A 12-week Comparative Prospective Open-label Randomized Controlled Study in Depression Patients Treated with Vilazodone and Escitalopram in a Tertiary Care Hospital in North India

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ABSTRACT

Background: Depression is a leading cause of morbidity in modern world and introduction of selective serotonin reuptake inhibitors (SSRIs) was a revolution for treating depression. However, sexual dysfunction and weight gain always remained an issue for patients leading to discontinuation of treatment. Vilazodone is a novel SSRI and literature show better efficacy and decrease weight gain and sexual dysfunction. Aim of study: This study aims to compare the efficacy, sexual dysfunction, and weight gain caused due to vilazodone and escitalopram. Methodology: This is an open-label randomized, controlled study; 60 patients diagnosed as depression were divided into two groups of 30 each. One group was started on vilazodone and one on escitalopram randomly. The groups were compared on the basis of efficacy, weight gain, and sexual dysfunction by applying Hamilton Depression Rating Scale (HDRS) and Arizona Sexual Experience Scale (ASEX) at baseline, 4, and 12 weeks interval. Statistical analysis was done by applying Chi-square, t-test, and fisher exact test and descriptive analysis. Results: Vilazodone group shows fall in HDRS with 18.77 ± 4.3, 14.83 ± 3.68, and 9.63 ± 3.06 while it was 18.8 ± 4.09, 14.3 ± 2.96, and 8.43 ± 2.1 at baseline, 4, and 12 weeks, respectively. ASEX score in vilazodone was found to have 16.87 ± 2.97, 15.37 ± 3.1, and 11.73 ± 3.55 while on escitalopram, 16.4 ± 3.35, 17.13 ± 3.48, and 18.37 ± 4.09 at first visit, 4, and 12 weeks, respectively. Patients on vilazodone had mean weight of 69.63 ± 7.7, 69.83 ± 7.83, and 69.9 ± 7.69 while on escitalopram, 72.47 ± 7.95, 72.87 ± 7.9, and 75.6 ± 8.46 at baseline, 4, and 12 weeks, respectively. Conclusions: Our study shows that vilazodone has better efficacy, lesser weight gain, and lesser sexual dysfunction.

Key words: Escitalopram, sexual dysfunction, vilazodone, weight gain

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INTRODUCTION

Depression is a major disorder of public health importance and is one of the major causes of morbidity as well as mortality, and it is predicted to be second leading cause of burden of disease worldwide by 2030.[1]

Depression also increases the risk of other medical conditions and further reduces the quality of life. The report on global burden of disease estimates the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women, and the 1-year prevalence has been estimated to be 5.8% for men and 9.3% for women.[1]

Introduction of antidepressants was a revolution in the treatment of depression. Response and remission remain the ultimate goal of treatment of depression. A response to treatment is defined as 50% reduction in Hamilton Depression Rating Scale (HDRS) or Montgomery–Asberg Depression Rating Scale score from the baseline because with older drugs only up to 50% response was possible, but the introduction of newer antidepressant drugs full remission is considered as the goal of treatment. As per studies up to 60% will achieve a response and 28% will have full remission. Selective serotonin reuptake inhibitor (SSRI) and serotonin–norepinephrine reuptake inhibitors (SNRIs) are the preferred class of antidepressants for depressive disorders. All antidepressants are not as effective as the other counterparts in all kinds of patient. Choice of antidepressants depends on various factors such as clinical features, medical, and psychiatric comorbidities and adverse effects such as weight gain and sexual dysfunction. Although relative efficacy, improved adverse effect profile and very less chances of toxicity in overdose as compared to older antidepressants, but still the adverse effects of SSRIs remain the most common reason for discontinuation of treatment because of which the risk of relapse and recurrence increases. The most common cause of discontinuation of SSRIs is the treatment emergent sexual dysfunction which is figured up to 24%–73%.[2]

Escitalopram is a SSRI, for which the research has shown better efficacy and least side effect profile as compared to other SSRIs and SNRIs.[1,3]

As all the SSRIs[3] and SNRIs have its own major side effects of delayed onset of action and sexual dysfunction which remained a major reason for discontinuing the treatment and overall increase in the burden of illness. Hence, there remains a need of a newer antidepressant which can have rapid onset of action and better tolerability and better side effect profile, including sexual dysfunction, weight gain, and other adverse effects.

Vilazodone has been termed as a serotonin partial agonist reuptake inhibitor SPARI which is partial agonist of 5HT1A. The daily recommended dose for use in depressive disorder is up to 40 mg. This is newer antidepressant which was approved by the Food and Drug Administration in January 2011. Dual action on serotonin reuptake inhibition and partial agonism on 5HT1A increase its antidepressant effect and its tolerability. Studies have shown that vilazodone has better side effect profile and early onset of action as compared to other SSRI.

As very few studies have been done on vilazodone, and no specific study has been done on comparison of escitalopram and vilazodone. Hence, this study was planned to compare vilazodone and escitalopram in terms of its efficacy in depressive disorder and also the sexual dysfunction and weight gain caused during the course of treatment.

METHODOLOGY

A longitudinal study (12 weeks) was conducted at the Department of Psychiatry, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana. Institutional Ethics Committee approval was obtained before the study. After obtaining informed consent, a total of sixty patients were chosen and randomly prescribed vilazodone or escitalopram (30 each).

Design of study

This was an open-label randomized, controlled study conducted in an outpatient setting. The randomization was adopted as per the study protocol. As per the clinical diagnosis of the principal investigator (MB), the patients were prescribed vilazodone or escitalopram; thereafter the rating was done by co-investigator (SA). The assessment of every patient recruited into the study was done at baseline/first visit; 4 weeks and 12 weeks interval.

Inclusion criteria

- Married patients (males/females) of age 21–50 years
- Patients who are meeting International Classification of Diseases 10 criteria for depressive episode or recurrent depressive disorder
- Patients who gave written consent.

Exclusion criteria

- Patients with comorbid psychiatric disorder (except depression or recurrent depression)
- Patients who were having comorbid substance dependence
- Patients with any other medical disorder which is confounding our inclusion diagnosis
- Patients requiring the use of other psychotropic
medication such as benzodiazepines, antipsychotics.

**Dosing**

Escitalopram was started in a dose of 10 mg once daily and gradually increased to a maximum of 20 mg/day if required. Vilazodone was also started in a dose of 10 mg once daily and gradually increased to a maximum of 40 mg/day if required. The dosage of both the drugs was increased only if tolerated well.

**Materials used**

1. Sociodemographic data, especially designed for the study
2. HDRS[4] to grade the severity of depression. It is a 17-item scale; 8 items are scored on a 5-point scale ranging from 0 to 4 and 9 items are scored from 0 to 2; it is a clinician administered scale
3. Arizona Sexual Experience Scale (ASEX)[5] to assess the sexual functioning. It is a 5-item rating scale that quantifies sex drive, arousal, vaginal lubrication/penile erection, ability to reach orgasm, and satisfaction from orgasm. Possible total scores range from 5 to 30, with the higher scores indicating more sexual dysfunction. It is a clinician-administered scale.

**Statistical analysis**

The statistical analysis was done using t-test, Chi-square, and Fisher exact test and descriptive analysis.

**RESULTS**

**Sociodemographic Profile**

In our study Table 1 shows the mean age ± S.D. of patients who were taking vilazodone was 40.23 ± 8.81 years while it was 37.27 ± 5.09 years who were on escitalopram. This difference was statistically insignificant. In our study, more number of females were included in both groups 66.67% (on vilazodone) and 60% (on escitalopram).

About one-third of the patients were males in patients on vilazodone as compared to the patients on escitalopram where 40% were males.

In our study, 50% of patients were from rural areas, and 50% were from urban areas in both the groups.

In our study, the patients who were working in an unskilled profession almost 36% of patients on vilazodone and 30% of patients on escitalopram while only about 13% of patients on vilazodone were semi-skilled compared to 20% of patients on escitalopram. Half of the patients in both groups were working in a skilled profession.

In our study, the patients who were on vilazodone almost were illiterate or poor education (i.e., up to fifth Grade) compared to 40% of patients on escitalopram. Almost one-third of the patients who were on vilazodone had studied above 5th Grade compared to 60% of patients on escitalopram.

In our study, all the patients in both groups were married.

In our study, patients who were on vilazodone 80% were Hindu; about 13% were Muslims; and 7% were Sikhs compared to those on escitalopram where 90% were Hindu; and 10% were Sikhs.

**Scoring on Hamilton depression rating scale**

Table 2 shows HDRS score on baseline/first visit when patients presented in the outpatient department, patients who were selected for vilazodone the mean score on HDRS scale was found to have 18.77 ± 4.3.

| Table 1: Association of sociodemographic factors with the two treatment groups |
| Vilazodone (n=30), Ecitalopram (n=30), P |
| --- | --- | --- |
| Sex | n (%) | n (%) |
| Male | 10 (33.33) | 12 (40) | 0.789 |
| Female | 20 (66.67) | 18 (60) | 1.000 |
| Locality | Urban | 15 (50) | 15 (50) | 0.741 |
| Rural | 15 (50) | 15 (50) | 1.000 |
| Occupation | Unskilled | 11 (36.66) | 9 (30) | 0.741 |
| Semiskilled | 4 (13.33) | 6 (20) | 1.000 |
| Skilled | 15 (50) | 15 (50) | 1.000 |
| Education | Up to Grade V | 20 (66.67) | 12 (40) | 0.070 |
| Above Grade V | 10 (33.33) | 18 (60) | 1.000 |
| Marital status | Married | 30 (100) | 30 (100) | 0.492 |
| Single | 0 | 0 | 1.000 |
| Religion | Hindu | 24 (80) | 27 (90) | 0.112 |
| Muslim | 4 (13.33) | 0 | 1.000 |
| Sikh | 2 (6.67) | 3 (10) | 1.000 |

Table 2: Mean±standard deviation score of subjects according to Hamilton Depression Rating Scale at 0, 4, and 12 weeks of treatment with vilazodone and escitalopram

| HDRS score | Mean±SD | t | P |
| --- | --- | --- | --- |
| Vilazodone | Ecitalopram | | |
| 0 weeks | 18.77±4.3 | 18.8±4.09 | -0.031 | 0.976 |
| 4 weeks | 14.83±3.68 | 14.3±2.96 | 0.619 | 0.539 |
| 12 weeks | 9.63±3.06 | 8.43±2.1 | 1.773 | 0.081 |

SD – Standard deviation; HDRS – Hamilton Depression Rating Scale
At 4 weeks and 12 weeks follow-up, the scores fell up to 14.83 ± 3.68 and 9.63 ± 3.06, respectively.

In patients who were selected for escitalopram found to have score of 18.8 ± 4.09, 14.3 ± 2.96, and 8.43 ± 2.1 at baseline/first visit, at 4 weeks and at 12 weeks, respectively.

There was fall in scores on HDRS in both the groups at 4 weeks and 12 weeks; however, the fall in scoring was more in patients who were on escitalopram, but the difference is found to be statistically insignificant.

Scoring on 3 Arizona Sexual Experience Scale
Table 3 shows ASEX score on baseline/first when patients presented in the outpatient department, patients who were selected for vilazodone found to have 16.87 ± 2.97 while the score decreased at 4 weeks and at 12 weeks, i.e., 15.37 ± 3.1 and 11.73 ± 3.55, respectively showing decline in ASEX scoring.

Patients who were selected for escitalopram were found to have 16.4 ± 3.33, 17.13 ± 3.48, and 18.37 ± 4.09 at first visit, at 4 weeks, and at 12 weeks, respectively, showing increasing score on ASEX.

Results showing that patients who were on escitalopram were having increasing score on ASEX with increasing duration than vilazodone and the difference was found to be significant at 4 and 12 weeks.

Weight of patients
As shown in Table 4 patients who were selected for vilazodone were found to have mean baseline weight ± S. D. of 69.63 ± 7.7 kg, and it was 69.83 ± 7.83 kg and 69.9 ± 7.69 kg at 4 and at 12 weeks, respectively.

While patients who were selected for escitalopram were having mean baseline weight of 72.47 ± 7.95 at 4 and at 12 weeks; it was 72.87 ± 7.9 and 75.6 ± 8.46, respectively.

It was found that patients who were on escitalopram put on more weight as compared to patients on vilazodone in whom the weight remains almost static. The difference was found to be statistically significant at 12 weeks.

DISCUSSION
In our study, we found that approximately two-third patients were males and one-third were females in the age group of 32–48 years. Half of them were from urban areas, and half were from rural areas, and among them, half were nonskilled professionals and half were skilled professionals with education level of secondary school.

All were married, and most of them were from Hindu community.

In our study, we have found that all the patients who were on vilazodone as well as on escitalopram had improvement in their depressive symptoms on HDRS scale as the days progressed and the difference between the drugs in terms of efficacy was not much. There are studies which have shown similar kind of results with vilazodone as well as with escitalopram in context of improvement of depressive symptoms. As we reviewed the past literature, we could not find any study against our finding though as such data are sparse for vilazodone as it is a newer antidepressant and needs to be studied further individually escitalopram is studied very less till now, and most of the studies are broadly on SSRI as a group.

Sexual dysfunction remains a major concern of patients with depressive illness. The distress per se is too much with the symptom, and on above that stigma attached to it in Indian setup enhances the distress associated with this. The causes of sexual problems are first it is a symptom with illness per se, second, it can be due the side effect of the antidepressants which leads to the discontinuation of the treatment. In our study, we have observed that sexual dysfunction occur with escitalopram but not with vilazodone rather there was improvement on the ASEX scale of sexual function. There was a study from the United States with consistent findings as that of our which was with vilazodone and citalopram showing higher sexual dysfunctions with citalopram, and there was an improvement in the same in patients who were on.

**Table 3: Mean±standard deviation score of subjects according to Arizona Sexual Experiences Scale at 0, 4, and 12 weeks of treatment with vilazodone and escitalopram**

| ASEX score | Mean±SD | t | P  |
|------------|---------|---|-----|
| Vilazodone | Ecitalopram |   |     |
| 0 weeks    | 16.87±2.97 | 16.4±3.35 | 0.571 | 0.570 |
| 4 weeks    | 15.37±3.1 | 17.13±3.48 | 2.075 | 0.042* |
| 12 weeks   | 11.73±3.55 | 18.37±4.09 | 6.708 | <0.001** |

* P value significant (<0.05); ** P value highly significant (<0.001).

**Table 4: Mean±standard deviation weight of subjects at 0, 4, and 12 weeks of treatment with vilazodone and escitalopram**

| Weight (kg) | Mean±SD | t | P  |
|------------|---------|---|-----|
| Vilazodone | Ecitalopram |   |     |
| 0 weeks    | 69.63±7.7 | 72.47±7.95 | 4.03 | 0.166 |
| 4 weeks    | 69.83±7.83 | 72.87±7.9 | 4.94 | 0.141 |
| 12 weeks   | 69.9±7.69 | 75.6±8.46 | 7.79 | 0.007* |

* P value significant (<0.05). SD – Standard deviation
vilazodone. There was a randomized, controlled trial with inconsistent findings showing that the patients on vilazodone were having higher sexual dysfunction than the placebo. This difference in finding can be explained by that our study was between vilazodone and the older SSRI which has an established side effect of sexual dysfunction while in that randomized controlled trial, and in the second study, the comparison was in between vilazodone and placebo which is not known to us that which drug or substance was given in the form of placebo; hence, whether it has sexual side effects or not.

Weight gain is one of the major risk factors for nonadherence to treatment. There can be multiple reasons of weight gain in patients with depressive illness. It can be (a) one of the symptoms of depression; (b) can be a side effect of the treatment. Weight gain always remains a problematic issue for patients of depression. First, patients of depression per se are at risk of cardiovascular diseases, and weight gain can aggravate the risk; second, weight gain raises the issue of drop outs leading to untreated illness. All these factors ultimately increase the burden on economy directly or indirectly. Thus, this issue needs to be addressed carefully. That’s why we have compared the two drugs for weight gain. In our study, we have seen that there is an increase in weight in patients who were prescribed escitalopram but patients who were prescribed vilazodone had almost the same weight as that of baseline.

Consistent results were found in many studies when we reviewed the literature for weight gain with escitalopram showing weight gain in acute phase as well as of chronic phase of treatment, but there was a pooled analysis which shows paradoxical effect that there is short-term weight loss with antidepressant treatment. The difference in the result in that study can be explained on the basis that the study was done on rodents and our one was done on human beings, and there might be differences in the neuroendocrine pathways of both. Second, in the study, the short-term weight loss during treatment may be a symptom of the underlying illness as antidepressants take time to act to show the results.

We found the consistent results for weight in vilazodone treatment. All the studies show that there is either no weight gain or there is weight loss, but we could not found any study revealing weight gain with vilazodone. However, our research for vilazodone is based on very sparse literature as it is a new drug and further studies need to be done to establish the fact. This is probably the only study comparing the weight gain and sexual side effects of vilazodone.

Strengths of study
1. This is the only study done in India regarding vilazodone’s sexual dysfunction, especially in area where sexual dysfunction is considered a stigma and patients do not report sexual problems
2. The study design was open-label randomized controlled, and the rater was not aware of the drug molecule being used
3. This is the only study comparing the vilazodone and escitalopram
4. As vilazodone is a novel SSRI so very sparse literature exists and our study may help the readers to enhance their knowledge regarding vilazodone
5. There were no drop outs
6. Use of other medications that could have also caused sexual dysfunction was avoided.

Limitations
1. Small sample size
2. There may be chance of biasing as scales used were clinician rated.

In view of these limitations, these finding could not be generalized.

CONCLUSIONS
In our study, we have reached to a conclusion that vilazodone and escitalopram have similar efficacy, but vilazodone has less weight gain and lesser sexual dysfunction as compared to escitalopram.

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Conflicts of interest
There are no conflicts of interest.

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