



Comparative evaluation of efficacy and tolerability of vilazodone, escitalopram, and amitriptyline in patients of major depressive disorder: A randomized, parallel, open-label clinical study

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Abstract:

OBJECTIVES: To evaluate and compare efficacy and tolerability of Vilazodone with Escitalopram and Amitriptyline in patients of major depressive disorder(MDD).

METHODS: This was a randomized, prospective, parallel-group, open label clinical study in which newly diagnosed patients of MDD were randomized to receive Tab Vilazodone 20 mg daily or Tab Escitalopram 20mg daily or Tab Amitriptyline 75mg daily for 12 weeks. Antidepressant activity was assessed by change in score from baseline to week 12 on HAMD-17 and MADRS scales while change in score on HAM-A scale was used to assess antianxiety effect. Change in scores on the three scales was also compared between the three treatment groups. Severity and causality of adverse events were assessed by the modified Hartwig & Siegel scale and Naranjo scale respectively. Data was analyzed in accordance with per protocol analysis.

RESULTS: Reduction in HAMD-17 and MADRS scores was significantly more in vilazodone group compared to the other two drugs indicating that vilazodone is more efficacious antidepressant. Number of remitters were also significantly more in the vilazodone group ($n=11$) compared to escitalopram ($n=4$) ($p<0.05$) and amitriptyline ($n=0$) ($p<0.001$) at 12 weeks. Similar results were also obtained with HAM-A score. Number of patients showing MADRS sustained response at 12 weeks was statistically significantly more in vilazodone ($n=12$) and escitalopram ($n=12$) groups compared to amitriptyline ($n=01$) ($p<0.001$). Reported adverse events were constipation and sedation(amitriptyline group); nausea and headache(escitalopram and vilazodone groups).These adverse events were of mild severity. Most adverse events belonged to probable category.

CONCLUSION: Vilazodone is more efficacious and well tolerated antidepressant compared to escitalopram and amitriptyline.

Keywords:

17-item Hamilton Depression Rating Scale, antidepressants, depression, Hamilton Anxiety Rating Scale, Montgomery-Asberg Depression Rating Scale

Introduction

Major depressive disorder (MDD) is a widespread, debilitating illness affecting >300 million people of all ages

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worldwide.^[1] Depression is associated with high rates of medical as well as psychiatric comorbidity, functional impairment, and significant personal and societal costs.^[2] The incidence of depression is 50% higher in women than men though it is the

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leading cause of disability in both.^[3] Currently available pharmacotherapeutic agents for the treatment of depression are tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors, and atypical antidepressants.^[4] TCAs are antagonists at nontarget receptors including histaminic, muscarinic, and α_1 -adrenergic receptors which are responsible for innumerable adverse effects such as sedation, weight gain, constipation, visual disturbances, and orthostatic hypotension. Another drawback of TCAs is their slow onset of action; as long as 3–4 weeks or more is required for their antidepressant effect to manifest.^[4]

SSRIs are currently the most commonly prescribed drugs in the treatment of depression despite their inadequate response and adverse drug reactions (ADRs) including gastrointestinal disturbances and sexual dysfunction in many patients.^[4,5] Although two-third of patients improve with initial treatment, only a third of patients remit.^[6] Furthermore, those who do remit often take weeks to do so. Lack of efficacy, in addition to tolerability issues, is the most common contributory factor to noncompliance.^[4] Hence, there is a need of newer antidepressant with equal/better efficacy and improved tolerability.^[7]

Vilazodone, introduced in the United States in 2011, has been described as the first member of the serotonin partial agonist reuptake inhibitor class of medications, combining serotonin reuptake inhibition with 5-HT_{1A} partial agonism. It potently and selectively inhibits reuptake of serotonin and binds selectively with high affinity to 5-HT_{1A} receptors.^[7] The high selectivity of vilazodone for the 5-HT_{1A} receptors could potentially lead to greater tolerability, due to less disruption of other neurotransmitter systems.^[8] Efficacy of vilazodone 40 mg/day in MDD was demonstrated in double-blind, placebo-controlled clinical trials of 8-week duration.^[9,10] Approximately one-half of all patients diagnosed with MDD have clinically significant levels of anxiety.^[11] Residual anxiety symptoms are associated with an increased risk of MDD relapse.^[12] Therapeutic effect of vilazodone in generalized anxiety disorder has also been demonstrated in different randomized, double-blind, placebo-controlled clinical trials.^[13] It is also suggested that vilazodone is an effective treatment option for patients with MDD who have symptoms of anxiety.^[14] Despite extensive literature search, we were unable to find any published studies evaluating the use of vilazodone in Indian population. Escitalopram and amitriptyline are commonly used antidepressants in this hospital. There is no direct study that has reported a head-to-head comparison of efficacy and tolerability of vilazodone, escitalopram, and amitriptyline. Hence, this study was planned to evaluate and compare the efficacy and tolerability of these three drugs in patients of MDD.

Materials and Methods

This was a randomized, prospective, comparative, parallel-group, open-label study conducted from February 2016 to October 2017 in the psychiatry outpatient department of a tertiary care teaching hospital. It was approved by the Institutional Ethics Committee and was carried out in accordance with Good Clinical Practice guidelines and the ethical principles as mentioned in the Declaration of Helsinki (Ethics Committee approval No. 862 EC/Pharmac/GMC/NGP Date: February 2, 2016).

Inclusion criteria: Newly diagnosed patients of MDD (as per the Diagnostic and Statistical Manual of Mental Disorders, Edition V),^[15] of either gender, aged between 18 and 60 years with 17-item Hamilton Depression Rating Scale (HAMD-17) score ≥ 22 ^[16] were included in our study. Patients of severe depression who may not respond to pharmacotherapy alone in the opinion of the psychiatrist; patients on treatment with electroconvulsive therapy within 3 months; those suffering from any other psychiatric disorders except generalized anxiety disorder; those with impaired renal/hepatic function; patients requiring other psychotropic medications, central nervous system (CNS) active drugs, or on drug therapy for any other systemic disorder; patients who have taken an investigational drug or participated in an investigational drug trial within the past 30 days; pregnant and lactating women; and women of reproductive age group who are not practicing a reliable method of contraception were excluded.

Study patients were selected in consultation with the treating psychiatrist. Patients meeting the selection criteria were briefed about the study. Written informed consent in vernacular language was obtained from those willing to participate. A detail medical history was obtained and physical examination was performed, and liver function, kidney function, and random blood glucose were estimated to rule out any systemic illness. Selected patients were randomly assigned using random number tables to receive either tablet vilazodone 20 mg daily (Tab Valz manufactured by Torrent Pharmaceuticals) or tablet escitalopram 20 mg daily (Tab Feliz S manufactured by Torrent Pharmaceuticals) or tablet amitriptyline 75 mg daily (Tab Amitone manufactured by Intas Pharmaceuticals) for 12 weeks. Regular counseling about the disease, its treatment, and treatment outcomes was provided to all patients in all the three study groups.

The primary efficacy parameter was change in score on HAMD-17 from baseline to week 12. More than or equal to 20% improvement in scores from baseline to the first 2 weeks of treatment is considered clinically meaningful

improvement.^[17] Remitters are defined as those with a HAMD-17 total score <7.^[18] The secondary efficacy parameters were change in score on Montgomery–Asberg Depression Rating Scale (MADRS) from baseline to week 12 and change in score on Hamilton Anxiety Rating Scale (HAM-A) from baseline to week 12. MADRS-sustained response was defined as MADRS total score ≤12 for at least last two consecutive visits.^[10] General clinical safety was monitored by vigilant follow-up of patients and recording of adverse events. Severity of adverse events was assessed by the Modified Hartwig and Siegel Scale.^[19] Causality of adverse events was assessed by the Naranjo ADR Probability Scale. Follow-up visits were carried out at 2, 4, and 12 weeks. Patients were asked to report at each follow-up visit with the empty blister packs so as to assess compliance to treatment. Eighty percent of adherence to treatment was considered as compliant. It was decided that, in the opinion of the psychiatrist, if any patient was not responding to drug therapy or his condition was worsening at any point during the course of study, the patient would be removed from the study and managed by the psychiatrist. At the end of the study, the treatment was continued or modified as per decision of the psychiatrist. No posttrial access to medicine was considered at the end of the study, and the same was intimated to the eager participants before their enrollment in the study.

Statistical analysis

The sample size was calculated based on change in HAMD score from baseline to week 12 (11) and standard deviation (SD) = 10.38 from previous studies, with level of significance $\alpha = 0.5\%$ and power = 80%. The required sample size turned out to be 16. However, considering dropout rate of 20%, we included 20 patients in each treatment group. The sample size was calculated

using Power and Sample Size Calculation software version 3.0.43 with the help of a statistician. Categorical data were analyzed by Chi-square test. For continuous variables, one-way ANOVA was used. All primary and secondary efficacy parameters were analyzed by Friedman test followed by Dunn's *post hoc* test for within-group comparison at different follow-up visits while Kruskal–Wallis test followed by Dunn's *post hoc* test was used for comparison between different groups. $P < 0.05$ was considered as statistically significant. GraphPad Prism version 5.01 (GraphPad software Inc., California, USA) was used for analysis.

Results

A total of sixty patients were randomized and allocated to three treatment groups, of which fifty patients completed the study according to the protocol with regular follow-up. There were ten dropouts: three in the amitriptyline group (two due to ADRs and one due to lack of efficacy), four in the escitalopram group (one due to ADRs, one due to lack of efficacy, and two lost to follow-up), and three in the vilazodone group (one due to ADRs and two lost to follow-up). Data were analyzed in accordance with per-protocol analysis.

The baseline demographic characteristics and clinical parameters of study patients are shown in Table 1.

Table 2 shows that HAMD-17 scores were statistically significantly lower at 4 and 12 weeks compared to baseline in all the three-group scores ($P < 0.001$).

It was observed that in all the three treatment groups, MADRS scores were statistically significantly lower at 4 and 12 weeks compared to baseline ($P < 0.001$) [Table 3].

Table 1: Baseline demographic characteristics and clinical parameters in study patients

| Parameters | Amitriptyline (n=17) | Escitalopram (n=16) | Vilazodone (n=17) | P |
|---------------------------|----------------------|---------------------|-------------------|-------------------|
| Gender ratio (men: women) | 8:9 | 10:6 | 9:8 | 0.66 ^s |
| Age (years) | 38.82 (13.46) | 34.43 (12.07) | 35.94 (13.68) | 0.62 [#] |
| Weight (kg) | 48.70 (4.17) | 47.93 (5.09) | 50.41 (4.06) | 0.27 [#] |
| HAMD-17 score | 24.94 (2.46) | 24.19 (2.66) | 24.47 (1.58) | 0.44 [#] |
| MADRS score | 27.59 (1.87) | 26.13 (2.06) | 26.47 (2.06) | 0.07 [#] |
| HAM-A score | 13.94 (0.96) | 13.25 (1.06) | 13.18 (0.95) | 0.06 [#] |

Values are expressed as mean (SD). ^sChi-square test, [#]One-way ANOVA test, ^{*}Kruskal-Wallis test. HAMD-17=17-item Hamilton Depression Rating Scale, MADRS=Montgomery-Asberg Depression Rating scale, HAM-A=Hamilton Anxiety Rating Scale, SD=Standard deviation

Table 2: Effect of study drugs on 17-item Hamilton Depression Rating Scale scores in patients of major depressive disorder

| Study drugs | HAMD-17 scores | | | |
|----------------------|----------------|--------------|---------------|---------------|
| | Baseline | 2 weeks | 4 weeks | 12 weeks |
| Amitriptyline (n=17) | 24.94 (2.46) | 21.53 (1.80) | 15.41 (2.15)* | 11.06 (1.98)* |
| Escitalopram (n=16) | 24.19 (2.66) | 19.25 (1.98) | 14.44 (2.12)* | 9.00 (3.05)* |
| Vilazodone (n=17) | 24.47 (1.58) | 17.59 (2.80) | 10.71 (2.61)* | 5.80 (1.50)* |

Values are expressed as mean (SD). * $P < 0.001$ when compared to baseline by Friedman test followed by Dunn's *post hoc* test. HAMD-17=17-item Hamilton Depression Rating Scale, SD=Standard deviation

Table 3: Effect of study drugs on Montgomery-Asberg Depression Rating scale scores in patients of major depressive disorder

| Study drugs | MADRS scores | | | |
|----------------------|--------------|--------------|---------------|---------------|
| | Baseline | 2 weeks | 4 weeks | 12 weeks |
| Amitriptyline (n=17) | 27.59 (1.87) | 24.06 (2.72) | 16.71 (3.49)* | 10.94 (2.56)* |
| Escitalopram (n=16) | 26.13 (2.06) | 19.06 (2.79) | 12.13 (3.32)* | 6.68 (3.09)* |
| Vilazodone (n=17) | 26.47 (2.06) | 17.71 (3.13) | 9.52 (3.67)* | 4.11 (1.57)* |

Values are expressed as mean (SD); * $P < 0.001$ when compared to baseline by Friedman test followed by Dunn's *post hoc* test. MADRS=Montgomery-Asberg Depression Rating scale, SD=Standard deviation

Table 4: Effect of study drugs on Hamilton Anxiety Rating Scale scores in patients of major depressive disorder

| Study drugs | HAM-A scores | | | |
|----------------------|--------------|--------------|--------------|--------------|
| | Baseline | 2 weeks | 4 weeks | 12 weeks |
| Amitriptyline (n=17) | 13.94 (0.96) | 11.65 (1.76) | 8.64 (2.02)* | 6.82 (1.70)* |
| Escitalopram (n=16) | 13.25 (1.06) | 10.88 (2.30) | 7.90 (1.90)* | 6.20 (1.70)* |
| Vilazodone (n=17) | 13.18 (0.90) | 9.05 (2.50) | 5.76 (1.78)* | 3.35 (0.99)* |

Values are expressed as mean (SD); * $P < 0.001$ when compared to baseline by Friedman test followed by Dunn's *post hoc* test. HAM-A=Hamilton Anxiety Rating Scale, SD=Standard deviation

Table 5: Comparison of reduction in 17-item Hamilton Depression Rating Scale, Montgomery-Asberg Depression Rating Scale, and Hamilton Anxiety Rating Scale score between study drugs in patients of major depressive disorder

| Study drugs | Reduction in score | | |
|----------------------|------------------------------|---------------------------|-------------------|
| | Amitriptyline (n=17) | Escitalopram (n=16) | Vilazodone (n=17) |
| HAMD-17 | | | |
| Baseline to 2 weeks | 3.41 (1.50)** | 4.93 (1.73) | 6.88 (3.23) |
| Baseline to 4 weeks | 9.52 (1.90)** | 9.75 (2.14) [§] | 13.76 (3.21) |
| Baseline to 12 weeks | 13.88 (2.69)** | 15.18 (3.14) [§] | 18.65 (2.14) |
| MADRS | | | |
| Baseline to 2 weeks | 3.52 (1.32) ^{#,**} | 7.06 (1.91) | 8.76 (2.86) |
| Baseline to 4 weeks | 10.88 (2.84) ^{#,**} | 14.00 (2.65) | 16.94 (3.92) |
| Baseline to 12 weeks | 16.65 (2.44) ^{#,**} | 19.44 (2.89)* | 22.35 (2.11) |
| HAM-A | | | |
| Baseline to 2 weeks | 3.52 (1.32) ^{#,**} | 7.06 (1.91) | 8.76 (2.86) |
| Baseline to 4 weeks | 10.88 (2.84) ^{#,**} | 14.00 (2.65) | 16.94 (3.92) |
| Baseline to 12 weeks | 16.65 (2.44) ^{#,**} | 19.44 (2.89)* | 22.35 (2.11) |

Values are expressed as mean (SD), Kruskal-Wallis test followed by Dunn's *post hoc* test. * $P < 0.05$ when compared to vilazodone, [§] $P < 0.05$ when compared to escitalopram, [#] $P < 0.01$ when compared to escitalopram, [§] $P < 0.01$ when compared to vilazodone, ** $P < 0.001$ when compared to vilazodone. HAMD-17=17-item Hamilton Depression Rating Scale, MADRS=Montgomery-Asberg Depression Rating scale, HAM-A=Hamilton Anxiety Rating Scale, SD=Standard deviation

In all the three treatment groups, there was a statistically significant reduction in HAM-A scores at 4 and 12 weeks compared to baseline [Table 4].

Table 5 shows that reduction in HAMD-17 score in the vilazodone group was statistically significantly higher compared to the amitriptyline group at all follow-up visits ($P < 0.001$). Reduction in score in the vilazodone group was statistically significantly higher compared to the escitalopram group at 4 and 12 weeks ($P < 0.01$) [Table 5]. Reduction in MADRS score in the vilazodone group was statistically significantly higher compared to the amitriptyline group at all follow-up visits ($P < 0.001$) [Table 5]. Table 5 also shows that reduction in HAM-A score in the vilazodone group was statistically significantly higher compared to both the amitriptyline and escitalopram groups at 2 weeks, 4 weeks ($P < 0.05$), and 12 weeks ($P < 0.001$).

The number of patients attaining remission was statistically significantly more in the vilazodone ($n = 11$) group compared to the escitalopram group ($n = 4$) ($P < 0.05$) and the amitriptyline group ($n = 0$) ($P < 0.001$) at 12 weeks. Patients attaining clinically meaningful improvement (having $\geq 20\%$ improvement in HAMD-17 score from baseline to 2 weeks) were 11.76% in the amitriptyline group, 56.25% in the escitalopram group, and 70.58% in the vilazodone group. The number of patients showing MADRS-sustained response at 12 weeks was statistically significantly more in the vilazodone ($n = 12$) and escitalopram ($n = 12$) groups compared to the amitriptyline group ($n = 1$) ($P < 0.001$).

Constipation ($n = 2$) and sedation ($n = 7$) were the reported adverse events in the amitriptyline group. Among the escitalopram and vilazodone groups, nausea ($n = 2$ in each group) and headache ($n = 3$ in the

vilazodone group; $n = 2$ in the escitalopram group) were the reported adverse events. On the basis of the Modified Hartwig and Siegel Scale of severity assessment, all the adverse events were categorized as mild (level 1) in severity. Causality of adverse events as assessed by the Naranjo Scale showed constipation, sedation, and nausea to be probable while headache was possible.

Discussion

In this study, a significant reduction in HAMD-17 and/or MADRS scores compared to baseline was evident at 4 weeks in the vilazodone group. It was reported that vilazodone in a dose of 40 mg/day led to a statistically significant decrease in HAMD-17 and/or MADRS scores following 8-week treatment of MDD in adults in different placebo-controlled studies.^[9,10] In various studies, a significant reduction in HAMD-17 and MADRS scores in patients of MDD following vilazodone treatment was reported as early as 1 or 2 weeks.^[9,10] However, most of the studies reporting a significant reduction of score with vilazodone at 2 weeks were placebo-controlled studies, and a significant reduction in HAMD-17/MADRS scores at week 1 or week 2 was in comparison to placebo. While in our study, reduction in scores at two weeks was significantly more with vilazodone than amitriptyline though it was similar to escitalopram. This indicates that even at 2 weeks, vilazodone was more efficacious than amitriptyline. In our study, reduction in HAMD-17 and MADRS scores was highest in the vilazodone group compared to the other two groups at week 4 and week 12, suggesting that vilazodone is more efficacious than the other two study drugs. Most of the published studies evaluating the antidepressant activity of vilazodone are placebo-controlled. We came across only one published study to date which included an SSRI comparator (citalopram), vilazodone (20 and 40 mg), and placebo. The results of this study indicated that each of the active medication-treated groups was superior to placebo, but there was no direct comparison between the active agents.^[5] Hence, we do not have published data about comparison of antidepressant activity of vilazodone with other antidepressants to compare with our study results.

Better efficacy of vilazodone observed in this study may be due to its unique mechanism of action: SSRI and 5-HT_{1A} receptor partial agonism. Although the exact mechanism of action of this combined activity is not known, it is believed that antidepressant effect of vilazodone derives mainly from the SSRI activity, which stimulates serotonergic transmission in the CNS by inhibiting the reuptake of serotonin by the serotonin transporter, while the 5-HT_{1A} partial agonist activity is thought to enhance the antidepressant effect by facilitating the desensitization of presynaptic 5-HT_{1A}

autoreceptors. It is postulated that vilazodone produces faster and greater desensitization of the presynaptic 5-HT_{1A} autoreceptors, thereby enhancing serotonin levels, presumed to be associated with antidepressant activity.^[20]

It is reported that patients who experience clinically meaningful improvement (i.e., $\geq 20\%$ improvement from baseline) in depressive symptoms in the first 2 weeks of treatment have a greater likelihood of stable treatment response and remission of symptoms.^[17] In the vilazodone group, the highest number (70.58%) of patients had $\geq 20\%$ reduction in scores from baseline to 2 weeks, suggesting that more number of patients are likely to achieve remission with vilazodone. The results of our study support this statement which can be seen from the frequency of remission (HAMD-17 score < 7) at 12 weeks which was significantly higher in the vilazodone group compared to both the amitriptyline and escitalopram groups. Remission rate was found to be 65% at the end of 12 weeks for vilazodone. Different rates of remission with vilazodone varying from 34% to 42.4% after 8 weeks of treatment have been reported in different studies.^[10,21] Remission rates with vilazodone observed in our study are higher as these are the rates after 12 weeks of treatment in contrast to the published literature which mentions remission rates at 8 weeks. Rates of remission are likely to be higher at 12 weeks than at 8 weeks because 8-week duration of the trials may have been insufficient for some patients to attain remission of symptoms, and more patients might have remitted with longer treatment.^[22] Remission rates with antidepressant medication are known to be cumulative and show an increase with increasing duration of treatment.^[23] Remission rates in our study cannot be compared with that reported in literature since this study did not have follow-up visit at 8 weeks which can be considered one of the lacunae of our study.

MADRS-sustained response (MADRS score ≤ 12 for at least the last two consecutive visits) was comparable in the vilazodone and escitalopram groups and was significantly higher than the amitriptyline group at 12 weeks. MADRS-sustained response is an efficacy outcome that was developed with guidance from the food and drug administration to show evidence of treatment benefits that are maintained beyond an individual time point in a short-term study.^[5] Comparable rates of MADRS-sustained response with vilazodone and citalopram have been reported.^[5] Higher rates of MADRS-sustained response as observed with vilazodone and escitalopram indicate that treatment benefits are maintained beyond a single time point.

Most of the published studies evaluating the efficacy of vilazodone have used a dose of 40 mg/day. However,

studies comparing doses of 20 mg and 40 mg/day of vilazodone have also reported statistically significant beneficial effects with no significant differences between the different vilazodone doses.^[5,24] One published study even reported that dose of vilazodone above 20 mg/day did not result in an additional decrease in MADRS scores.^[25] Further, one study has reported that tolerability is better with 20 mg dose of vilazodone than 40 mg.^[5] Hence, we chose 20 mg dose of vilazodone in our study, while the doses of escitalopram and amitriptyline that we used are the standard doses of these drugs as mentioned in standard textbooks.^[4]

Reduction in HAM-A score was observed in the vilazodone group at 4 and 12 weeks compared to baseline suggesting beneficial effect of vilazodone in anxiety. Therapeutic effect of vilazodone in dose of 20 mg/40 mg/day in generalized anxiety disorder has been demonstrated in double-blind, randomized, placebo-controlled clinical trials, wherein a significant reduction in HAM-A scores from baseline to week 8 was reported.^[13] Efficacy of vilazodone has also been reported in patients of MDD with prominent anxiety symptoms in a pooled analysis of two Phase III studies.^[14] Even SSRIs, including escitalopram, are considered to be effective therapy for anxiety disorders.^[26] Although TCAs are comparable in efficacy to the SSRIs for anxiety disorders, they are usually not preferred for this condition due to poor tolerability profile.^[27] An extensive search of literature did not reveal any published study comparing antianxiety effect of vilazodone with an active comparator. In our study, all the three study drugs demonstrated a significant reduction in HAM-A score at 4 weeks though the reduction was significantly higher in the vilazodone group. This indicates that vilazodone is more efficacious antianxiety agent than the other two study drugs. Of all diagnosed patients of MDD, about one-half have clinically meaningful levels of anxiety, which complicates clinical management and can affect treatment outcomes.^[12] Hence, it is desirable to have an antidepressant with significant antianxiety action for these patients. In addition to being a SSRI, vilazodone also acts as a partial agonist at the 5-HT_{1A} receptor, which may contribute to its anxiolytic property.^[28] There was no statistically significant change in any of the laboratory parameters in all the three treatment groups at 12 weeks.

Adverse effects with antidepressant drugs are common and can negatively impact patient outcomes. In this study, the percentage of patients having adverse events was comparable in the vilazodone (29.41%) and escitalopram (25%) groups, while it was significantly higher in the amitriptyline group (52.94%). Intolerability to medication is one of the most common reasons of discontinuation of antidepressant treatment.^[29] Constipation and sedation were major adverse events

reported with amitriptyline, which are known adverse effects of this drug. Nausea and headache were major adverse events reported in both the escitalopram and vilazodone groups. Gastrointestinal adverse events such as nausea, vomiting, and diarrhea are reported in almost every published study that evaluated the safety and efficacy of vilazodone.^[5,9,30] These adverse events were of mild severity, lasted for a short period, and resolved over time. Sexual dysfunction is a common adverse effect of SSRIs which are currently the most commonly used antidepressants.^[4] Published literature about vilazodone suggests that it has lesser adverse effects on sexual function.^[30] However, in our study, no adverse effect on sexual function was reported in either the escitalopram or vilazodone group. One of the reasons for this might be the small sample size in our study, and second, we did not use any measurable criterion (e.g., various scales) for evaluating effect of study drugs on sexual function.

Limitations

First, this was an open-label study, so more chances of bias. Second, the small sample size in our study restricts the generalizability of study results to wider population. Third, assessing adverse effects on sexual functions was difficult since we did not use any measurable criteria for the same.

Conclusion

Although the results of our study show that vilazodone is more efficacious antidepressant compared to escitalopram and amitriptyline, the small sample size of this study does not allow generalization of the study results. Further, high cost of vilazodone can be another hindrance in the use of this drug. Hence, it can be suggested that vilazodone can be considered as a treatment option in selected group of MDD patients who have coexisting anxiety and who do not respond satisfactorily to the already established drugs. However, even this needs to be substantiated by large-scale studies with larger sample size and having an active comparator group.

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Conflicts of interest

There are no conflicts of interest.

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