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Abstract

Efficacy and safety of escitalopram versus desvenlafaxine in the treatment of major depression: A preliminary 1-year prospective randomized open label comparative trial

Aim and Objective: To compare efficacy and safety of escitalopram with desvenlafaxine in the treatment of major depression. **Materials and Methods:** A total of 60 patients of depression were randomized into two groups after meeting inclusion criterion. In the first 3 weeks, escitalopram 10 mg/day was given and then 20 mg/day for the next 3 weeks in group 1 ($n = 30$). Desvenlafaxine in the first 3 weeks was given 50 mg/day and 100 mg/day for the next 3 weeks in group 2 ($n = 30$). The parameters evaluated during the study were efficacy assessments by Hamilton Scale of Rating Depression (HAM-D), Hamilton Rating Scale of Anxiety (HAM-A), and Clinical Global Impression (CGI). Safety assessments were done by UKU-scale. **Results:** Escitalopram and desvenlafaxine significantly ($P < 0.001$), reduced HAM-D, HAM-A, and CGI scores from their respective base lines. However, on comparison failed show any statistical difference at 3 and 6 weeks of treatment. Escitalopram and desvenlafaxine were both found to be safe and well-tolerated and there was not much difference between the two groups as evident from UKU Scale and their effect on various biochemical parameters. **Conclusion:** The present study demonstrated similar efficacy and safety in reducing depression and anxiety with both escitalopram and desvenlafaxine, but clinical superiority of one drug over the other cannot be concluded due to limitations of the small sample size.

Key words: Anxiety, desvenlafaxine, escitalopram, major depression

INTRODUCTION

Major depressive disorder is a prevalent and disabling illness worldwide, associated with significant impairment in physical and social functioning as well as increased morbidity and mortality.^[1] At its worst, depression can lead to suicide. Fewer than 25% of those affected have access to effective

treatments. A large selection of effective antidepressant medications is available, but their clinical utility is limited by adverse events or some or other problems. Indeed, the clinical success of the selective serotonin reuptake inhibitors (SSRIs) over the past decade relative to their therapeutic predecessors, such as tricyclic antidepressants, has been

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attributed to their improved tolerability, ease of use and far greater safety.^[2] However, the safety and tolerability of individual SRIs vary within the class^[3] and it is clear that many patients may not respond optimally to an acute course of any given treatment. Thus, there is a constant need of search for new better effective treatment.

The efficacy and the tolerability of escitalopram, aSSRI and desvenlafaxine, a non-selective SRI has been well-established.^[4-21] Most of the studies establishing their efficacy and safety are available from western population and whatever available has compared these drugs respectively with placebo. Thus, there are very limited studies available directly comparing efficacies of escitalopram with desvenlafaxine in treatment of major depression.

Hence, a preliminary 1-year prospective randomized open label trial comparing efficacy and safety of escitalopram with desvenlafaxine in the treatment of major depression was undertaken.

MATERIALS AND METHODS

A total of 60 patients from psychiatry outpatient department of a tertiary level hospital diagnosed with major depression were included in the study after they fulfilled the inclusion criteria. A total of 30 patients were taken in each group. A written informed consent was obtained from first relative after explaining the nature and purpose of the study along with reverse consent from the patients on their clinical improvement was taken. The study was approved by institutional ethics committee, GMC, Jammu vide number 36A/Pharma/IEC/2010/528 dated 27. 10. 2010. The flow diagram of the study is shown in Figure 1.

Patients with major depression of both sexes in the age group of 18-55 years with a Hamilton Scale of Rating Depression (HAM-D) score >20; who meet Diagnostic and Statistical Manual of Mental Disorders-IV criteria for depression,^[4] with a minimum total score of 20 on the 24-item Hamilton Scale for Depression,^[5] non pregnant females and without any comorbid conditions like DM, HT, and IHD were included in the study.

Exclusion criteria

“Patients with the following conditions were excluded from the study - those taking any antidepressant in the last 6 weeks; intake of any drug which may causes depressive state, psychosis or anxiety; any chronic ailment; any substance abuse; and those patients intolerant or allergic to the drug.

In case any exacerbation of disease or ADR event during the study, the data from this population were decided to be included in statistical analysis at the time of their exclusion.

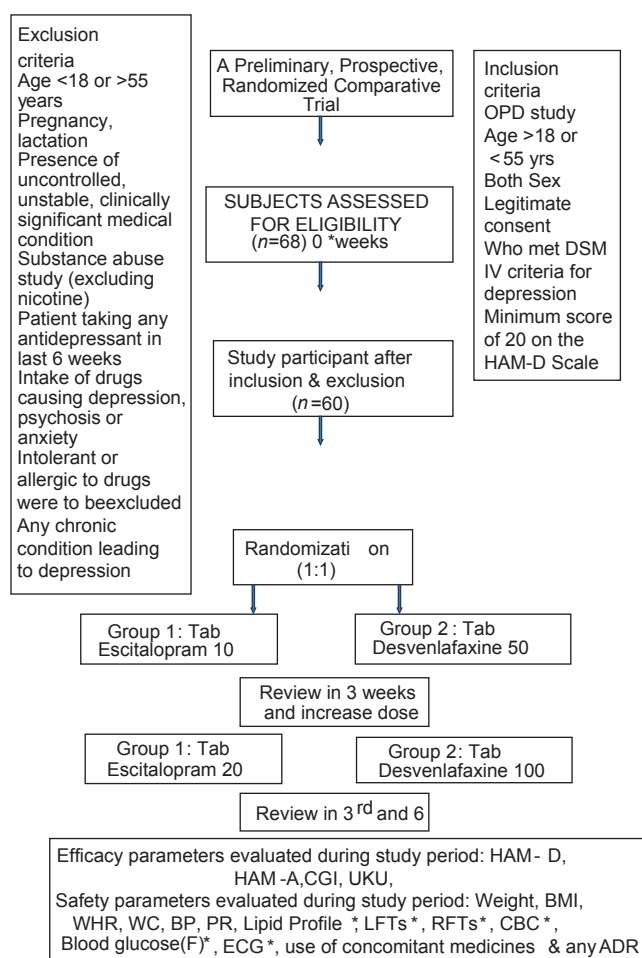


Figure 1: Study flow diagram

Patients meeting eligibility criteria at the screening visit were assigned randomly in 1:1 ratio to either receive escitalopram or desvenlafaxine. The total duration of study was 6 weeks. The dose of study medication was to be increased after 3 weeks in accordance with the approved labelling information. In the first 3 weeks, escitalopram 10 mg/day was given and then 20 mg/day for the next 3 weeks. Dose of desvenlafaxine in the first 3 weeks was 50 mg/day and 100 mg/day for the next 3 weeks. The primary endpoints were HAM-D, Hamilton Rating Scale of Anxiety (HAM), and Clinical Global Impression (CGI).

Adverse event monitoring was done by using UKU-scale. Furthermore, some of biochemical parameter like blood sugar, LFT, and RFT were also analyzed and compared among two treatment arms for safety assessment.

Statistical analysis

All the analysis was carried out with the help of computer software SPSS version 15 for windows. The evaluation of patients in two groups was done by applying HAM-D, HAM-A, and CGI and will be reported as mean \pm standard deviation scores. The score were reported as % change from

the baseline and were assessed by use of paired/unpaired “t” test/analysis of covariance whichever was applicable. Categorical variables were reported as percentage and the statistical analysis done by use of Chi-square test. A $P < 0.05$ was considered statistically significant. All P values reported analyses were two-tailed. The analysis was done on intention-to-treat basis.

RESULTS

The base line parameters of both the group has been shown in Table 1. Both escitalopram as well as desvenlafaxine significantly ($P < 0.001$) reduced HAM-D, HAM-A, and CGI scores from their respective base

lines [Table 2]. However, on comparison failed show any statistical difference at 3 and 6 weeks of treatment [Table 3].

Escitalopram and desvenlafaxine were both safe and well-tolerated and there was not much difference between the two groups as evident from UKU-scale [Table 4].

Escitalopram and desvenlafaxine were both safe and well-tolerated and there was not much difference between the two groups as far the effect on various biochemical parameters was concerned [Table 5].

Side effects seen in the present study with escitalopram were headache ($n = 6$), nausea ($n = 4$), vomiting ($n = 1$), diarrhea ($n = 2$), palpitations ($n = 3$), sexual dysfunction

Table 1: Baseline characteristics of patients (mean±standard deviation)

Parameter mean±SD	Escitalopram	Desvenlafaxine	Statistical inference	
			t	P value
Age (years)	34.23±9.19	33.60±9.95	0.25	0.79
Sex: Male: Female	13:17	15:15	χ^2 0.27	0.60
HAM-D	23.96±2.20	23.66±2.07	0.54	0.58
HAM-A	14.56±3.35	14.96±2.77	-0.50	0.61
CGI	5.76±0.67	5.56±0.77	1.06	0.29
Pulse	81.53±5.47	82.50±7.97	-0.54	0.58
BP systolic mm/hg	124.93±3.31	125.40±4.30	-0.47	0.64
BP diastolic mm/hg	79.66 ±	80.63 ±	-1.00	0.32
Weight (kg)	65.23±11.99	65.93±12.45	-0.22	0.82
Height (cm)	166.56±9.34	166.86±8.70	-0.12	0.89
BMI (kg/m ²)	23.34±2.48	23.60±3.24	-0.35	0.72
Waist circumference	81.90±6.65	80.96±9.08	0.45	0.65
Blood sugar (R)	107.96±3.47	105.90±5.26	1.79	0.07
Serum urea	27.83±1.08	28.16±0.69	-1.41	0.16
Serum creatinine	0.58±0.092	0.57±0.053	0.51	0.61
Serum sodium	142.26±1.08	142.16±0.79	0.40	0.68
Serum potassium	4.24±0.104	4.24±0.107	0.12	0.90
Serum bilirubin	0.81±0.07	0.82±0.04	-0.85	0.39
SGOT	32.43±4.32	31.60±2.54	0.90	0.36
SGPT	34.06±12.03	32.06±7.07	0.78	0.43
Hb (g)	11.24±0.89	11.28±0.96	-0.19	0.84
Total WBC/cumm	6066.66±784.91	5666.66±606.47	2.20	0.03
Platelet count lakh/cumm	1.90±0.173	1.91±0.178	-0.21	0.83

BP=Blood pressure, BMI=Body mass index, CGI=Clinical global impression, HAM-A=Hamilton rating scale of anxiety, HAM-D=Hamilton scale of rating depression, Hb=hemoglobin, SD=Standard deviation, SGPT=Serum glutamate pyruvate transaminase, SGOT=Serum glutamate oxaloacetate transaminase, WBC=White blood cell

Table 2: Effect of treatment across escitalopram (n=30) and desvenlafaxine (n=30) groups over time: Scores within subjects (mean±standard deviation)

Variables	0 week	3 rd week	6 th week	Pillai's trace F (within subjects)	P value
HAM-D total score					
Escitalopram	23.97±2.21	19.70±1.91	16.30±1.57	490.94	<0.001*
Desvenlafaxine	23.67±2.07	20±4.19	17.1±3.52		
HAM-A total score					
Escitalopram	14.57±3.56	11.87±3.17	9.63±3.02	342.1	<0.001*
Desvenlafaxine	14.97±2.77	11.9±3.49	9.17±3.11		
CGI score					
Escitalopram	5.77±0.68	2.90±0.31	2.47±0.51	420.88	<0.001*
Desvenlafaxine	5.57±0.77	2.93±0.25	2.53±0.57		

* $P < 0.05$ =Significant (two-tailed), CGI=Clinical global impression, HAM-A=Hamilton rating scale of anxiety, HAM-D=Hamilton scale of rating depression

Table 3: Effect of treatment across escitalopram (n=30) and desvenlafaxine (n=30) groups over time: Scores between subjects (mean±standard deviation)

Variables	1 st week	3 rd week	6 th week	Pillai's trace F (within subjects)	P value
HAM-D score					
Escitalopram	23.97±2.21	19.70±1.91	16.30±1.57	3.014	0.057
Desvenlafaxine	23.67±2.07	20±4.19	17.1±3.52		
HAM-A score					
Escitalopram	14.57±3.56	11.87±3.17	9.63±3.02	2.596	0.083
Desvenlafaxine	14.97±2.77	11.9±3.49	9.17±3.11		
CGI score					
Escitalopram	5.77±0.68	2.90±0.31	2.47±0.51	0.754	0.475
Desvenlafaxine	5.57±0.77	2.93±0.25	2.53±0.57		

* $P < 0.05$ = Significant (two-tailed). CGI: Clinical Global Impression, HAM-A: Hamilton Rating Scale of Anxiety, HAM-D: Hamilton Scale of Rating Depression

Table 4: Effect of escitalopram (n=30) and desvenlafaxine (n=30) On UKU scale at 6 weeks

Parameter	Escitalopram	Desvenlafaxine	Statistical inference	
			t	P
UKU mean±SD	0.93	1.13	0.96	0.33

SD=Standard deviation, UKU=Udvalg for kliniske undersøgelser

($n = 1$), loss of appetite ($n = 1$), insomnia ($n = 3$), and constipation ($n = 1$). Whereas, with desvenlafaxine were headache ($n = 4$), nausea ($n = 9$), palpitations ($n = 2$), insomnia ($n = 3$), constipation ($n = 3$), giddiness ($n = 4$), dry mouth ($n = 3$), and restlessness ($n = 1$).

DISCUSSION

In the present study, it was seen that escitalopram-reduced depression levels with a decrease from the baseline value HAM-D from 3 weeks onward till the end of the study. The above findings are in concurrence with various published reports in which these drugs, individually were efficacious in decreasing depression and anxiety in comparison to placebo.

A similar reduction in depression by escitalopram is also reported by Burke *et al.*,^[6] and Leopolo *et al.*,^[7] who showed that escitalopram significantly improved MADRS scores in comparison to placebo starting with in within one week of treatment and persisting till 8 weeks of therapy at both the doses (10 mg and 20 mg).

Rapaport *et al.*,^[8] showed that the time to depression relapse was significantly longer ($P = 0.013$) and the cumulative rate of relapse was significantly lower in patients who received escitalopram (26% escitalopram vs. 40% placebo; hazard ratio = 0.56; $P = 0.01$). Moore *et al.*,^[9] showed that the Montgomery-Åsberg Depression Rating Scale (MADRS)

score decreased more in the escitalopram than in the citalopram arm (-22.4 ± 12.9 vs. -20.3 ± 12.7 ; $P < 0.05$). There were more treatment responders with escitalopram (76.1%) than with citalopram (61.3%, $P < 0.01$).

In the present study, it was seen that desvenlafaxine produced a decrease from the baseline value of HAM-D from 3 weeks onward till the end of the study, that is, at 6 weeks. Desvenlafaxine has also been shown to cause a significant reduction in depression in several studies.^[10-13] These studies found out that mean HAM-D scores for desvenlafaxine 50, 100, 200, and 400 mg/day were significantly lower than placebo, respectively.

In the present study, there was a trend toward the higher overall response of escitalopram in decreasing depression and anxiety than with desvenlafaxine ($F = 3.014$, $P = 0.057$). Our results are almost in accordance to those put forth by Soares *et al.*,^[14] who reported a similar reduction in depression with escitalopram and desvenlafaxine. Reductions in HAM-D₁₇ total score at acute phase end point were similar for desvenlafaxine and escitalopram-treated women (-13.6 vs. 14.3 , respectively, $P = 0.24$). No significant difference was observed between groups at continuation phase end points in the proportion of who maintained response (desvenlafaxine, 82%; escitalopram, 80%, $P = 0.70$).

Limited studies have directly compared the efficacy of escitalopram with desvenlafaxine in treatment of major depression, otherwise escitalopram has been compared with class SNRI's in other studies. Kornstein *et al.*,^[15] showed that mean reduction in MADRS score from baseline to week 8 was significantly greater for the escitalopram group versus the SNRI group.

In the present study, it was seen that escitalopram produced a decrease from the baseline value of HAM-A, from 3 weeks onward till the end of the study, that is, at

Table 5: Effect of escitalopram (n=30) and desvenlafaxine (n=30) on various biochemical parameters (mean±standard deviation)

Variables	1 st week	3 rd week	6 th week	Pillai's trace F (within subjects)	P value
Blood sugar					
Escitalopram	107.96±3.47	105.50±5.45	107.56±5.40	0.697	0.502
Desvenlafaxine	105.90±5.26	105±4.41	105.03±4.58		
Serum urea					
Escitalopram	27.83±1.085	27.96±0.61	28.03±1.03	1.874	0.163
Desvenlafaxine	28.16±0.69	28.13±0.77	28±0.69		
Serum creatinine					
Escitalopram	0.58±0.092	0.56±0.071	0.58±0.089	0.311	0.734
Desvenlafaxine	0.57±0.053	0.56±0.062	0.56±0.061		
Desvenlafaxine	5.57±0.77	2.93±0.25	2.53±0.57		
Serum bilirubin					
Escitalopram	0.81±0.073	0.81±0.07	0.82±0.04	0.020	0.981
Desvenlafaxine	0.82±0.061	0.83±0.047	0.83 ± 0.047		
Serum SGOT					
Escitalopram	32.43±4.32	31.66±2.46	32.70±4.12	0.301	0.741
Desvenlafaxine	31.20±2.60	32.86±2.08	32.86 ± 2.08		
Serum SGPT					
Escitalopram	34.06±12.034	32.36±7.07	32.30±6.43	0.207	0.814
Desvenlafaxine	32.06 ± 7.07	32.53 ± 8.01	31.60 ± 6.41		

* $P < 0.05$ = Significant (two-tailed). SGPT = Serum glutamate pyruvate transaminase, SGOT = Serum glutamate oxaloacetate transaminase

6 weeks indicating additional antianxiety activity. Similar reductions in anxiety by escitalopram were put forth by Malin *et al.*,^[16] who consistently demonstrated significant anxiolytic properties in addition to antidepressant efficacy with escitalopram. It also showed efficacy in treating panic disorder and generalized and social anxiety disorders.

Bandelow *et al.*,^[17] documented the efficacy of escitalopram, on symptoms of anxiety in patients with major depressive disorder. Similarly, escitalopram was shown significantly more effective compared to placebo in treating both anxiety symptoms and the entire depression in the total depressive population, as well as in depressive patients with a high degree of anxiety by Cyril and Jaromir.^[18]

In the present study, it was seen that desvenlafaxine also produced a decrease from the baseline value of HAM-A, from 3 weeks onward till the end of the study, that is, at 6 weeks. Similar reductions in anxiety by desvenlafaxine were put forth by Tourian *et al.*^[19] In this secondary analysis, desvenlafaxine-treated patients experienced significant improvement in anxiety symptoms compared with placebo-treated patients.

In current study, there is no significant difference in the efficacy of escitalopram and desvenlafaxine in reducing anxiety ($F = 2.596$, $P = 0.083$). Similar results are shown by Soares *et al.*,^[14] where there are no differences in the efficacy of escitalopram and desvenlafaxine in reducing anxiety.

In the present study, it was seen that escitalopram produced a decrease from the respective baseline value of CGI from

3 weeks onward till the end of the study, that is, at 6 weeks. A similar reduction in CGI by escitalopram is also reported by, Olić *et al.*,^[20] and Yevtushenko *et al.*^[21]

In the present study, it was seen that desvenlafaxine also produced a decrease from the respective baseline value of CGI from 3 weeks onward till the end of the study, that is, at 6 weeks. Similar reductions in CGI were seen in other studies also.^[14,19]

In current study, there is no significant difference in the CGI scores of escitalopram group and desvenlafaxine group ($P = 0.475$) Scores between subjects. Similar results were seen by Soares *et al.*,^[14] with almost same reduction in both escitalopram and desvenlafaxine group.

In the present study, escitalopram and desvenlafaxine were safe and well-tolerated. UKU scale is used to evaluate side effects and the values are (0.93 and 1.13), respectively in escitalopram and desvenlafaxine group. There is no statistically significant difference between the two groups ($t = 0.96$, $P = 0.33$). There was no other discontinuation due to any other reasons including adverse effects in the present study. Similar side effect profile was put forth by Soares *et al.*,^[14] who showed both desvenlafaxine and escitalopram were generally safe and well-tolerated.

The present study does have some limitations. First, it is a short-term study with less number of patients and effect of small sample size cannot be ruled out on results of the study.

CONCLUSION

The present study demonstrated almost similar efficacy and safety in reducing depression and anxiety with both escitalopram and desvenlafaxine, but clinical superiority of one drug over the other cannot be definitely be concluded due to small sample size. Escitalopram and desvenlafaxine were well-tolerated.

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Conflicts of interest

There are no conflicts of interest.

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