Original Article

Comparative Efficacy and Safety of Escitalopram versus Desvenlafaxine in Postmenopausal Women with Depression and Anxiety: A Randomized, Open-Label, Comparative Trial

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Abstract

Aims and Objectives: The aim was to evaluate the comparative efficacy and safety of escitalopram versus desvenlafaxine in postmenopausal women with depression and anxiety in our study cohort. **Materials and Methods:** A randomized, open-label, intention-to-treat, comparative study was conducted over a period of 1 year. Group 1 (n = 20) patients received tablet escitalopram 10 mg once daily orally which was increased to 20 mg/day when needed at the first follow-up. Group 2 (n = 20) patients received tablet desvenlafaxine 50 mg once daily orally which was increased to 100 mg/day when needed at the first follow-up. Patients were followed at 3 and 6 weeks. Primary endpoints were change in baseline scores (recorded as mean ± standard deviation) of Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A), and safety was also assessed and compared. **Results:** Forty patients completed the study. Escitalopram was statistically better than desvenlafaxine in reducing depression after 6 weeks of treatment ($P < 0.05$). Both the drugs were found to be equally effective in treating anxiety. Furthermore, they showed comparable safety and tolerability. **Conclusion:** Escitalopram appears to be more effective on short-term basis in treating depression, and both the drugs appear equally effective in combating anxiety. Furthermore, they appear to be equally safe and well tolerated in postmenopausal women with depression and anxiety.

Keywords: *Anxiety, depression, desvenlafaxine, escitalopram, postmenopausal women*

Introduction

Postmenopausal women experience a wide spectrum of vasomotor, psychosomatic, psychological, and urinary symptoms. Although well tolerated by some, these can be very distressing in others. With increasing life expectancy, women spend a significant part (one-third) of their lives in postmenopausal state demanding health-care priority.[1]

Decrease in estrogen levels in menopause reduces the levels of serotonin and norepinephrine, thus contributing to depression.[2]

Depression accounts for 3.8% of the global disability-adjusted life years and 8.3% of the global years lived with disability.[3] Depression is more prevalent in women (10%–25%), i.e., 1.5–3 times compared to men (5%–12%).[4] As evident from the risk factors and physiology of menopause, postmenopausal women are predisposed to depression.

There is also a substantial prevalence of anxiety symptoms in women in midlife.[5] Anxiety is strongly associated with depression, functional impairment, poor quality of life, and suicidal tendencies with excessive burden on the health-care resources.[6]

Access this article online

Quick Response Code:

Website: www.jmidlifehealth.org

DOI: 10.4103/jmh.JMH_139_18

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How to cite this article: Mahajan SS, Tandon VR, Arora M, Mahajan A, Kotwal S. Comparative efficacy and safety of escitalopram versus desvenlafaxine in postmenopausal women with depression and anxiety: A randomized, open-label, comparative trial. J Mid-life Health 2019;10:141-6.

Selective serotonin reuptake inhibitors (SSRIs) are contemplated as initial choice for treatment of depression in view of their overall efficacy, superior safety profile, more tolerable side effects, and ease of use.[7] The efficacy and safety of desvenlafaxine for the treatment of depression is also well established.[8-10] Both SSRIs and selective norepinephrine reuptake inhibitors (SNRIs) have been reported to be effective in treating anxiety associated with depression.[11,12]

SSRIs have been found to be less effective in postmenopausal women than premenopausal women and also in older women (≥50 years) as compared to younger ones.[13,14] On the other hand, SNRIs have reported consistent efficacy in women of different age groups, including the peri- and postmenopausal ones.[14,15]

The difference in response is speculated to be due to the effects of estrogen on mood regulation, both directly and indirectly through modulation of monoamine neurotransmitters.[16-18] Thus, the lack of estrogen in menopause can have a significant impact on the effectiveness of antidepressants.

There is paucity of data regarding the best therapeutic option for postmenopausal women suffering from depression and anxiety and that available, is from the western countries. Furthermore, in the Indian setup, there are only a few studies making direct head-to-head comparisons between escitalopram and desvenlafaxine in the adult patients of depression, and they also fail to provide any conclusive results regarding superiority of one over the other.[19,20]

Hence, a randomized, open-label, comparative study was undertaken to evaluate the comparative efficacy and safety of escitalopram versus desvenlafaxine in postmenopausal women with depression and anxiety in our study cohort.

Materials and Methods

A randomized, open-label, intention-to-treat, comparative study was conducted in the Department of Pharmacology in collaboration with the Department of Psychiatry, Government Medical College (GMC), Jammu, over a period of 1 year from November 2016 to October 2017. The study was undertaken after prior approval from the Institutional Ethics Committee, GMC, Jammu.

A written, informed consent was obtained from the first-degree relative as well as reverse consent was obtained from participants at the end of study or at the stage when a clinician permitted for it.

The study participants included were all postmenopausal women attending the psychiatry outpatient department and newly diagnosed with depression and anxiety after considering all inclusion and exclusion criteria for eligibility.

All principles of bioethics were followed throughout the conduct of the study.

Inclusion criteria

- Newly diagnosed patients of depression as per the Diagnostic and Statistical Manual of Mental Disorders-V criteria[21]
- Postmenopausal women with natural or surgical menopause
- A total score of ≥18 on the Hamilton Depression Rating Scale (HDRS)[22]
- A score of ≥18 on the Hamilton Anxiety Rating Scale (HAM-A)[23]
- Age 40–65 years
- Any uncomplicated comorbid condition.

Exclusion criteria

- Uncontrolled hypertension
- Uncontrolled diabetes mellitus
- Severe renal disease
- Cirrhosis of liver
- Angle-closure glaucoma
- Gastrointestinal diseases or patients taking omeprazole
- Patients already on psychotropic medications and prescription/over-the-counter drugs
- Patients on hormonal therapy, hormonal contraceptives, selective estrogen receptor modulators, and aromatase inhibitors
- History of major depressive episode/drug or alcohol abuse
- Suicidal attempt
- Bipolar disorder
- Endometrial or ovarian cancer
- Myocardial infarction, angina pectoris, cerebrovascular events, or stroke
- Any hospitalized/ambulatory patient with acute illness
- Intolerance or allergic reaction to the drugs during the study.

The study participants were randomized by block permutation method in a ratio of 1:1 into two treatment groups for a period of 6 weeks.

Treatment protocol

- Group 1: Patients received tablet escitalopram 10 mg once daily orally which was increased to 20 mg/day when needed at the first follow-up
- Group 2: Patients received tablet desvenlafaxine 50 mg once daily orally which was increased to 100 mg/day when needed at the first follow up.

The doses of escitalopram (10–20 mg/day) and desvenlafaxine (50–100 mg/day) used in the study were selected as they are the recommended therapeutic doses.[24-26] The mean dose required was computed and compared separately. Tablet lorazepam 1–2 mg/day was given as rescue therapy to patients when required.

At the baseline visit, the demographic details and relevant history of the patients were recorded. Vital parameters such as pulse rate and blood pressure were noted. Baseline evaluation of the HAM-D and HAM-A scores was done. The patients were called for follow-up at 3 weeks and 6 weeks.

Primary endpoints

The primary endpoints assessed were change in baseline scores (recorded as mean ± standard deviation [SD]) of:

1. Hamilton Depression Rating Scale (HDRS/HAM-D)
2. HAM-A.

Efficacy of the study drugs was evaluated by reduction in the mean baseline scores and percentage reduction in HAM-D and HAM-A at 3 weeks and 6 weeks. Intergroup comparison was done at baseline, 3, and 6 weeks.

For the safety assessment and comparison between the two groups, adverse drug events (ADEs) were recorded on the adverse drug reaction (ADR) form provided by the Pharmacovigilance Programme of India (PvPI).[27] A causal relationship was assessed, and severity and seriousness of the reactions were recorded as per the standard operating procedure of PvPI and relevant comparisons were made thereof.

Statistical analysis

The analysis was done on an intention-to-treat basis. Data were recorded as N (%) or mean ± SD. Continuous variables (normal distribution) were compared within the group by paired *t*-test and between groups by unpaired *t*-test. Categorical variables were reported in percentages and their analysis was done using Chi-square test. $P < 0.05$ was considered to be statistically significant.

Results

Of the 50 patients recruited, 40 patients completed the study with 20 each in both the arms.

The demographic details of these patients were comparable ($P > 0.05$), as depicted in Table 1.

It was observed that both escitalopram and desvenlafaxine produced a significant reduction ($P < 0.001$) in HAM-D scores at 3 and 6 weeks from their respective baselines. Furthermore, escitalopram was found to be statistically ($P < 0.05$) better than desvenlafaxine after 6 weeks of treatment [Table 2].

In addition, both the drugs were also significantly ($P < 0.001$) effective in reducing the HAM-A scores from their respective baselines at 3 and 6 weeks. However, they were comparable on intergroup comparisons at both follow-ups [Table 3].

There was no statistically significant difference ($P > 0.05$) in the mean dose required of both the drugs at 3 weeks and 6 weeks [Figure 1].

It was observed that 4 (20%) patients in the escitalopram arm and 6 (30%) patients in the desvenlafaxine arm required rescue treatment with tablet lorazepam. On intergroup comparison, the difference was not statistically significant ($P > 0.05$).

Both the drugs were found to be of comparable safety. The ADEs seen in escitalopram treatment arm were gastritis in 3 (50%) patients, dryness of mouth in 2 (33.3%) patients, and dizziness in 1 (16.7%) patient. Similarly, those in the desvenlafaxine group

Table 1: Demographic characteristics of patients

Demographic variable	Mean±SD		Mean difference	*t*	*P*
	Escitalopram (*n*=20)	Desvenlafaxine (*n*=20)			
Age	51.60±7.76	48.95±6.81	2.650	1.148	0.258 (NS)
Age at menopause	45.88±5.05	44.45±5.50	1.425	0.853	0.399 (NS
Duration since menopause	5.7±3.97	4.50±3.44	1.225	1.043	0.303 (NS)
Demographic variable	**Frequency (%)**		χ^2		***P***
	Escitalopram (*n*=20)	**Desvenlafaxine (*n*=20)**			
Nature of menopause					
Natural	19 (95)	18 (90)	0.360		0.548 (NS)
Surgical	1 (5)	2 (10)			
Residence					
Urban	12 (60)	13 (65)	0.107		0.744 (NS)
Rural	8 (40)	7 (35)			

Comparison between the groups' baseline scores with unpaired Student *t*-test and Chi-square test: NS: Nonsignificant. SD: Standard deviation

Table 2: Comparative effect of escitalopram and desvenlafaxine on Hamilton Depression Rating Scale scores

Time	Mean±SD Mean difference (percentage change)		*t*	*P*
	Escitalopram (*n*=20)	Desvenlafaxine (*n*=20)		
0 week	21.20±2.91	21.50±3.36	−0.302	0.765 (NS)
3 weeks	11.60±5.48***	11.95±4.63***	−0.218	0.829 (NS)
	−09.60±6.00 (45.28)	−09.55±4.15 (44.41)		
6 weeks	7.25±3.65***	9.60±3.49***	−2.081	0.044†
	−13.95±4.16 (65.80)	−11.90±4.64 (55.35)		

Paired *t*-test in comparison to respective baselines. ***P<0.001; Comparison between groups at baseline, 3 weeks and 6 weeks with unpaired Student's *t*-test. †P<0.05; NS: Nonsignificant, SD: Standard Deviation

Table 3: Comparative effect of escitalopram and desvenlafaxine on Hamilton Anxiety Rating Scale scores

Time	Mean±SD Mean difference (percentage change)		*t*	*P*
	Escitalopram (*n*=20)	Desvenlafaxine (*n*=20)		
0 week	21.00±3.43	20.10±3.52	0.818	0.418 (NS)
3 weeks	12.95±5.38***	11.05±3.66***	1.306	0.199 (NS)
	−08.05±4.69 (38.33)	−09.05±3.38 (45.02)		
6 weeks	07.90±4.51***	08.75±3.71***	−0.651	0.519 (NS)
	−13.10±4.28 (62.38)	−11.35±3.33 (56.47)		

Paired *t*-test in comparison to respective baselines. ***P<0.001; Comparison between groups at baseline, 3 weeks and 6 weeks with unpaired Student's *t*-test. NS: Nonsignificant, SD: Standard Deviation

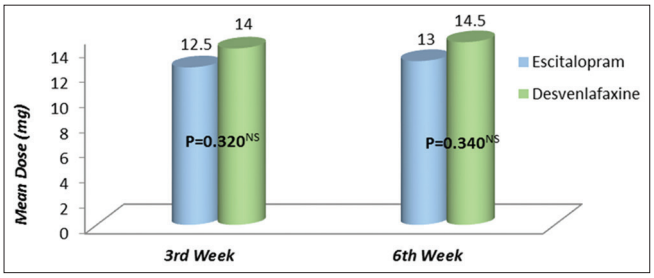

Figure 1: Mean dose required of escitalopram and desvenlafaxine (with correction)

were gastritis, dizziness, and headache in 3 (37.5%), 3 (37.5%), and 2 (25%) patients, respectively. All the ADRs were possible on causality assessment and mild-to-moderate in nature, and none of the reactions warranted withdrawal or change of treatment.

Discussion

In our study, both escitalopram and desvenlafaxine showed a significant reduction in the mean HAM-D score from their respective baselines at 3 and 6 weeks ($P < 0.001$), thus suggesting their antidepressant efficacy in postmenopausal women. Similar findings were observed in a study by Soares *et al.*, 2010, wherein both the drugs showed a significant reduction in HAM-D scores of postmenopausal women from their respective baselines after 8 weeks of treatment.[28] Furthermore, their antidepressant efficacy is well established in adult patients of depression.[19,20]

Escitalopram was found to be statistically better than desvenlafaxine after 6 weeks of therapy on neck-to-neck comparison, thereby proving its superiority ($P < 0.05$). Kennedy *et al.*, 2009, also observed that escitalopram was superior to all comparators, i.e., SSRIs such as citalopram, fluoxetine, paroxetine, and sertraline and SNRIs such as duloxetine and venlafaxine-XR in overall treatment effect with a significant estimated mean treatment difference on Montgomery-Asberg Depression Rating Scale (MADRS) ($P < 0.0001$) in adult patients of depression.[29]

However, our results differed from those by Soares *et al.*, 2010, wherein both the drugs were comparable to each other ($P = 0.24$) on intergroup comparison after 8 weeks of treatment. The disparity in results could be explained on the basis of a larger sample size, different study design, treatment schedule and longer duration of the study, differences in the doses used, and difference in the epidemiological and demographic profiles of the study participants.[28]

Both the drugs were significantly ($P < 0.001$) effective in reducing anxiety symptoms in postmenopausal women with depression after 3 and 6 weeks of treatment in our study. Numerous studies have also reported the efficacy of escitalopram in improving the mean HAM-A score from baseline in adult patients with anxiety symptoms.[30,31] Furthermore, the efficacy of desvenlafaxine in treating anxiety was substantiated by Tourian *et al.*, 2010.[32]

However, in the present study, they did not vary significantly from each other on intergroup comparison at both 3 and 6 weeks, failing to establish their

superiority over each other in treating anxiety. Various other studies corroborated similar results on neck-to-neck comparison.[20,28]

In our study, the mean dose of escitalopram required was 12.50 ± 4.44 mg and 13.00 ± 4.70 mg at 3 and 6 weeks of treatment and that of desvenlafaxine was 14 ± 5.03 mg at 3 weeks and 14.5 ± 5.10 mg at 6 weeks. These findings differed from those of Soares *et al*., 2010.[28]

Both the drugs were found to be equally safe and well tolerated in our study. Similar findings have been reported previously.[20,28]

Limitations of our study were that it was a short duration study to conclusively comment on the efficacy of antidepressants and results may vary in general population because of the small number of patients in the study. Furthermore, no attempt was made to study the mechanism of action and dose–response relationship.

Conclusion

Escitalopram appears to be more effective on short-term basis in treating depression, and both the drugs appear equally effective in combating anxiety. Furthermore, they appear to be equally safe and well tolerated in postmenopausal women with depression and anxiety.

Even though the results of the current study are very encouraging and in the favor of escitalopram, in view of its limitations a larger randomized controlled comparative clinical trial needs to be done to establish and confirm the results before it is widely recommended for clinical treatment of depression and anxiety in particular strata of postmenopausal women.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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