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Original Research Article

Effectiveness and side-effect profile of Vilazodone and Escitalopram in major Depressive Disorder – An observational study

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ABSTRACT

Background : Major depressive disorder (MDD) is characterized by a cluster of emotional, behavioral, and cognitive features causing functional impairment. Escitalopram and Vilazodone are approved drugs in management of MDD. Escitalopram is found to be efficacious in patients with MDD. However, sexual dysfunction and weight gain are of a primary concern leading to discontinuation of treatment. Vilazodone is efficacious for patients who do not respond to SSRI/SNRI monotherapy. Evidence suggests it to be associated with a better side effect profile.

Aim : To study the effectiveness and side effect profile of vilazodone and escitalopram in patients diagnosed with MDD.

Materials and Methods : All patients diagnosed with MDD and commenced for the first time on vilazodone or escitalopram were included in the study via purposive sampling. Effectiveness and side effect profiles of the patients were studied by applying HAM-D and ASEC, respectively, at baseline, at weeks 1, 2, 4, 6, and 8.

Results : There was a statistically significant difference in weeks 2, 4, and 6 for both the drugs. On intergroup comparison, no significant difference was found in terms of response rates. The number of side-effects was more in the escitalopram group.

Conclusion : Taken together with our results, vilazodone appears to be equally effective as escitalopram in treating patients of MDD. However, vilazodone has the advantage of better tolerability as compared to escitalopram.

Key messages: Vilazodone was found to be equally effective as escitalopram in patients with MDD and has the advantage of better tolerability as compared to escitalopram.

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1. Introduction

Major depressive disorder (MDD) is a chronic disorder characterized by a cluster of emotional, behavioural, and cognitive features causing functional impairment. It has a lifetime prevalence of 16.6%. Globally, depressive disorders are ranked as the single largest contributor to non-fatal health loss (7.5% of all Years Lived with Disability). As per the WHO report 2017, over 300 million people are estimated to suffer from depression at a global level.[1] Twelve months prevalence of MDD in the United States is approximately 7%.[2] In India, 4.5% of the population is estimated to be living with depression.[1]

The essential feature of MDD as per the DSM V criteria is at least two weeks of depressed mood or the loss of interest and pleasure in almost all daily activities. The patient must also have at least five additional symptoms from a change in appetite or weight, sleep, psychomotor activity, decreased energy, feelings of guilt, and thoughts of death or suicidal ideation.[2]

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Fewer than half of the patients typically attain response (50% improvement in symptoms) or remission (full resolution of symptoms) during the initial treatment.[3]

The primary goal of treatment in a long-term perspective remains the prevention of recurrence and achieving full recovery to the premorbid functioning level.

Selective serotonin reuptake inhibitors (SSRIs) are drugs of choice for the treatment of MDD.[4,5] Escitalopram is one of the most frequently used SSRI. Based on pooled and meta-analysis studies, escitalopram demonstrates superior efficacy compared with citalopram and with SSRIs combined.[6,7] It is found to be efficacious, cost-effective, and is associated with the highest probability of remission.[8,9]

The success of the pharmacological treatment depends on the response rates as well as tolerance of the drug. Treatment with antidepressants is limited by factors that affect patients' compliance, including delay in onset of therapeutic effects, intolerable side effects, and other safety concerns.[10,11] SSRI's have sexual dysfunction and weight gain as two of the most observed side effects.

Theoretically, SPARI action could lead to faster antidepressant onset, better efficacy with fewer side effects.[12] Vilazodone is a novel dual-acting serotonergic antidepressant approved by the US Food and Drug Administration in 2011 for the treatment of MDD in adults. It is the first member of the serotonin partial agonist-reuptake inhibitor (SPARI) class of medications, combining serotonin-reuptake inhibition with 5-HT_{1A} partial agonism. Evidence has suggested that the partial agonism of vilazodone at the 5-HT1A receptor increases endogenous serotonin levels more than an SSRI alone. Its unique SPARI mechanism of action could also be efficacious for patients who do not respond to SSRI/SNRI monotherapy.[13]

In a 12-week comparative prospective open-label randomized controlled study conducted in north India comparing the efficacy and safety of escitalopram and vilazodone in MDD, vilazodone has been found to have better efficacy, lesser weight gain, and lesser sexual dysfunction.[14] Kudyar P et al. reported that escitalopram was more efficacious and better tolerated than vilazodone in patients with MDD.[8]

This observational study is undertaken with the aim to assess the effectiveness and side effects of vilazodone and escitalopram in patients diagnosed with major depressive disorder.

2. Materials and Methods

The present study is an observational study conducted in the psychiatry department of a tertiary care hospital over one year from January 2019 to December 2019 after obtaining approval from the Institutional Ethics Committee.

All the patients diagnosed with Major Depressive Disorder as per DSM V criteria and commenced for the first time on either vilazodone or escitalopram, were taken as subjects of the study by purposive sampling method. Patients in the age group of 18 and 55 years and willing to participate in the study were included. History of any other comorbid psychiatric disorders, including substance abuse, medical disorders, neurological disorders and sexual dysfunction, pregnant or lactating women, use of other medications with well established drug interactions were excluded from the study.

Informed consent was obtained from all participants after they were explained about the nature and purpose of the study and verbally assured about their information confidentiality.

At the baseline, sociodemographic details were obtained, including age, gender, region, socioeconomic status, family type (joint/nuclear), educational status, and occupation. Clinical parameters such as blood pressure, both systolic and diastolic, were noted, along with the patients' height and weight. Blood sugar levels, total leukocyte counts (TLC), serum urea, serum creatinine, and hemoglobin were estimated. Hamilton depression rating scale (HAM D) was applied to assess the severity of symptoms of MDD.[15] Antidepressant Side-Effect Checklist (ASEC) was also applied.[16]

Patients in both the groups were assessed at week 1, week 2, week 4, week 6, and week 8 by applying the HAM D scale and ASEC. Blood sugar levels, total leukocyte counts (TLC), serum urea, serum creatinine, hemoglobin, blood pressure, and weight were estimated at week 4 and week 8.

HAM-D, also known as Hamilton depression rating scale, is a multiple item questionnaire used to indicate depression and as a guide for evaluating recovery. 21-item HAM-D scale was used in the current study to evaluate the patients' symptoms of depression. Each item on the questionnaire is scored on a 3 or 5 point scale, and depending on the item, the total score is calculated. A score of 0–7 is normal, scores 8–13 indicate mild depression, 14–18 indicate moderate depression, 19–22 indicate severe depression and >23 indicate very severe depression. The primary efficacy outcomes were the change from the baseline in the scores on the HAM-D.[15]

Antidepressant Side-Effect Checklist (ASEC) is a self-reporting checklist for monitoring adverse events in patients using antidepressants. It has well-defined items developed to provide a comprehensive rating of side effects with antidepressant medications.[16]

Statistical analysis was done using SPSS 21 software. The change in the scores from baseline was noted and assessed by the use of independent t-test. From the data collected, subjects were assigned to two groups those receiving vilazodone as group A and escitalopram as group B. Intergroup comparison between two groups was also made by using independent t-test.

A Probability value of less than 0 05 has been taken as statistically significant

3. Results

3.1. Sample characteristics

Of the 117 patients taken into the study, 44 were excluded as they were not meeting the fixed criteria, and the remaining 73 patients were assigned to two groups, those receiving vilazodone as group A which included 32 patients, and those receiving escitalopram as group B which included 41 patients. All the patients were followed up over 8 weeks and analyzed at the end of the study, of which 4 were lost to follow up.

The number of patients on whom the study is carried out is 31 in the vilazodone group and 38 in the escitalopram group.

The sample characteristics are summarized in Table 1.

In both groups, sociodemographic details were noted. On intergroup comparison using Chi-square test, no significant difference was seen pertaining to age, socioeconomic status, family type, educational status, and occupation.

More females were included in both the groups in our study.

Sample characteristics are shown in Table 2.

On treatment with the drugs vilazodone and escitalopram, HAM-D scores were calculated at the baseline and over 8 weeks. On evaluation, there was a statistically significant difference in weeks 2, week 4, and week 6 for both the drugs ($P < 0.001$), as summarized in Table 2. On intergroup comparison, no significant difference was found between the two groups in terms of response rates.

Adverse effects were recorded over 8 weeks in both groups of patients. Nausea/vomiting was the most common adverse effect (n = 10), followed by decreased libido (n = 9) and increased appetite (n = 8) in the escitalopram group. In the vilazodone group, the most common adverse effect was diarrhea (n = 3), followed by nausea/vomiting and headache (n =2). ASEC was applied to evaluate adverse effects in both groups of patients. The number of adverse effects was more in the escitalopram group leading to a higher score on ASEC as shown in Table 3.

4. Discussion

The present study was conducted to assess the effectiveness and tolerability of vilazodone and escitalopram in outpatients diagnosed with MDD.

Patients' mean age in the vilazodone group was 33.03±8.62 years, while it was 33.16±9.06 years in the escitalopram group. A similar trend in the age group of patients with MDD, as observed in our study, was reported by Jiang et al., 2017 and Kishi et al., 2017 in their respective randomized controlled trials.[17,18]

In our study, 62.3% of the total patients were females, of which 19(61.3%) were taking vilazodone, and 24 (63.2%) were on escitalopram. As per the WHO report 2017, depression has been more common among females (5.1%) than males (3.6%).[1] In a 12-week comparative prospective open-label randomized controlled study in depression patients treated with vilazodone and escitalopram, Manish Bathla et al., 2018 reported that more females were receiving treatment as compared to males, which is in agreement with our results.[14]

The HAM-D scores calculated during the study were significantly lowered by vilazodone and escitalopram ($P < 0.001$). On intergroup comparison using independent t-test, vilazodone was found to cause more lowering of HAM-D score than escitalopram ($P < 0.02$). However, the difference was not statistically significant.

HAM-D score has a significant role in assessing the improvement or deterioration of depression. In the current study, both vilazodone and escitalopram decreased the HAM-D score significantly in a similar fashion ($P < 0.001$). When vilazodone and escitalopram were compared, as summarized in Table 2, the HAM-D score was more effectively reduced with vilazodone than with escitalopram at weeks 2, 4, and 6 ($P < 0.02$), but the difference was not statistically significant. Studies have shown similar kinds of results with vilazodone and escitalopram in the context of improvement of depressive symptoms.[13,19] In a network meta-analysis, escitalopram emerged as the most efficacious agent among the SSRIs and was the best tolerated of all the antidepressants that were analyzed.[20] Similarly, vilazodone has also been shown to decrease HAM-D score in patients with MDD.[21] Manish B et al., in a randomized controlled study comparing the efficacy of vilazodone and escitalopram in MDD, found vilazodone to have better efficacy, which is consistent with our results.[14] A study conducted by Kudyar P et al., 2015 comparing the efficacy and safety of vilazodone and escitalopram in MDD demonstrated that escitalopram is more efficacious in causing a decline in HAM-D score, which is in contradiction to our results.[8]

In the current study, safety was evaluated by the adverse drug reactions (as demonstrated by ASEC). Adverse drug reactions across both groups are shown in Table 3. Vilazodone was found to be better tolerated than escitalopram numerically. There is a lesser incidence of nausea/vomiting, lesser weight gain, and sexual dysfunction with vilazodone.

Patients on escitalopram in our study reported increased appetite while those on vilazodone did not. A study from North India reported similar findings as our study.[14] Studies reported that there is no weight gain or weight loss with vilazodone.[21] Despite our best efforts, we could not find any study reporting weight gain with vilazodone, which probably may be due to vilazodone being a new drug having

Table 1: Sample characteristics

Variables		Group A	Group B	Total	P (Chi-square test)
Age (Mean +SD)		33.03±8.62	33.16±9.06		0.95
Gender	Male	12 (38.7%)	14 (36.8%)	26 (37.7%)	0.87
	Female	19 (61.3%)	24 (63.2%)	43 (62.3%)	
Region	Rural	20 (64.5%)	22 (57.9%)	42 (60.9%)	0.57
	Urban	11 (35.5%)	16 (62.1%)	27 (39.1%)	
Socioeconomic status	Lower	19 (61.3%)	20 (52.6%)	39 (56.5%)	0.47
	Middle	12 (38.7%)	18 (67.4%)	30 (43.5%)	
Family type	Nuclear	18 (58.1%)	21 (55.3%)	39 (56.5%)	0.81
	Joint	13 (41.9%)	17 (44.7%)	30 (43.5%)	
Educational status	Illiterate	4 (12.9%)	4 (10.5%)	8 (11.6%)	0.73
	Primary	7 (22.6%)	13 (34.3%)	20 (29.1%)	
	Upper primary	6 (19.4%)	4 (10.5%)	10 (14.5%)	
	Secondary	4 (12.9%)	5 (13.2%)	9 (13.0%)	
	Senior secondary	5 (16.1%)	4 (10.5%)	9 (13.0%)	
	Under graduate	1 (3.2%)	4 (10.5%)	5 (7.2%)	
	Graduate	4 (12.9%)	4 (10.5%)	8 (11.6%)	
Occupation	Unskilled	14 (45.2%)	18 (47.4%)	32 (46.4%)	0.92
	Semi-skilled	5 (16.1%)	4 (10.5%)	9 (13%)	
	Home-maker	9 (29%)	12 (31.6%)	21 (30.4%)	
	Student	3 (9.7%)	4 (10.5%)	7 (10.2%)	

Table 2: Efficacy ofvilazodone and escitalopram on HAM-D scores between the groups

		Mean+SD	P (independent t-test)
Baseline	Group A	18.61±2.73	0.24
	Group B	19.39±2.75	
1 week	Group A	15.97±2.75	0.07
	Group B	17.13±2.59	
2 weeks	Group A	12.65±3.10	0.02*
	Group B	14.37±3.09	
4 weeks	Group A	9.29±2.95	0.02*
	Group B	10.95±3.09	
6 weeks	Group A	5.77±3.25	0.02*
	Group B	7.61±3.22	
8 weeks	Group A	3.23±2.99	0.16
	Group B	4.26±3.05	

*P<0.05; HAM-D: Hamilton rating scale for depression

sparse literature available.

In our study, we have observed that sexual dysfunction occurred with escitalopram but not with vilazodone. Consistent results were found in a multicenter, randomized, placebo-controlled, and active-controlled, double-blind, fixed-dose study conducted in the United States. They have observed higher sexual dysfunction with citalopram and improvement in the same in patients on vilazodone.[21] Escitalopram has an established side effect of sexual dysfunction.[12]

The current study results have demonstrated that both vilazodone and escitalopram are effective in treating patients of MDD. Vilazodone is better tolerated than escitalopram pertaining to its lesser incidence of nausea/vomiting, weight gain, and sexual dysfunction.

4.1. Strengths of the study

Patients with comorbid psychiatric disorders, including substance abuse, medical and neurological disorders, pregnant and lactating females, were excluded; hence, most other possible causes of intolerability are avoided. Use of other medications that could have also caused sexual dysfunction was avoided. Scales used to measure response rates and side effects were validated. As vilazodone is a comparatively recent drug, sparse literature exists. So our study may help the readers to enhance their knowledge about vilazodone.

Table 3: Adverse drug reactions across both groups

Side-effects	Vilazodone (n =31)	Escitalopram (n =38)
Dry Mouth	0	3
Nausea/Vomiting	2	10
Diarrhea	3	2
Constipation	0	0
Headache	2	0
Tremors	0	0
Feeling like the room's spinning	0	5
Blurred vision	0	0
Disorientation	0	0
Insomnia	1	4
Drowsiness	0	3
Decreased libido	1	9
Erectile dysfunction	0	2
Delayed ejaculation	0	2
Palpitations	1	0
Feeling light-headed on standing	0	0
Increased appetite	0	8
Decreased appetite	0	0
Weight gain	2	5
Problems with urination	0	0
Sweating	0	0
Increased body temperature	0	0
Yawning	0	0

5. Limitations of the study

This study was preliminary, done in a single-center with less number of patients. Furthermore, being an observational study, no blinding was done for the evaluation of both the drugs. This study did not include a placebo arm. Lack of pharmacokinetic data may also be considered as one of the limitations of this study.

Hence, further research with a greater number of participants and using randomised sampling is required to confirm the clinical advantage of one drug over the other.

6. Conclusion

Taken together with our results, newer antidepressant vilazodone appears to be equally effective as escitalopram in treating patients of MDD. However, vilazodone has the advantage of better tolerability as compared to escitalopram.

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9. Conflict of Interest

The authors declare that they have no conflict of interest.

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