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Original Research Article

A Randomized, Open-Labeled, Comparative Study on Safety and Efficacy of Desvenlafaxine with Escitalopram among the Patients of Depression Associated with Anxiety

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Abstract:

Background: Higher levels of chronicity, symptom severity, substantial functional impairment, and a poor response to medication treatment are all related to anxious depression. There is, however, little data supporting first-choice antidepressants in individuals with anxious depression. The purpose of this study was to assess the safety and effectiveness of desvenlafaxine and escitalopram in the acute treatment of anxious depression.

Methods: The study included a total of 100 participants who were diagnosed with anxiety and depression. At random, the patients were divided into two groups with a 1:1 ratio. The test group received desvenlafaxine, whereas the control group received the usual medicine of escitalopram. For a total of eight weeks, both drugs were taken orally once daily. In the first, fourth, and eighth weeks, the patients were monitored. The effectiveness ratings of the Hamilton depression rating scale (HAM-D) and the Hamilton anxiety rating scale (HAM-A) were contrasted. Patients who showed a 50% decrease in rating ratings from baseline or less during follow-up visits were deemed to be responding to treatment. To assess safety and tolerability, changes in laboratory data, vitals, and reported side effects were taken into consideration.

Results: Both the escitalopram and desvenlafaxine groups' HAM-D and HAM-A scores markedly declined from their respective baselines ($P < 0.001$). However, neither group was able to show a statistically significant difference at 4 or 8 weeks of treatment. It was concluded that both escitalopram and desvenlafaxine were safe; however, escitalopram exhibited a higher tolerance and a much lower number of side effects than desvenlafaxine.

Conclusion: Desvenlafaxine and escitalopram both worked equally well to lessen the symptoms of depression associated with anxiety. It was shown that escitalopram was well tolerated.

Keywords: Desvenlafaxine, Escitalopram, Anxiety, Depression.

Introduction

Anxiety symptoms are prevalent in those suffering from depression disorders. Few patients in the clinical setting have pure anxiety or depressive disorder [1,2]. In addition, 60–96% of patients with depression report having anxious symptoms [3]. The prognosis is poor when anxiety symptoms coexist with depression because the patients exhibit worse social dysfunctions, increased symptom severity, increased chronicity, and a poor response to medication treatment [4,5].

Furthermore, patients with co-occurring anxiety and depression are more susceptible to the negative effects of therapeutic medications and exhibit poor treatment compliance, stopping their medication before it is finished [5]. According to earlier research, comorbid anxiety is a significant clinical component; thirty to sixty percent of patients with depressive disorders do not respond to antidepressant medication, and studies show that treatment resistance rises when anxiety symptoms are present [6, 7].

Numerous treatments have been suggested for the treatment of anxious depression under the aforementioned clinical focus. The current guidelines available for medication-assisted depression treatment often prescribe the "administration of antidepressants as first-line treatment," regardless of whether anxiety symptoms emerge concurrently [8–10]. For the most part due to a lack of data, they are unable to

suggest the best class of antidepressants for individuals suffering from anxious depression. The antidepressants that are not prioritized are prescribed based on meta-analyses of these studies or on placebo-control trials of several antidepressant classes[11,12].

While there are few direct comparison studies, there are a fair number of indirect comparisons. Thus, a comparison of the clinical results of antidepressants for anxious depression in a head-to-head trial is required. Antidepressants that were largely designed based on their pharmacokinetic features are the mainstay of treatment for depressive disorders that are accompanied by anxiety symptoms in current clinical practice [5,13].

These suggestions, however, are still only theories, and there is a dearth of data drawn from real-world practice settings. There are currently few therapeutic options for depressive disorders in which anxiety coexists; as a result, clinical treatment plans founded on the practitioners' empirical ideas have taken precedence. The research hypothesis on anxiety symptoms linked to depression was frequently not provided beforehand in previous clinical trials, and the change in anxiety symptoms was frequently not examined as a primary outcome variable [14].

Furthermore, even if some placebo-controlled trials consider the reduction of anxiety symptoms to be a secondary goal, the findings of these studies do not establish which class of antidepressants is best for reducing anxiety symptoms in patients with anxious depression. We designed this head-to-head study to directly compare the efficacy and safety of antidepressants that have recently been developed and widely used classes of antidepressants, escitalopram, desvenlafaxine, and vortioxetine, for the acute treatment of anxious depression. This will help to rationalize drug treatment strategies for anxious depression. The most recently developed drug, vortioxetine, has accumulated evidence showing effects on anxious depression [18]. Desvenlafaxine, a metabolite of venlafaxine, is the recommended treatment option for anxious depression as a serotonin−norepinephrine reuptake inhibitor (SNRI) [17]. Escitalopram, on the other hand, has been used increasingly as a selective serotonin reuptake inhibitor (SSRI) for the treatment of anxious depression in numerous studies [15,16].

Material and Methods

At the Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, this randomized, open-label, parallel, prospective, comparative study was carried out over the course of a year, from January 2022 to December 2022, by the Department of Pharmacology in cooperation with the Department of Psychiatry. After receiving information about the purpose and scope of the study, all study participants or, if applicable, their legally recognized relative, provided signed informed consent. Every participant in the outpatient psychiatry program at BMIMS, Pawapuri, Nalanda, Bihar, was chosen at random and given sufficient information regarding the purpose and aims of the study.All eligible patients who visited the psychiatry outpatient department (OPD) and fell within the age range of 18 to 60 (both sexes) for a clinical diagnosis of major depressive disorder (MDD) and who had recently been diagnosed with depression according to the Diagnostic and Statistical Manual of Mental Disorders were included in the trial. Patients with mild-to-moderate depression who scored between 7 and 18 on the Hamilton Depression Rating Scale (HAM-D) and a score of 12 on the Hamilton Anxiety Rating Scale (HAM-A) were included in the study.

Individuals who had taken antidepressants for more than a month, pregnant or nursing women, people with comorbid conditions like uncontrolled diabetes, hypertension, liver cirrhosis, chronic renal failure, ischemic heart disease, and cancers, suicidal thoughts and catatonic features, people taking medications that negatively interact with study drugs like quetiapine, duloxetine, bupropion, cough syrups, aspirin, fluoxetine, sertraline, and monoamine oxidase inhibitors, noncompliant participants or guardians, abnormal liver and renal function tests, and patients with epilepsy were not allowed to participate in this study.

Random selection was used to choose study participants from among patients who satisfied the eligibility criteria. 138 patients had been screened and recruited; 110 of them met the requirements to be randomly assigned using a 1:1 distribution ratio of computer-generated numbers. Patients were split into two groups: group B received Tab. Escitalopram 10 mg orally once daily, and group A received Tab. Desvenlafaxine 50 mg orally once daily for the duration of the experiment. At the time of study subject enrollment, comprehensive historical and demographic data were collected. The clinical examinations, HAM-D and HAM-A score screening, and laboratory investigations were finished at baseline, the fourth week, and the end of the eighth week.

The effectiveness outcome was measured by comparing the HAM-D and HAM-A scores at the start and end of the research. The HAM-D scale is an observer scale consisting of 17–21 questions that is used to assess the severity of depression in patients. The 17-item HAM-D scale is scored 0–4 (absent, uncertain, mild, moderate, and severe) on the first nine items, and 0–2 (0–2 = absent, doubtful, and certainly present) on the remaining eight items. The 14-item HAM-A scale, which is useful for evaluat-

ing psychological and bodily anxiety, is explained by a number of indicators. A reduction of 50% or more from the baseline in HAM-D and HAM-A scores was deemed indicative of a therapeutic response.The safety was evaluated using the participant reports of unfavorable treatment-related events and the clinician's reports collected at each follow-up visit. As part of the safety assessment, laboratory parameters including the liver function test, blood urea and serum creatinine, random blood sugar (RBS) level, complete blood count, and serum creatinine were measured at baseline and at the end of the eighth week.

Baseline HAM-D and HAM-A scores were gathered at study visits, together with a thorough clinical history and a history of all previously and currently taken drugs, including any drug allergies. Two post-baseline visits were scheduled for eight and four weeks apart. Clinical assessments of both research groups were conducted using HAM-D and HAM-A scores at every follow-up visit. At the baseline and fourth week visits, prescription drugs were given. Any negative occurrences that occurred in the past were documented. Pill counting was another technique used to keep track of patients' compliance with their medication. Every time there was a follow-up visit after then, safety and effectiveness measures were assessed.

All statistical analysis was done using the computer-assisted program SPSS version 21 for Windows. All study participants' levels of depression and anxiety were measured using the HAM-D, HAM-A, and laboratory tests at baseline, week 4, and week 8. The results were presented as mean and standard deviation values. The proper statistical techniques, such as the paired t-test, students' independent t-test, and analysis of variance, were employed to examine the results, which were expressed as a percentage change from the beginning point. The incidence of adverse effects was calculated as a percentage among the research groups using the Chi-square test. A probability of less than 0.05 was considered to be a statistically significant outcome.

Results

A modified intention-to-treat analysis revealed that 10 subjects were not followed up, making 90 of the 100 randomized patients (test group with desvenlafaxine = 46 and control group with escitalopram = 44) eligible. For the desvenlafaxine group, the mean age was calculated as 38.44 ± 10.65 years, while for the escitalopram group, it was 39.38 ± 11.50 years. There was no statistically significant difference (P = 0.19) between the groups. Among all research participants, the prevalence of depression was found to be 31% in men and 69% in women, meaning that depression is twice as common in men and women across both treatment arms.The gender distribution between the study groups did not differ significantly. Baseline values for both groups are shown in Table 1.

Table 1: Baseline characteristics of patients

Parameter	Mean±SD		Statistical inference	
	Desvenlafaxine (Group A)	Escitalopram (Group B)	t–value	P-value
Age (years)	38.4±10.65	39.38±11.50	−0.46	0.64
Sex (male: female)	17:33	14:36		
HAM-D	22.80±6.64	22.14±8.78	−0.424	0.673
HAM-A	16.66±5.07	17.08±5.65	0.208	0.835
Pulse	78.50±7.87	80.54±5.48	−1.00	0.322
SBP	124.66±3.36	125.36±3.83	−0.47	0.643
DBP	80.63	78.66	−1.00	0.322
Hb (g)	11.26±0.6	11.22±0.8	−0.196	0.846
WBC	5866.66±646.47	6266.66±764.6	2.20	0.03
Platelet count	1.91±0.176	1.90±0.172	−0.12	0.83
RBS	106.90±5.26	108.46±3.47	1.79	0.07
Blood urea	21.60±1.44	21.66±1.46	−0.195	0.846
Serum creatinine	0.78±0.09	0.80±0.10	−1.001	0.322
SGPT	17.84±2.49	19.10±1.50	−3.068	0.007
SGOT	14.72±1.70	15.10±1.45	−1.203	0.232

HAM-D: Hamilton Depression Rating Scale, HAM-A: Hamilton Anxiety Rating Scale, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, Hb: Haemoglobin, WBC: White blood cell, RBS: Random blood sugar, SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase, SD: Standard deviation, Hemoglobin (Hb%), white blood cells (WBCs), RBCs, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, HAM-D, HAM-A, diastolic blood pressure, and systolic blood pressure.In the desvenlafaxine group, the mean baseline HAM-D score was 22.80, while in the escitalopram group, it was 22.14. Be-

tween the two therapy groups, there was no discernible difference in the mean baseline HAM-D score. Patients are deemed to be responding to treatment if their HAM-D scores have dropped by more than 50% from their starting points. Analysis of the response rates within and between the two treatment groups was done using the improvement in mean scores at the follow-up visits at the fourth and eighth weeks.

The mean HAMD score dropped at the end of the 4-week treatment period, starting from a baseline value of 22.80–12.40 in the desvenlafaxine group and 22.14–12.62 in the escitalopram group. After 4 weeks of treatment, it was feasible to ascertain that the mean HAM-D scores in both study groups had fallen statistically significantly ($P < 0.001$) [Table 2]. This was done using a paired t-test within each group.

Table 2: Treatment effect across Desvenlafaxine (n=50) and Escitalopram (n=50) group: (Mean±standard deviation) scores within the study subjects

Variables	Baseline	4th week	8th week	F-test	P-value
Mean HAM-D score					
Desvenlafaxine	22.80±6.64	12.40±3.86	6.16±1.77	205.753	<0.001
Escitalopram	22.14±8.78	12.62±4.24	6.10±1.93	119.305	<0.001
Mean HAM-A score					
Desvenlafaxine	16.66±5.07	10.62±4.56	6.42±2.98	237.468	<0.001
Escitalopram	17.08±5.65	10.78±5.16	5.44±1.77	266.858	<0.001

HAM-D: Hamilton Depression Rating Scale, HAM-A: Hamilton Anxiety Rating Scale As shown in Table 3, there was no statistically significant ($P = 0.673$) difference in the mean HAM-D scores between the groups at the end of the 4-week treatment session.

Like desvenlafaxine, escitalopram also demonstrated a statistically significant ($P < 0.001$) decrease in mean HAM-D score following 8 weeks of medication; baseline values for both groups were 22.80 to 6.16 and 22.14 to 6.10, respectively, as indicated in Table 2. This demonstrates that the clinical response to an antidepressant's mechanism of action will take time to show, as the percentage of responders increases correspondingly as treatment duration increases from 4 to 8 weeks.

Table 3 shows that at the end of the eighth week, there was no statistically significant difference in the mean HAM-D ratings between the escitalopram and desvenlafaxine groups ($P = 0.787$).Since there is no difference in the overall score reduction between the groups analyzed, it can be concluded that the therapeutic efficacy of the drugs used in the study and the control groups was similar.

Table 3: Comparison of mean Hamilton depression rating scale scores in both the groups over time (mean±standard deviation) Scores between the subjects

HAM-D score	Group A (Desvenlafaxine)	Group B (Escitalopram)	t-value	P-value
Baseline	22.80±6.64	22.14±8.78	−0.424	0.673
Week 4	12.40±3.86	12.62±4.24	0.424	0.673
Week 8	6.16±1.77	6.10±1.93	−0.271	0.787

HAM-D: Hamilton depression rating scale

The mean baseline HAM-A scores for the two treatment arms, which were 17.08 for the escitalopram group and 16.66 for the desvenlafaxine group, did not significantly differ from one another. The mean HAM-A score dropped from the baseline value after 4 weeks of medication, going from 16.66 to 10.62 in the desvenlafaxine group and from 17.08 to 10.78 in the escitalopram group. Table 2 displays the statistically significant ($P < 0.001$) decrease in mean HAM-A scores in both treatment arms following 4 weeks of treatment, as determined by within-group analysis using paired t-tests.Table 3 indicates that at the 4-week mark, the mean reduction in HAM-A scores did not demonstrate a statistically significant difference between the two treatment groups ($P = 0.696$). The average HAM-A score in the desvenlafaxine group fell from 16.66 to 6.42 after 8 weeks of pharmaceutical therapy; this difference was statistically significant ($P < 0.001$). Table 2.

The mean HAM-A score reduction in the escitalopram group likewise showed statistical significance ($P < 0.001$), declining from a baseline value of 17.08 to 5.44 at the end of the 8-week treatment term.Table 4 illustrates that, after 8 weeks, there was no statistically significant difference ($P = 0.870$) in the mean HAM-A scores between the escitalopram group (5.44) and the desvenlafaxine group (6.42).

Table 4: Comparison of mean Hamilton anxiety rating scale scores in both the groups over time (mean ± standard deviation) Scores between the subjects

HAM-A score	Group A (Desvenlafaxine)	Group B (Escitalopram)	t-value	P-value
Baseline	16.66 ± 5.07	17.08 ± 5.65	0.208	0.835
Week 4	10.62 ± 4.56	10.78 ± 5.16	−0.391	0.696
Week 8	6.42 ± 2.98	5.44 ± 1.77	−0.164	0.870

The results of the current study indicate that the Desvenlafaxine group experienced a larger decline in mean HAMA Score at the end of 8 weeks compared to the escitalopram group (baseline 17.08–5.44).

A score loss of roughly 50% shows more importance in clinical practice than a full score reduction.Of the 23 trial participants, 17 were in the desvenlafaxine group and 6 were in the escitalopram group who reported adverse events.

Out of the 100 participants in the study, 30.8% were assigned to the desvenlafaxine group and 10.6% to the escitalopram group. Figure 1 shows the specifics of these adverse drug reactions.

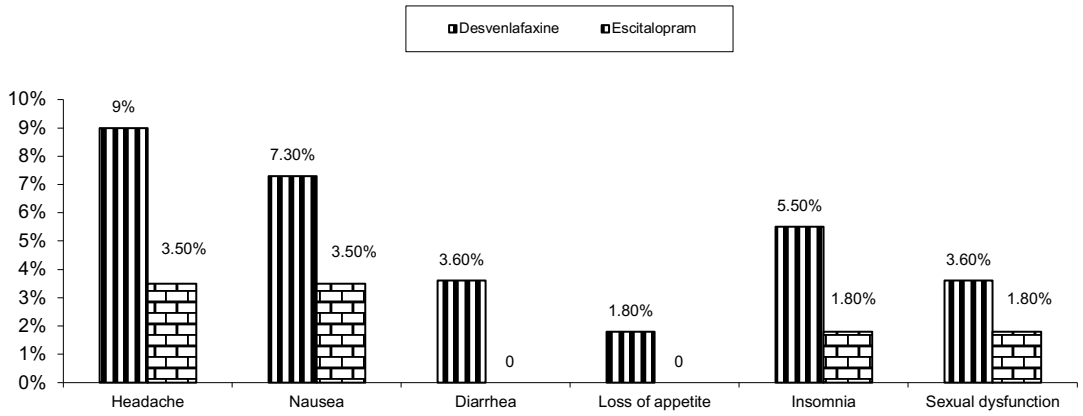

Figure 1: Percentage of adverse events reported in both the research groups

The group treated with desvenlafaxine reported more adverse events than the group treated with escitalopram. Further investigation is required because there was no statistically significant difference in the proportions of negative effects between the groups taking escitalopram (group B) and desvenlafaxine (group A) ($P > 0.05\%$). There were no significant adverse events reported during the study. There were no unfavorable impacts on the study participants in either group, and dropouts were due to other circumstances. There is no appreciable difference in the laboratory results between the study's end and baseline visit.

Discussion

The results of the study showed that the HAM-D and HAM-A ratings of the desvenlafaxine and escitalopram groups were significantly ($P < 0.001$) lower than their respective baselines. However, a comparison of the groups at 4 and 8 weeks of treatment did not show any statistically significant change. Desvenlafaxine with escitalopram were found to be safe. Escitalopram was better tolerated than desvenlafaxine because statistically significantly fewer side events were reported. Comparing both drugs to a placebo, it was found that they were equally effective at lowering anxiety connected to depression (several published articles confirmed these findings). Age-related increases in the prevalence of depression are consistent with the findings of the Wild et al. observational research.[20] Within the entire study group, depression was found in 69% of female participants and 31% of male participants in the current study. This suggests that depression in women is twice as common as depression in men in both categories. According to a study by Maier et al.[19], there is a comparable female majority in depression prevalence. From the start of the trial until the end, both groups' mean HAM-D scores significantly dropped. Similar drops in depression caused by escitalopram were noted in trials by Burke et al.[21], Lepola et al.[22], and other researchers. Desvenlafaxine has also been shown in multiple studies [23–26] to dramatically diminish depression. In this study, escitalopram has shown further antianxiety effects by reducing the HAM-A score from the start to the finish. In addition to its efficacy as an antidepressant, escitalopram has been frequently demonstrated to possess additional anxiolytic characteristics in studies conducted by Malin et al. [27].The mean HAM-A score decreased from the beginning to the end of the study due to desvenlafaxine as well. A study conducted by Tourian et al. has established the antianxiety characteristics of desvenlafaxine.[28] The group treated with desvenlafaxine

shown a substantial improvement in their anxiety symptoms as compared to the group receiving escitalopram medication in this trial. Both work just as well to lessen the anxiety that sadness causes.The current study's findings are in line with a randomized, double-blind, placebo-controlled, multicentric, flexible-dose trial conducted by Bose et al. in adult patients with generalized anxiety disorder[29]. Additionally, this study's findings are consistent with adverse events that have been previously reported for the same study drugs.[21, 22; 30–32]Within the group, both before and after desvenlafaxine and escitalopram treatment, HAM-D and HAM-A ratings fell statistically significantly; however, in later visits, there was no statistically significant difference between the two treatment groups. Escitalopram was shown to be more well-tolerated and to have a significantly lower risk of side effects.

The study short duration of 8 weeks and small subject count were its main drawbacks. To compare the absolute efficacy of escitalopram and desvenlafaxine, there was no placebo group. It is necessary to do additional research as the quality of life after therapy was not looked at. A closer look at the pharmacoeconomic effects of these drugs is necessary.

Conclusion

According to the current study, desvenlafaxine was more effective than escitalopram in reducing symptoms of depression. However, both drugs did so in a comparable way. It is not feasible to declare with certainty, though, that one medication is more clinically effective than another because of the tiny sample size. Escitalopram was better tolerated and had a statistically lower likelihood of adverse effects than desvenlafaxine. On the other hand, it is crucial to consider the differences in cost and tolerability while choosing treatments.

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