ORIGINAL RESEARCH

A Comparative Evaluation of Antidepressant Medications: SSRIs vs. SNRIs in Treating Major Depressive Disorder

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ABSTRACT

Aim: The aim of this study was to compare the efficacy and safety of Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) in treating patients diagnosed with Major Depressive Disorder (MDD), focusing on the response rates, side effects, and overall improvement in mood and quality of life. **Materials and Methods:** This prospective, randomized, open-label, parallel-group study included 120 patients with MDD. Participants were randomly assigned to receive either SSRIs (fluoxetine, sertraline, or escitalopram) or SNRIs (venlafaxine or duloxetine) over 8 weeks. The primary outcome was the change in Hamilton Depression Rating Scale (HAM-D) score from baseline to 8 weeks. Secondary outcomes included response rate (≥50% reduction in HAM-D), remission rate (HAM-D ≤7), side effects (measured using the FIBSER scale), and quality of life (assessed with the WHOQOL-BREF scale). **Results:** Both treatment groups demonstrated significant reductions in HAM-D scores, with no significant difference in scores between SSRIs (5.8 ± 2.0) and SNRIs (5.7 ± 2.1) at Week 8 ($p=0.89$). The response rates were 70% for the SSRI group and 75% for the SNRI group ($p=0.45$). The remission rates were 50% for the SSRI group and 53.3% for the SNRI group ($p=0.70$). Common side effects included nausea, insomnia, and dizziness, with no significant differences between groups. Both groups showed significant improvements in all domains of the WHOQOL-BREF scale ($p<0.001$). **Conclusion:** SSRIs and SNRIs were found to be equally effective in reducing depressive symptoms and improving quality of life in patients with MDD. Both treatments had similar efficacy and safety profiles, making them both viable options for treating MDD, with patient preferences and tolerability potentially guiding treatment decisions.

Keywords: SSRIs, SNRIs, Major Depressive Disorder, Response Rate, Quality of Life

INTRODUCTION

Major Depressive Disorder (MDD) is a prevalent and debilitating mental health condition that affects millions of individuals worldwide. Characterized by persistent feelings of sadness, hopelessness, and a lack of interest or pleasure in daily activities, MDD can severely impact an individual's quality of life, relationships, and overall functioning. The treatment of MDD typically involves a combination of pharmacotherapy, psychotherapy, and lifestyle changes. Among the pharmacological treatments, antidepressant medications play a central role in managing the symptoms of depression, with selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) being two of the most commonly prescribed classes of drugs.[1]SSRIs and SNRIs are both considered first-line treatment options for MDD due to their relative safety, tolerability, and effectiveness. Although both classes of medications share some similarities in their mechanisms of action, they also exhibit key differences that can influence their efficacy, side-effect profiles, and suitability for individual patients. SSRIs primarily target serotonin, a neurotransmitter believed to play a key role in mood regulation, while SNRIs target both serotonin and norepinephrine,

another neurotransmitter involved in mood and arousal. These differences in pharmacological action may lead to varying clinical outcomes, and understanding the comparative effectiveness of these two drug classes is crucial for optimizing treatment strategies for individuals suffering from MDD.[2]This paper aims to provide a comprehensive evaluation of SSRIs and SNRIs in the context of treating MDD. By comparing their mechanisms of action, clinical efficacy, side effects, and patient outcomes, this evaluation seeks to offer insights into how these medications perform in real-world settings and provide guidance for clinicians in selecting the most appropriate treatment for their patients.The primary distinction between SSRIs and SNRIs lies in their mechanisms of action. SSRIs, as the name suggests, selectively inhibit the reuptake of serotonin, thereby increasing its availability in the synaptic cleft and enhancing serotonergic neurotransmission. This action is thought to contribute to the mood-lifting effects of SSRIs, making them particularly effective in treating symptoms of depression, anxiety, and other mood disorders. Common SSRIs include fluoxetine, sertraline, escitalopram, and paroxetine.[3]In contrast, SNRIs have a dual mechanism of action, affecting both serotonin and norepinephrine. By inhibiting the reuptake of both neurotransmitters, SNRIs enhance serotonergic and noradrenergic transmission in the brain, which is believed to have a more broad-spectrum effect on mood regulation and emotional arousal. SNRIs such as venlafaxine, duloxetine, and desvenlafaxine have been shown to be effective in treating depression, as well as certain types of anxiety disorders and chronic pain conditions. The dual mechanism of SNRIs may offer advantages in treating patients who have not responded to SSRIs, or those who present with additional symptoms, such as fatigue or pain, that may benefit from the increased norepinephrine activity.[4]Both SSRIs and SNRIs have been extensively studied in clinical trials, with numerous studies demonstrating their efficacy in treating MDD. In general, both classes of drugs have been shown to be more effective than placebo in reducing depressive symptoms. However, some research suggests that SNRIs may have a slight advantage in terms of efficacy, particularly in patients with more severe forms of depression or those who also experience significant anxiety or pain. For example, venlafaxine has been found to outperform SSRIs in certain populations, particularly in patients with treatment-resistant depression or those with comorbid conditions such as generalized anxiety disorder.[5]Despite these findings, SSRIs remain the first-line treatment for MDD due to their favorable safety profile and lower risk of adverse effects. For many patients, SSRIs are effective in alleviating depressive symptoms, especially when the depression is mild to moderate in severity. However, for patients who do not respond to SSRIs or who experience insufficient symptom relief, SNRIs may offer a valuable alternative, particularly when there is a clear need for enhanced norepinephrine modulation.[6]A critical aspect of antidepressant therapy is the tolerability and side-effect profile of the medications. While both SSRIs and SNRIs are generally well tolerated, they are not without their side effects. SSRIs are often associated with gastrointestinal disturbances, sexual dysfunction, weight gain, and sleep disturbances. These side effects, though generally mild and transient, can be bothersome for patients and may lead to discontinuation of therapy or poor adherence.[7]SNRIs, due to their dual action on serotonin and norepinephrine, have a somewhat different side-effect profile. In addition to the common SSRI-related effects, SNRIs are more likely to cause increased blood pressure, particularly at higher doses of medications such as venlafaxine. This can be a concern for patients with preexisting hypertension or those at risk for cardiovascular issues. Other potential side effects of SNRIs include dizziness, dry mouth, and increased sweating. Nonetheless, for many patients, the benefits of SNRIs outweigh these potential risks, particularly when treating patients with severe or refractory depression.

MATERIALS AND METHODS

This was a prospective, randomized, open-label, parallel-group study conducted to compare the efficacy and safety of Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) in treating patients diagnosed with Major Depressive Disorder (MDD). The study aimed to evaluate the response rates, side effects, and overall improvement in mood and quality of life in patients undergoing treatment with SSRIs and SNRIs.The study included 120 patients diagnosed with Major Depressive Disorder, as defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). Participants were recruited from outpatient clinics and were between the ages of 18 and 65 years. Inclusion criteria included a diagnosis of MDD with a baseline Hamilton Depression Rating Scale (HAM-D) score $\geq$ 18. Exclusion criteria included a history of bipolar disorder, schizophrenia, other psychotic disorders, substance abuse, and significant medical conditions that could affect the study's outcomes.

Randomization and Treatment Groups

The 120 patients were randomly assigned into two groups using a computer-generated randomization list:

- **Group 1: SSRI Group (n=60)**: This group was treated with one of the following SSRIs: fluoxetine, sertraline, or escitalopram. The dose was titrated according to the clinical response and tolerability, with the maximum dose set according to standard guidelines for each drug.
- **Group 2: SNRI Group (n=60)**: This group was treated with one of the following SNRIs: venlafaxine or duloxetine. As with the SSRI

group, the dose was titrated based on clinical response and tolerability, with maximum doses following standard clinical guidelines.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Age between 18 and 65 years
- Diagnosis of Major Depressive Disorder (DSM-5)
- Hamilton Depression Rating Scale (HAM-D) score ≥ 18
- Written informed consent

Exclusion Criteria

- History of bipolar disorder or schizophrenia
- Substance abuse or dependence
- Significant medical conditions (e.g., cardiovascular disease, uncontrolled diabetes)
- Pregnancy or breastfeeding
- History of hypersensitivity to SSRIs or SNRIs

Study Procedure

After obtaining informed consent, baseline assessments including the HAM-D, FIBSER, and WHOQOL-BREF were administered. Participants were randomly assigned to one of the two treatment groups. The medications were prescribed based on the group allocation, and patients were followed up at 2, 4, 6, and 8 weeks. At each visit, patients' HAM-D scores were assessed, and side effects were recorded using the FIBSER scale. At the end of 8 weeks, patients completed a final assessment using the WHOQOL-BREF scale to evaluate changes in their quality of life.

The primary outcome measure of the study was the change in the Hamilton Depression Rating Scale (HAM-D) score from baseline to 8 weeks of treatment. This provided a direct assessment of the overall severity of depressive symptoms in the participants. Secondary outcomes included several additional measures to assess the treatment's impact. The response rate was defined as a ≥50% reduction in the HAM-D score, indicating a clinically significant improvement in depression severity. The remission rate was considered as a HAM-D score of ≤ 7, indicating a near-complete resolution of depressive symptoms. Side effects were systematically recorded using the Frequency, Intensity, and Burden of Side Effects Rating (FIBSER) scale, which provided a comprehensive evaluation of the adverse effects experienced by participants. Additionally, participants' quality of life was assessed using the World Health Organization Quality of Life (WHOQOL-BREF) scale, which measured the broader impact of treatment on the patients' well-being and functioning.

Statistical Analysis

Data were analyzed using SPSS (version 21). Continuous variables were expressed as means ± standard deviation, while categorical variables were presented as frequencies and percentages. Between-group comparisons for demographic variables, clinical outcomes, and side effects were conducted using independent t-tests for continuous data and chi-square tests for categorical data. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographics and Clinical Characteristics of Participants

The baseline demographics and clinical characteristics of the study participants are summarized in Table 1. The SSRI group (n=60) had a mean age of 45.3 ± 10.2 years, while the SNRI group (n=60) had a mean age of 44.8 ± 9.7 years, with no significant difference between the two groups (p=0.76). The gender distribution was slightly skewed toward females, with 35 females and 25 males in the SSRI group, and 32 females and 28 males in the SNRI group. Overall, the study included 53 males and 67 females. Both groups had similar baseline severity of depression, as indicated by their Hamilton Depression Rating Scale (HAM-D) scores, with the SSRI group having a mean score of 22.1 ± 3.4 and the SNRI group scoring 22.3 ± 3.2 (p=0.76). The average duration of depression was also similar between the groups, with the SSRI group having 5.2 ± 3.1 years and the SNRI group having 5.0 ± 3.0 years (p=0.72). Furthermore, the presence of comorbidities such as hypertension and diabetes was comparable across the two groups, with 18 patients with hypertension and 12 with diabetes in the SSRI group, and 20 patients with hypertension and 10 with diabetes in the SNRI group.

Table 2: Change in HAM-D Score from Baseline to 8 Weeks

Table 2 displays the changes in the Hamilton Depression Rating Scale (HAM-D) scores from baseline to 8 weeks for both treatment groups. At baseline, both groups had similar HAM-D scores (SSRI: 22.1 ± 3.4, SNRI: 22.3 ± 3.2, p=0.76), indicating no significant difference in the severity of depression. Over the course of the study, both groups showed significant improvement in their depression scores. At Week 2, the SSRI group had a mean HAM-D score of 16.4 ± 3.1, while the SNRI group had a score of 16.7 ± 3.0 (p=0.58). By Week 4, both groups continued to improve, with the SSRI group showing a mean score of 12.3 ± 2.8 and the SNRI group at 12.1 ± 2.6 (p=0.75). At Week 6, the SSRI group had a mean score of 9.1 ± 2.3, and the SNRI group had 9.4 ± 2.5 (p=0.65). At the final assessment at Week 8, the improvement remained consistent, with the SSRI group at 5.8 ± 2.0 and the SNRI group at 5.7 ± 2.1 (p=0.89). The lack of significant differences in the change of HAM-D scores across the time points suggests that both SSRIs and SNRIs were equally effective in reducing depressive symptoms.

Table 3: Response and Remission Rates at 8 Weeks
Table 3 outlines the response and remission rates at 8 weeks. The response rate, defined as a ≥50% reduction in the HAM-D score, was slightly higher in the SNRI group (75%) compared to the SSRI group (70%), though the difference was not statistically significant (p=0.45). The overall response rate in the entire sample was 72.5%. Similarly, the remission rate, defined as a HAM-D score of ≤ 7, was 50% in the SSRI group and 53.3% in the SNRI group, with no significant difference between the two groups (p=0.70). These results suggest that both SSRIs and SNRIs were similarly effective in achieving response and remission in patients with Major Depressive Disorder.

Table 4: Side Effects Reported During Treatment (FIBSER Scale)
Table 4 presents the side effects reported by participants in both treatment groups, as measured using the Frequency, Intensity, and Burden of Side Effects Rating (FIBSER) scale. The most common side effects across both groups included nausea, insomnia, and dizziness. The SSRI group had 30% of participants report nausea, while the SNRI group had 36.7% report the same side effect. Similarly, 23.3% of participants in the SSRI group experienced insomnia, compared to 28.3% in the SNRI group. Dizziness was reported by 20% of the SSRI group and 25% of the SNRI group. Other common side effects included sexual dysfunction (16.7% in the SSRI group, 21.7% in the SNRI group), weight gain (8.3% in the SSRI group, 11.7% in the SNRI group), and dry mouth (10% in the SSRI group, 8.3% in the SNRI group). However, there were no significant differences between the two groups in terms of side effect prevalence, with all p-values being greater than 0.45, indicating that both SSRIs and SNRIs had similar safety profiles.

Table 5: Quality of Life (WHOQOL-BREF) Scores at Baseline and 8 Weeks
Table 5 shows the changes in quality of life as assessed by the WHOQOL-BREF scale, both at baseline and at the end of the study (Week 8). Significant improvements were observed in all four domains of quality of life (Physical Health, Psychological Well-Being, Social Relationships, and Environment) across both treatment groups. For physical health, the mean score improved from 50.4 ± 9.3 at baseline to 65.2 ± 8.4 at Week 8 ($p<0.001$). Psychological well-being also showed a significant improvement, with the score rising from 45.8 ± 10.1 at baseline to 60.5 ± 9.7 at Week 8 ($p<0.001$). Social relationships improved from 52.3 ± 8.6 to 64.1 ± 7.5 ($p<0.001$), and the environment domain increased from 55.7 ± 7.9 to 67.3 ± 6.8 ($p<0.001$). These significant improvements in quality of life demonstrate that both SSRIs and SNRIs not only reduced depressive symptoms but also enhanced the overall well-being of patients.

Table 1: Baseline Demographics and Clinical Characteristics of Participants

Characteristic	SSRI Group (n=60)	SNRI Group (n=60)	Total (n=120)
Age (Mean ± SD)	45.3 ± 10.2	44.8 ± 9.7	45.0 ± 9.9
Gender (Male:Female)	25:35	28:32	53:67
HAM-D Score (Mean ± SD)	22.1 ± 3.4	22.3 ± 3.2	22.2 ± 3.3
Duration of Depression (Years)	5.2 ± 3.1	5.0 ± 3.0	5.1 ± 3.1
Comorbidities (Hypertension/Diabetes)	18/12	20/10	38/22

Table 2: Change in HAM-D Score from Baseline to 8 Weeks

Time Point	SSRI Group (Mean ± SD)	SNRI Group (Mean ± SD)	p-value
Baseline	22.1 ± 3.4	22.3 ± 3.2	0.76
Week 2	16.4 ± 3.1	16.7 ± 3.0	0.58
Week 4	12.3 ± 2.8	12.1 ± 2.6	0.75
Week 6	9.1 ± 2.3	9.4 ± 2.5	0.65
Week 8 (Final)	5.8 ± 2.0	5.7 ± 2.1	0.89

Table 3: Response and Remission Rates at 8 Weeks

Outcome Measure	SSRI Group (n=60)	SNRI Group (n=60)	Total (n=120)	p-value
Response Rate (≥50% Reduction in HAM-D)	42 (70%)	45 (75%)	87 (72.5%)	0.45
Remission Rate (HAM-D ≤ 7)	30 (50%)	32 (53.3%)	62 (51.7%)	0.70

Table 4: Side Effects Reported During Treatment (FIBSER Scale)

Side Effect	SSRI Group (n=60)	SNRI Group (n=60)	Total (n=120)	p-value
Nausea	18 (30%)	22 (36.7%)	40 (33.3%)	0.56
Insomnia	14 (23.3%)	17 (28.3%)	31 (25.8%)	0.64

Dizziness	12 (20%)	15 (25%)	27 (22.5%)	0.58
Sexual Dysfunction	10 (16.7%)	13 (21.7%)	23 (19.2%)	0.47
Weight Gain	5 (8.3%)	7 (11.7%)	12 (10%)	0.63
Dry Mouth	6 (10%)	5 (8.3%)	11 (9.2%)	0.72

Table 5: Quality of Life (WHOQOL-BREF) Scores at Baseline and 8 Weeks

Domain	Baseline (Mean ± SD)	Week 8 (Mean ± SD)	p-value
Physical Health	50.4 ± 9.3	65.2 ± 8.4	<0.001
Psychological Well-Being	45.8 ± 10.1	60.5 ± 9.7	<0.001
Social Relationships	52.3 ± 8.6	64.1 ± 7.5	<0.001
Environment	55.7 ± 7.9	67.3 ± 6.8	<0.001

DISCUSSION

The results of this study indicate that both SSRIs and SNRIs were equally effective in reducing depressive symptoms in patients with Major Depressive Disorder (MDD), as measured by the Hamilton Depression Rating Scale (HAM-D). At baseline, both the SSRI and SNRI groups had similar HAM-D scores (22.1 ± 3.4 for SSRI and 22.3 ± 3.2 for SNRI), reflecting comparable severity of depression. This baseline similarity aligns with findings from other studies that have reported no significant differences in baseline depression severity between treatment groups (Thase et al., 2013).[7] In the current study, both groups showed marked improvements in HAM-D scores over the 8-week period, with no significant difference between the groups at any time point, including at Week 8 (5.8 ± 2.0 for SSRI vs. 5.7 ± 2.1 for SNRI). This is consistent with results from a large-scale meta-analysis by Cipriani et al. (2018), who found no substantial difference in the efficacy of SSRIs and SNRIs in reducing depressive symptoms.[8]

The response rates in this study, defined as a ≥50% reduction in the HAM-D score, were 70% for the SSRI group and 75% for the SNRI group, with no statistically significant difference (p=0.45). These response rates are comparable to those observed by Papakostas et al. (2007), who reported response rates of 66% for SSRIs and 72% for SNRIs. Although the response rates were slightly higher in the SNRI group, the lack of statistical significance between the groups suggests that both classes of antidepressants are similarly effective in achieving significant symptom reduction in MDD patients.[9] Similarly, the remission rates, defined as a HAM-D score of ≤ 7, were also comparable between the two groups (50% for SSRIs and 53.3% for SNRIs), reflecting similar treatment efficacy in terms of achieving remission. This aligns with the findings of Trivedi et al. (2006), who noted no significant differences in remission rates between SSRI and SNRI treatments.[10]

Regarding side effects, both groups experienced similar adverse effects, including nausea, insomnia, dizziness, and sexual dysfunction, with no significant differences in the frequency of these side effects between the two groups (Table 4). These results are consistent with previous studies, such as those by Wilson et al. (2010), who found that both SSRIs and SNRIs commonly cause side effects like nausea and sexual dysfunction but with no major differences in side effect profiles.[11] In this study, the most commonly reported side effect was nausea (30% for SSRIs and 36.7% for SNRIs), followed by insomnia (23.3% for SSRIs and 28.3% for SNRIs), which is consistent with the findings from other clinical trials comparing these medications (Fava et al., 2006). Importantly, the data suggests that while side effects are prevalent in both groups, they do not significantly affect the overall tolerability between SSRIs and SNRIs.[12]

One of the key findings in this study was the significant improvement in the quality of life among participants in both treatment groups. All domains of the WHOQOL-BREF scale (Physical Health, Psychological Well-Being, Social Relationships, and Environment) showed significant improvements from baseline to Week 8, with p-values less than 0.001. This result is consistent with a study by Demyttenaere et al. (2008), who also found significant improvements in quality of life with both SSRIs and SNRIs, particularly in the psychological and social domains. The improvements observed in this study suggest that the reduction in depressive symptoms achieved by both treatments had a positive impact on the patients' overall well-being, highlighting the importance of considering quality of life outcomes in antidepressant treatment trials.[13]

Finally, when comparing these results with other studies on SSRIs and SNRIs, it is evident that while there are minor differences in efficacy and side effects, the overall findings support the clinical equivalence of these two classes of antidepressants. The consistent improvements in depressive symptoms and quality of life observed in this study are in line with previous literature, which supports the broad applicability of SSRIs and SNRIs in treating MDD (Gartlehner et al., 2011). Despite some variation in response and side effect profiles, both treatments remain viable options for the management of depression.[14]

CONCLUSION

In conclusion, this study demonstrates that both SSRIs and SNRIs are equally effective in reducing depressive symptoms and improving quality of life in patients with Major Depressive Disorder. Both treatment groups showed significant improvements in

HAM-D scores, response rates, and remission rates, with no significant differences between them. Additionally, the side effect profiles were similar across both groups. These findings suggest that both classes of antidepressants are viable and effective options for treating MDD, with clinical decision-making potentially guided by individual patient preferences and tolerability.

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