Original Article

# A Comparative Study of Vilazodone and Escitalopram in Major Depressive Disorder

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## ABSTRACT

***Introduction:*** Several Selective serotonin reuptake inhibitors (SSRIs) have been developed to enhance treatment outcomes for Major Depressive Disorder (MDD). Vilazodone is recommended as an effective treatment option for patients diagnosed with MDD who exhibit symptoms of anxiety. Although escitalopram is a frequently prescribed antidepressant, there is a shortage of knowledge about the usage and outcomes of vilazodone use. This study was conducted to evaluate and compare the efficacy of escitalopram and vilazodone in MDD.

***Methodology:*** 100 patients were allotted equally into two different groups as per a computer-generated random table. Group A received escitalopram 10 mg/day and group B received vilazodone 20 mg/day. Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) were evaluated at baseline and at 4, 8, and 12 weeks.

**Result:** Patients with depression showed lower HAM-D scores after both escitalopram and vilazodone treatment at 4, 8, and 12 weeks as compared to baseline. Both escitalopram and vilazodone-treated groups decrease HAM-A scores at 4, 8, and 12 weeks. In both groups more decrease in HAM-A score at 12 weeks was found as compared to 8 weeks. At 12 weeks, a more lowering of HAM-A score was found with escitalopram as compared to vilazodone (p-value < 0.0001).

***Conclusion:*** No significant difference in the primary outcome of depression between vilazodone and escitalopram groups as both these drugs were equally efficacious in decreasing HAM-D score whereas escitalopram was found to be better in reducing the HAM-A score than vilazodone.

**Keywords:** Escitalopram, Vilazodone, Major Depressive Disorder (MDD), Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale.

## INTRODUCTION

Depression is a common mental disorder characterized by depressed mood or loss of pleasure or interest in activities for long periods.[1] As per the March 2023 report by the World Health Organization (WHO), around 3.8% of the population experiences depression, with rates of 5% among adults and 5.7% among adults aged over 60 years.[1] Depression commonly occurs alongside chronic medical illnesses and can exacerbate their associated health outcomes. Depression was found to coexist in 9% to 23% of individuals with at least one chronic physical illness like angina, arthritis, asthma, or diabetes and this incidence was significantly higher than depression in the general population.[2] These findings highlight the need for safe and effective treatments for individuals diagnosed with comorbid depression. Approaches that decrease hospitalization rates and support a return to active employment could substantially alleviate the impact of depression.

In recent years, several antidepressants with dual nor-epinephrine and serotonin action like those seen with tertiary amine tricyclic antidepressants, but with minimal or no non-selective histaminergic or cholinergic effects have been developed. The introduction of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) has enhanced treatment outcomes for Major Depressive Disorder (MDD).

Escitalopram, the S-enantiomer of citalopram, is among the most commonly prescribed SSRIs for treating MDD in individuals aged 12 and older. It is effective, affordable, and linked to the highest likelihood of remission.[3] A meta-analysis indicates that escitalopram outperforms other SSRIs.[4] Vilazodone is a relatively new antidepressant that strongly and selectively inhibits serotonin reuptake and binds with high affinity to 5-HT1A receptors.[5] The effectiveness of vilazodone at a dosage of 40 mg/day in treating Major Depressive Disorder (MDD) was established through double-blind, placebo-controlled clinical trials lasting 8 weeks.[6,7] Vilazodone is also recommended as an effective treatment option for patients diagnosed with Major Depressive Disorder (MDD) who exhibit symptoms of anxiety.[5] Although escitalopram is a frequently prescribed antidepressant, there is a shortage of knowledge about the usage and outcomes of vilazodone use.

This study was conducted to evaluate and compare the efficacy of escitalopram and vilazodone in MDD. This study will greatly assist treating clinicians and the public in selecting a more effective treatment option.

## METHODOLOGY

The Department of Pharmacology, in collaboration with the Department of Psychiatry at SGT Medical College and Hospital, Gurugram, conducted a 12-week open-label study, from April 2020 to June 2020 after approval of IEC vide number IEC/FMHS/F/17/02/20-7. The study included 100 patients diagnosed with major depression from the psychiatry outpatient department (OPD) who met the inclusion criteria. Inclusion criteria are (1) Patients who have been symptomatic for at least 2 weeks & who fulfil the diagnostic criteria for a single or recurrent major depressive disorder, as defined by the International Classification of Diseases (ICD-10) will be enrolled in the study, (2) Patients in the age group of 18-65 years, (3) Patients with intelligent quotient (IQ) within normal range, (4) Patients with whom a reliable informant is available, and (5) Patients who were drug naive or who have not been on any antidepressant in last 2 weeks before screening. Exclusion criteria are (1) Patients with Bipolar depression, (2) Patients with severe depressive disorders with psychotic symptoms, (3) Patients with co-morbid substance-related disorders except nicotine, and (4) Patients with a history of treatment-resistant depression. For this study, treatment-resistant depression will be defined as failure to respond to 2 adequate trials of antidepressants from different classes for at least 6 weeks of duration, (5) Patients with a history of hypersensitivity to escitalopram and vilazodone in the past, (6) Patients who are pregnant and lactating, (7) Any history of medical, surgical, neurological complication or any other condition in which these medications are contraindicated, and (8) History of previous nonresponse to escitalopram and vilazodone.

After enrolment written informed consent was obtained from a legal guardian after explaining the nature & purpose of the study. 100 patients were allotted equally into two different groups as per a computer-generated random table. Group A received escitalopram 10 mg/day and group B received vilazodone 20 mg/day. Concomitant medications like intermediate-acting benzodiazepines (lorazepam, alprazolam) for sleep disturbances, and beta-blockers for somatic anxiety were permitted. To ensure compliance, patients were asked to bring the empty strips of medicine on follow-up visits. The Hamilton Depression Rating Scale (HAM-D) is a clinician-administered tool used to assess the severity of depression. It consists of 17 items, with 8 items scored on a 5-point scale ranging from 0 to 4, and 9 items scored on a 3-point scale ranging from 0 to 2.[8] The Hamilton Anxiety Rating Scale (HAM-A) comprises 14 items, each rated on a scale from 0 (not present) to 4 (severe), with a total score ranging from 0 to 56.[9] Both scales were evaluated at baseline and at 4, 8, and 12 weeks.

### Statistical Analysis

Statistical analysis was done on those participants who completed the study. Continuous variable data were presented as mean ± SD and categorical variable data as percentages. One-way ANOVA with Sidak's post-hoc test was used to assess statistical significance in treated groups. A p-value of $< 0.05$ was considered statistically significant. Graph Pad Prism 8.0.2 software was used for statistical analysis.

## RESULTS

Eight participants out of 100 lost in follow-up (4 from each group). Finally, 92 participants were included in the statistical analysis. In escitalopram and vilazodone treatment groups 54.3% and 50.0% were female and the average age of the participants was 37±12 and 39±11 (mean±SD) years respectively. The baseline variable detail of participants is given in Table 1.

Baseline analysis using both HAM-D and HAM-A scales showed that the patients were with moderate depression and moderate anxiety respectively (Fig 1 and 2) and there was no baseline differences in the groups treated with escitalopram and vilazodone.

**Table 1:** Demographic variables of participants at baseline.

| Variables | | Escitalopram (n=46) | Vilazodone (n=46) |
|---|---|---|---|
| Female | | 54.3% (n=25) | 50.0% (n=23) |
| Age (years), Mean ± SD | Female | 37.6±12.5 | 39.1±11.5 |
| | Male | 37.1±12.4 | 39.1±11.4 |
| Employment | Employed | 26 | 27 |
| | Unemployed | 19 | 17 |
| | Retired | 1 | 2 |
| Education | uneducated | 6 | 5 |
| | Secondary school | 16 | 16 |
| | High secondary | 12 | 10 |
| | Graduate | 9 | 11 |
| | Postgraduate | 3 | 4 |
| living in urban areas | | 27 | 30 |

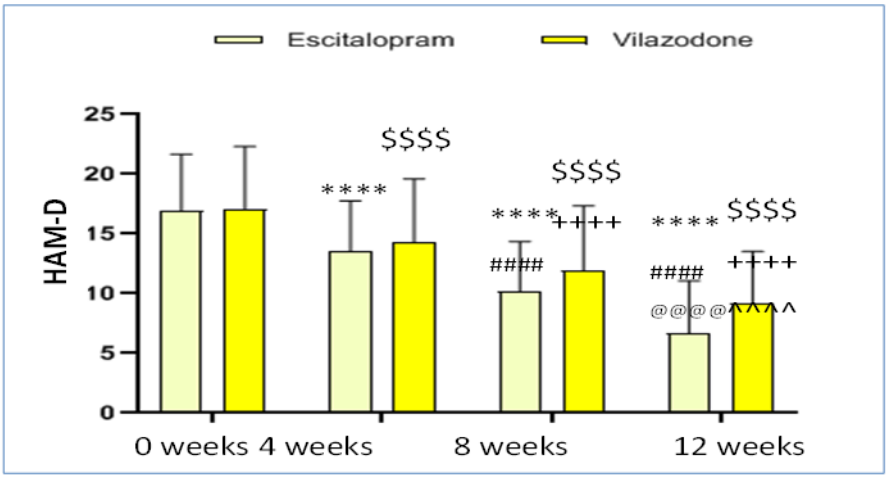


**Figure 1:** Hamilton depression rating scale (HAM-D) scores in patients treated with escitalopram (10 mg) and vilazodone (20 mg) at 0, 4, 8, and 12 weeks. *As compared to escitalopram 0 week; # as compared to escitalopram 4 weeks; @ as compared to escitalopram 8 weeks; $ as compared to vilazodone 0 week; + as compared to vilazodone 4 weeks; ^ as compared to vilazodone 8 weeks.

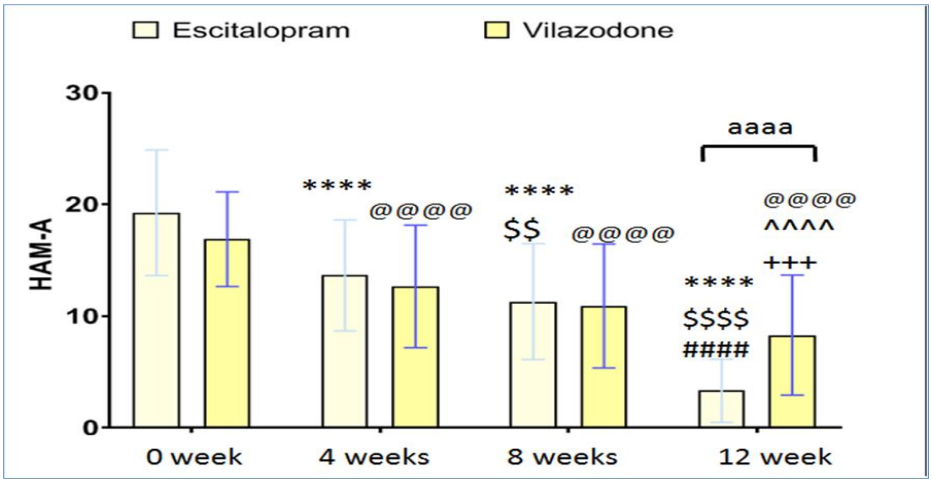


**Figure 2:** Hamilton anxiety rating scale (HAM-A) scores in patients treated with escitalopram (10 mg) and vilazodone (20 mg) at 0, 4, 8, and 12 weeks. * As compared to escitalopram 0 week; $ as compared to escitalopram 4 weeks; # as compared to escitalopram 8 weeks; @ as compared to vilazodone 0 week; ^ as compared to vilazodone 4 weeks; + as compared to vilazodone 8 week.

Patients with depression showed lower HAM-D scores after both escitalopram and vilazodone treatment at 4, 8, and 12 weeks as compared to baseline (fig 1) (each p-value < 0.0001; ANOVA with Sidak's post-hoc test). Both escitalopram and vilazodone-treated groups decrease HAM-A scores at 4, 8, and 12 weeks (each p-value < 0.0001; ANOVA with Sidak's post-hoc test) (fig 2). In both groups, more decrease in HAM-A score at 12 weeks was found as compared to 8 weeks (escitalopram p-value < 0.0001 and vilazodone p-value = 0.0008). At 12 weeks, a more lowering of HAM-A score was found with escitalopram as compared to vilazodone (p-value < 0.0001).

## DISCUSSION

The present study was conducted to compare the effectiveness of vilazodone which is comparatively a newer antidepressant drug with escitalopram a widely used antidepressant in patients with MDD and coexisting anxiety in outpatient settings. Escitalopram is a selective serotonin reuptake inhibitor whereas Vilazodone exerts its action through multiple mechanisms like SERT inhibition along with partial agonistic action on the 5HT1A receptor.[10]

WHO 2017 report on depression shows that the number of females (5.1%) suffering from depression is more as compared to their male (3.6%) counterparts.[11] Our study also had more females (52.17%) out of which 25 were in the escitalopram group and 23 were in the vilazodone group. However, the difference in the number of female and male patients enrolled was not significant.

Lella S et al., 2021 & Bathla M et al., 2018 in their respective study also had more females taking treatment for depression in comparison to males, which is in agreement with our result.[12,13]

In our study, the mean age group of patients was 37.35±12.45 in the escitalopram group and 39.1±11.45 in the vilazodone group. Lella S et al., 2021, Jiang et al., 2017

and Kishi et al., 2017 in their respective studies demonstrated similar trends in the MDD patient's age group as observed in our study.[12,14,15]

The present study used the Hamilton depression rating scale (HAM-D 17) to assess the severity of depression. Baseline analysis using HAM-D showed that the patients were with moderate depression and there was no baseline differences in the groups treated with escitalopram and vilazodone. Patients with depression showed significantly lower HAM-D scores (each p-value < 0.0001) after both escitalopram and vilazodone treatment at 4, 8, and 12 weeks as compared to baseline. Also, a further decline in HAM-D score was seen at 8 weeks as compared to 4 weeks and at 12 weeks as compared to the 8$^{th}$ week in both the vilazodone and escitalopram groups. Similarly, a study done by Kishi T et al 2017,[14] Jiang K et al 2017,[15] and Urade et al. 2015,[16] found escitalopram to be more efficacious in causing a decrease in HAM-D score. Mathews M et al. 2015 demonstrated that vilazodone caused a decline in HAM-D score in patients presenting with MDD.[17]

In a study conducted by Kadam RL et al 2020, Ankushe RD et al 2022, S. Lella et al 2021, and Adiyogi A et al 2020, Vilazodone was found to be causing more decline in HAM-D scores than escitalopram in patients with depression.[5,10,12,18] However, in our study on intergroup comparison after 12 weeks, the difference between HAM-D score of patients treated with vilazodone and escitalopram was not found to be statistically significant. Similar results as observed in our study were noticed in a study done by Kadam RL 2020, Shweta C et al 2018, Kumar PNS et al 2023, Sinha S et al 2021 and Bathla M et al 2018 where they also found no statistically significant difference in lowering HAM-D score on intergroup comparison between vilazodone and escitalopram group.[5,13, 19,20,21] Contrary to our result, a study conducted by and Kudyar P et al 2018 demonstrated more fall in HAM-D score by the escitalopram-treated group than the vilazodone group.[22]

The secondary efficacy outcome of our study was the HAM-A score. Baseline analysis using HAM-A scales showed that the patients were with moderate anxiety and there was no baseline differences in the groups treated with escitalopram and vilazodone. Both escitalopram and vilazodone treated groups demonstrated a significant decrease in HAM-A score at 4, 8, and 12 weeks as compared to baseline.

In both groups more decrease in HAM-A score at 12 weeks was found as compared to 8 weeks (escitalopram p-value < 0.0001 and vilazodone p-value = 0.0008). At 12 weeks, a more lowering of HAM-A score was found with escitalopram as compared to vilazodone (p-value < 0.0001).

Kudyar P et al 2018 in their study also documented that escitalopram is more efficacious in causing a fall in HAM-A score as compared to vilazodone, which is in agreement with our results but we failed to find any other similar report in review of literature.[22] Contrary to our result, Kadam RL 2020 and Ankushe RD et al 2022 found that vilazodone is more efficient in causing a decline in HAM-A score than escitalopram in their study.[5,10] whereas Sinha S et al 2021 concluded that vilazodone is non inferior to escitalopram in decreasing HAM-A score.[21]

There were few limitations in our study. Firstly, it was an open-label study so the chances of bias cannot be ruled out. The second limitation is small sample size so the results cannot be generalized to wider population. Thirdly, we did not evaluate the safety of these drugs.

## CONCLUSION

Our study demonstrated that there's no significant difference in the primary outcome of depression between vilazodone and escitalopram groups as both these drugs were equally efficacious in decreasing HAM-D score whereas escitalopram was found to be better in reducing the HAM-A score than vilazodone. However, we need a larger sample size to extrapolate our study results.

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