nasir, Müller-Vahl, & Bloch, 2019).

Fluoxetine, one of the first SSRIs introduced, **is known** for its long half-life, which **helps stabilize** drug levels in the body. Sertraline **is** often favored since it is well-tolerated and is a relatively safer choice during pregnancy and breastfeeding. Fluvoxamine **is also a widely prescribed medication**, particularly for the treatment of obsessive-compulsive disorder.

Despite the well-established overall efficacy of SSRIs, individual responses to different drugs within this class **vary**. Subtle differences in pharmacokinetics, pharmacodynamics, side effect profiles, and efficacy on specific symptoms of each disorder **make** choosing the most appropriate SSRI for a particular patient a clinical challenge. Some studies **have compared** these drugs pairwise. For example, one study compared the efficacy of fluvoxamine and sertraline in treating major depression (Rossini et al., 2005). Furthermore, systematic reviews and meta-analyses **have attempted** to evaluate the comparative efficacy of different SSRIs, but the results **have sometimes been** inconclusive, and the need for further research on safety and efficacy profiles in specific populations **remains**.

There is also a notable absence of studies that directly compare the effectiveness of fluoxetine, fluvoxamine, and sertraline in a randomized controlled clinical trial. Such a trial would simultaneously test all three drugs against each other for treating the three common disorders: anxiety, depression, and obsessive-compulsive disorder. This kind of research would offer crucial evidence to help clinicians make better decisions, allowing them to select the most suitable treatment for a patient based on their specific needs and the unique profile of each drug.

Therefore, the aim of this randomized controlled clinical trial **is** to compare the efficacy of fluoxetine, fluvoxamine, and sertraline in patients with anxiety disorders, depression, and/or obsessive-compulsive disorder. The results of this research are expected to help clarify the differences and similarities between these three drugs and provide more practical guidance for clinical practitioners in selecting the most appropriate treatment for patients.

SSRIs **are established** as a first-line psychopharmacological treatment for Major Depressive Disorder (MDD), anxiety disorders, and OCD due to their favorable efficacy and tolerability profiles. Among the most widely prescribed agents in this class **are** sertraline, fluoxetine, and fluvoxamine, each supported by a substantial body of evidence validating its use for these conditions. However, despite their widespread application, the question of their comparative efficacy **remains** a subject of ongoing clinical debate. While individual studies **have demonstrated** the effectiveness of each medication, there **is** a notable lack of comprehensive, head-to-head research that directly compared the superiority of one over the others across the distinct diagnostic categories of OCD, anxiety, and depression. This gap in the literature, compounded by variations in patient response and side-effect profiles, **complicates** clinical decision-making and **gives rise** to a critical research question: **Is** there a demonstrable priority of efficacy among sertraline, fluoxetine, and fluvoxamine in the treatment of these highly prevalent disorders?

Material and Methods

This study was conducted at Imam Hossein Hospital in Tehran, Iran from September 2022 to September 2024.

2.1. Assessment Instruments

To assess the severity of anxiety, depression, and obsessive-compulsive symptoms among participants, the following standardized and validated self-report questionnaires **were administered**:

Beck Anxiety Inventory (BAI): The Beck Anxiety Inventory (BAI) is a 21-item self-report instrument designed to assess the severity of anxiety symptoms. Each item describes a common anxiety symptom, and the respondent indicates how much they have been bothered by that **symptom during the past week**, based on a four-point Likert scale ranging from 0 (not at all) to 3 (severe, I couldn't stand it). The total score, calculated by summing the individual item scores, can range from 0 to 63. Based on the total score, anxiety severity is classified as follows: 0–7 = minimal anxiety, 8–15 mild anxiety, 16–25 moderate anxiety, and 26–63 = severe anxiety (Beck, Epstein, Brown, & Steer, 1993).

Beck Depression Inventory-Second Edition (BDI-II): The Beck Depression Inventory-II (BDI-II) is a 21-item self-report instrument used to measure the intensity of depressive symptoms in individuals aged 13 and older over the past two weeks, including the day of assessment. Each item presents a set of four statements (scored 0 to 3) that reflect the severity of a specific depressive symptom, and the respondent selects the option that best describes their feelings. The total score ranges from 0 to 63. Based on the total score, depression severity is classified as follows: 0–13 minimal, 14–19 mild, 20–28 moderate, and 29–63 severe depression (Jackson-Koku, 2016).

Yale-Brown Obsessive Compulsive Scale (Y-BOCS): The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is a specialized instrument consisting of 10 items designed to assess the severity

of obsessive-compulsive disorder symptoms over the past week. The first five items assess obsessions, and the second five assess compulsions, with each item evaluating aspects such as the time spent, functional impairment, distress, resistance, and control on a five-point Likert scale from 0 (no symptoms) to 4 (extremely severe symptoms). The total score **is the sum of all 10 items, ranging from 0 to 40**, with higher scores indicating greater severity of OCD symptoms. Generally, 0–7 = subclinical, 8–15 mild, 16–23 moderate, 24–31 severe, and 32–40 very severe (Goodman et al., 1989).

2.2. Procedures

Patients were randomly assigned to one of three treatment groups: fluoxetine (20 mg), fluvoxamine (150 mg), or sertraline (100 mg). After an eight-week treatment period, patients completed the questionnaires again. This allowed for the assessment of improvement by comparing their scores before and after the treatment.

All questionnaires **were validated Persian translations of the original English versions.**

2.3. Ethics Code

This study was conducted in accordance with ethical guidelines and received approval from **Shahid Beheshti University of Medical Sciences Ethics Committee (Ref: IR.SBMU.PHNS.REC.1402.142)**. Informed consent was obtained from all participants.

2.4. Statistical Analysis

For the BDI-II test, a reduction of 17.5% **or at least 11 points in the total score was considered a treatment response.**

For the BAI test, a reduction of 36% **or at least 22 points in the total score was considered a treatment response.**

For the Y-BOCS test, a reduction of 32% **or at least 14 points in the total score was considered a treatment response.**

In this study, **GraphPad Prism (version 8) was used.** Paired t-tests were applied for pre- and post-treatment comparisons. The Kolmogorov-Smirnov test **confirmed that data were normally distributed.** One-way ANOVA was used to compare the three drug groups in reducing questionnaire scores. The significance level for all tests was set at $p < 0.05$.

Results

A total of 90 participants were enrolled in the study. Of these, 33 (36.7%) were male and 57 (63.3%) were female.

Distribution of participants in treatment groups by gender (Table 1): The study enrolled 30 participants in each of the three treatment arms: the sertraline group (10 males, 20 females), the fluoxetine group (14 males, 16 females), and the fluvoxamine group (9 males, 21 females).

Age characteristics of participants by gender (Table 2): Male participants (n=33) had a mean age of 34.9 years (SD 1.8), ranging from 18 to 60 years. Female participants (n=57) had a mean age of 38.5 years (SD 1.6), **ranging from 17 to 68 years.**

The efficacy of the three drugs—fluoxetine, fluvoxamine, and sertraline—in reducing anxiety symptoms was evaluated using changes in Beck Anxiety Inventory scores (Δ BAI). All three treatment groups showed a reduction in mean anxiety scores **over the treatment period.**

Specifically, the mean reduction in anxiety score (Δ BAI) was 20.07 (SD 16.56) in the fluoxetine group, 17.93 (SD 10.12) in the fluvoxamine group, and 15.73 (SD 15.55) in the sertraline group.

Although numerical differences **were observed** in the mean reduction of scores between the three groups (such that fluoxetine showed the largest mean reduction and sertraline the smallest), the results of the one-way ANOVA indicated that these differences **were** not statistically significant (Table 3, Figure 1).

The effect of the three drugs—fluoxetine, fluvoxamine, and sertraline—on reducing depressive symptoms was evaluated by examining changes in BDI-II questionnaire scores (Δ BDI-II). Each group included 30 participants.

As shown in the mean scores, all three drugs, on average, reduced depression scores, indicating symptomatic improvement. The fluoxetine group showed the largest mean reduction (15.53), followed by the fluvoxamine group (14.70) and the sertraline group (13.13).

However, despite these numerical differences, the result of the one-way ANOVA test showed that these differences **were not** statistically significant. Based on the findings of this study and the statistical analysis performed, none of the three drugs—fluoxetine, fluvoxamine, or sertraline— was identified **as** superior in reducing the severity of depressive symptoms compared to the others. In other words, all three drugs were generally effective in improving depressive symptoms, but the observed difference did not reach statistical significance.

This finding suggests that, in the studied sample, all three drugs showed broadly similar therapeutic effects on depressive symptoms. The reported standard deviations, particularly for the fluoxetine and sertraline groups, suggested considerable variability in individual responses to these treatments (Table 4, Figure 1).

In this study, the efficacy of the three drugs—fluoxetine, fluvoxamine, and sertraline—in reducing obsessive-compulsive symptoms was evaluated using changes in Yale-Brown Obsessive Compulsive Scale scores (Δ Y-BOCS). Each treatment group included 30 participants.

The mean reduction in Y-BOCS scores was 12.57 (SD 11.21) in the fluoxetine group, 14.93 (SD 7.44) in the fluvoxamine group, and 11.97 (SD 9.05) in the sertraline group.

As demonstrated by the mean scores, each of the three drugs led to a decrease in Y-BOCS ratings, thereby indicating a positive symptomatic response in individuals with OCD.

On this scale, the fluvoxamine group showed the largest mean reduction (14.93), followed by the fluoxetine (12.57) and sertraline (11.97) groups. Additionally, the standard deviation in the fluvoxamine group was lower than that in the other two groups, indicating less dispersion and greater homogeneity in the treatment response. However, despite these numerical differences in mean reductions and standard deviations, the result of the one-way ANOVA test showed that these differences were not statistically significant. Based on these findings, none of the three drugs—fluoxetine, fluvoxamine, or sertraline—was identified as superior in reducing the severity of obsessive-compulsive symptoms. All three drugs were generally effective, but the observed differences did not reach statistical significance or reflect a true difference in the wider population.

Discussion

This study compared the effectiveness of three common SSRIs—fluoxetine, fluvoxamine, and sertraline—for treating anxiety disorders, major depressive disorder, and OCD. The results showed that fluoxetine, fluvoxamine, and sertraline were equally effective in reducing anxiety, depression, and obsessive-compulsive symptoms. The absence of significant differences among the three drugs is consistent with prior evidence suggesting comparable efficacy of SSRIs. Given this similarity, treatment choice should be based on other clinical factors, including side effect profiles, potential interactions, pharmacokinetic characteristics, patient comorbidities, and individual preferences. The variability in patient responses observed in this study further emphasizes the need for individualized treatment and careful monitoring.

Some limitations should be noted. The eight-week duration may not capture long-term outcomes, and the relatively small sample size may have limited detection of subtle differences. Subgroup analyses could also clarify whether specific patient characteristics predict differential response. Future studies with larger, more diverse populations, longer follow-up periods, and broader outcome measures such as functional recovery and quality of life are recommended. Investigating biomarkers of treatment response may also contribute to more personalized therapeutic strategies.

Conclusion

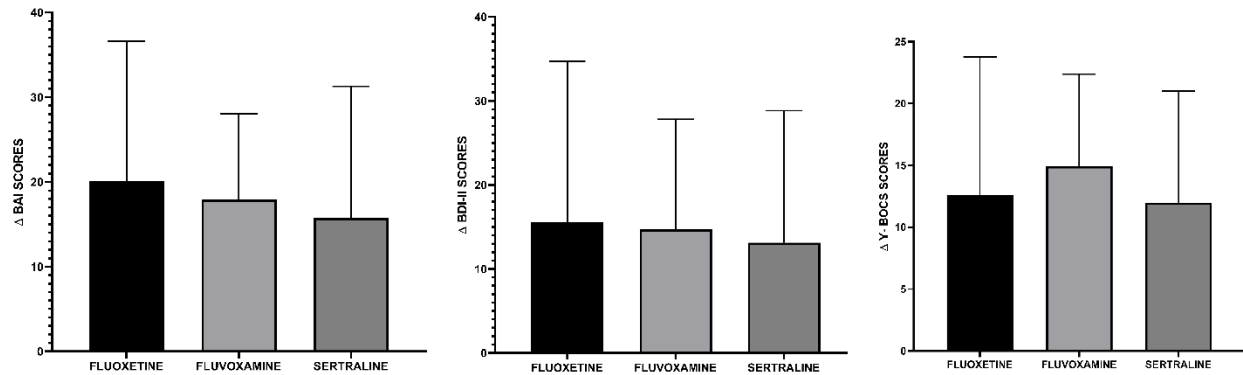
This randomized controlled trial demonstrated that fluoxetine, fluvoxamine, and sertraline are equally effective in reducing symptoms of anxiety, depression, and obsessive-compulsive disorder.

Since no significant differences in efficacy were observed, treatment decisions should primarily rely on clinical considerations such as side effect profile, drug interactions, availability, cost, and

patient preference. The findings support the use of all three SSRIs as first-line options while emphasizing individualized treatment planning.

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Figures and Tables

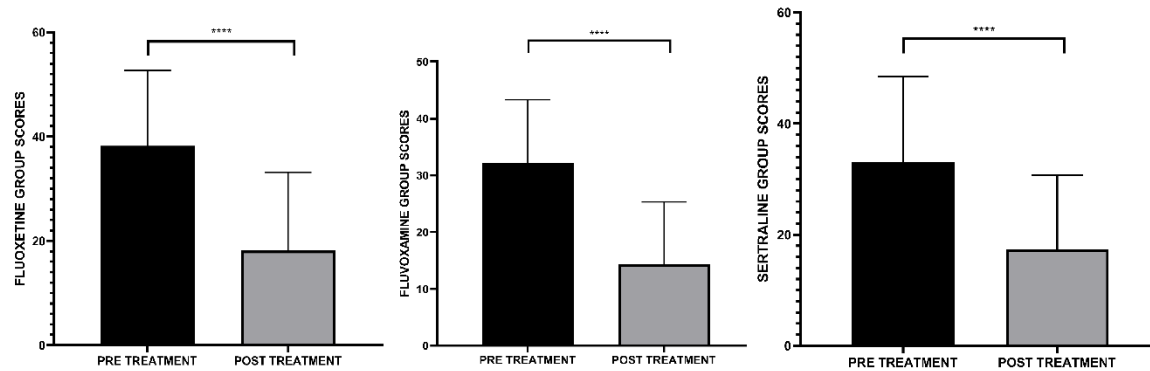


Figure

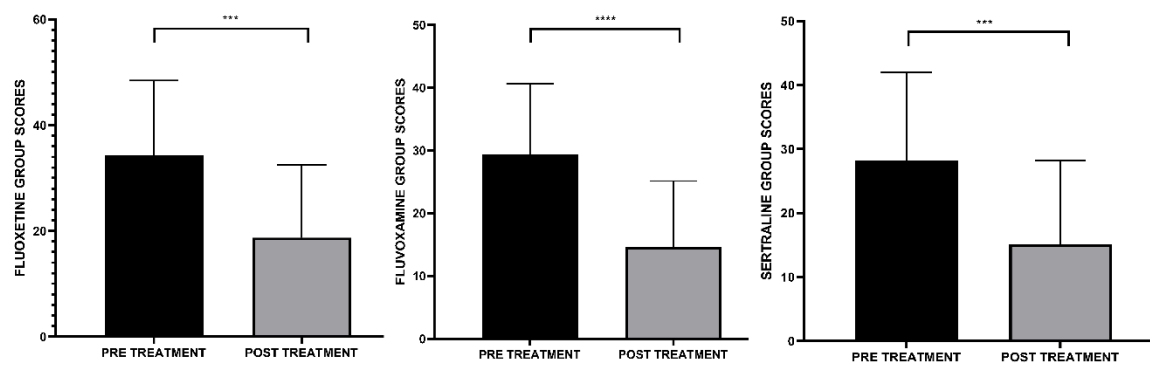
1.

Changes in BAI, BDI-II, and Y-BOCS scores following 8 weeks of treatment with fluoxetine, fluvoxamine, and sertraline in patients with anxiety, depression, and obsessive-compulsive disorder (OCD) (n = 30 per group). The bar graphs **show mean changes (Δ scores)** in (A) Beck Anxiety Inventory (BAI), (B) Beck Depression Inventory-II (BDI-II), and (C) Yale-Brown Obsessive Compulsive Scale (Y-BOCS), with error bars **representing standard deviations**. One-way ANOVA revealed no significant differences **in improvement among** the fluoxetine, fluvoxamine, and sertraline groups for BAI ($p = 0.72$), BDI-II ($p = 0.65$), and Y-BOCS ($p = 0.81$), **indicating comparable efficacy across the three drugs**.

BAI TEST (A)



BDI-II TEST (B)



Y-BOCS TEST (C)

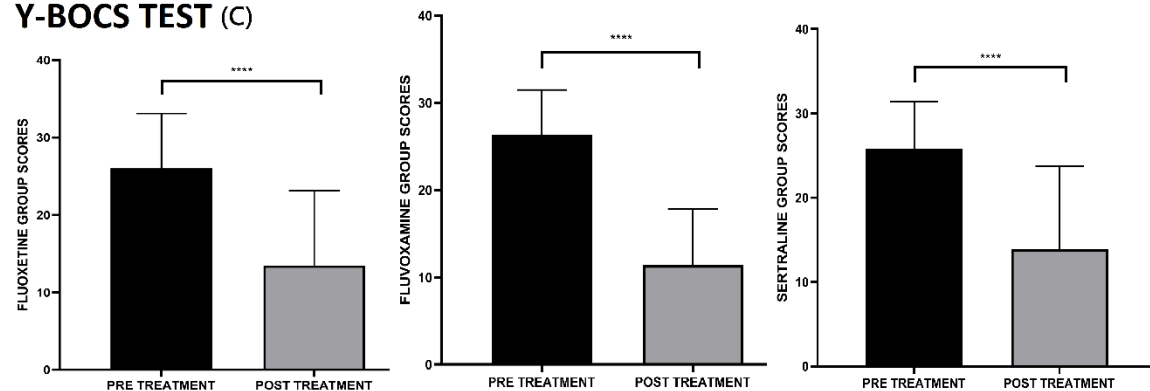


Figure 2. Pre- and post-treatment scores for BAI, BDI-II, and Y-BOCS in patients treated with fluoxetine, fluvoxamine, or sertraline with anxiety, depression, and obsessive-compulsive disorder (OCD) (n = 30 per group). The bar graphs **display** mean scores for (A) Beck Anxiety Inventory (BAI), (B) Beck Depression Inventory-II (BDI-II), and (C) Yale-Brown Obsessive Compulsive Scale (Y-BOCS) before (**black bars**) and after (**gray bars**) 8 weeks of treatment, with error bars indicating standard deviations. Paired t-tests revealed significant reductions in scores across all three measures in each treatment group ($p < 0.05$), confirming improvements in anxiety, depression, and OCD symptoms.

Table 1. Distribution of participants across treatment groups by gender

Treatment Group	Male (n)	Female (n)	Total (n)
Sertraline	10	20	30
Fluoxetine	14	16	30
Fluvoxamine	9	21	30
Total	33	57	90

Table 2. Demographic characteristics and age distribution of participants by gender

Characteristic	Male	Female
Number of participants (n)	33	57
Mean age (SE)	34.9 (1.8)	38.5 (1.6)
Age range (years)	18–60	17–68

SE, standard error.

Table 3 Descriptive statistics for changes (Δ) in Beck Anxiety Inventory (BAI) scores across treatment groups

Statistic	Fluoxetine	Fluvoxamine	Sertraline
N	30	30	30
Mean	20.07	17.93	15.73
Standard Deviation	16.56	10.12	15.55
Std. Error of Mean	3.024	1.848	2.839
Minimum	-5.00	1.00	-12.00
Maximum	49.00	45.00	47.00

Δ , change from baseline to 8 weeks; BAI, Beck Anxiety Inventory.

Table 4. Descriptive statistics for changes (Δ) in Beck Depression Inventory-II (BDI-II) scores across treatment groups

Statistic	Fluoxetine	Fluvoxamine	Sertraline
N	30	30	30
Mean	15.53	14.70	13.13
Standard Deviation	19.16	13.11	15.69
Std. Error of Mean	3.499	2.394	2.865
Minimum	-28	-8	-11
Maximum	48	34	39

Δ , change from baseline to 8 weeks; BDI-II, Beck Depression Inventory-Second Edition.

Table 5. Descriptive statistics for changes (Δ) in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores across treatment groups

Statistic	Fluoxetine	Fluvoxamine	Sertraline
N	30	30	30
Mean	12.57	14.93	11.97
Standard Deviation	11.21	7.446	9.05
Std. Error of Mean	2.046	1.359	1.652
Minimum	-18	-1	-5
Maximum	31	27	25

Δ , change from baseline to 8 weeks; Y-BOCS, Yale-Brown Obsessive Compulsive Scale.