A Double-Blind Comparison of Escitalopram and Venlafaxine Extended Release in the Treatment of Major Depressive Disorder

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Background: Escitalopram is the most selective serotonin reuptake inhibitor (SRI) antidepressant available. Venlafaxine is a nonselective SRI that also inhibits noradrenergic reuptake. This study compared escitalopram and venlafaxine extended release (XR) in depressed outpatients at the highest doses recommended in the United States.

Method: In this randomized trial, patients (diagnosis of DSM-IV–defined major depressive disorder; baseline Hamilton Rating Scale for Depression score of ≥ 20) received 1 week of single-blind placebo treatment, followed by 8 weeks of double-blind, fixed-dose treatment with either escitalopram or venlafaxine XR (rapidly titrated to 20 mg/day and 225 mg/day, respectively, in accordance with prescribing information). The primary efficacy variable was change from baseline to week 8 in Montgomery-Asberg Depression Rating Scale (MADRS) total score. Data were collected from May to December 2002.

Results: Mean baseline MADRS scores for the escitalopram (N = 97) and venlafaxine XR (N = 98) groups were 30.7 and 30.0, respectively. There were no significant differences in measures of efficacy between the 2 antidepressants. Mean changes from baseline to endpoint in MADRS total score for escitalopram and venlafaxine XR were –15.9 and –13.6, respectively. Remission (MADRS score of ≤ 10) rates at endpoint were 41.2% for escitalopram and 36.7% for venlafaxine XR. Response (≥ 50% reduction from baseline MADRS score) rates for the escitalopram and venlafaxine XR groups were 58.8% and 48.0%, respectively. Tolerability measures favored escitalopram over venlafaxine XR treatment. The venlafaxine XR group had a higher incidence than the escitalopram group of treatment-emergent adverse events (85.0% vs. 68.4%) and discontinuation due to adverse events (16.0% vs. 4.1%; $p < .01$).

Conclusion: Results of this study indicate that, when titrated rapidly to their maximum recommended doses, escitalopram is at least as effective as venlafaxine XR and significantly better tolerated. These results do not support the hypothesis that nonselective SRIs have greater efficacy than selective SRIs.

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Major depressive disorder is a prevalent and disabling illness, associated with significant impairment in physical and social functioning,[1] as well as increased morbidity and mortality.[2] Depression is also a relapsing condition that requires long-term treatment.[3] Tolerability issues can affect patient compliance with pharmacotherapy, both acutely and during continuation treatment when psychiatric symptoms have become less severe.[4,5]

A large selection of effective antidepressant medications is available, but their clinical utility can be limited by adverse events. Indeed, the clinical success of the serotonin reuptake inhibitors (SRIs) over the past decade relative to their therapeutic predecessors, such as the tricyclic antidepressants, has been attributed to their improved tolerability, ease of use, and far greater safety in overdose.[6,7] However, the safety and tolerability of individual SRIs vary within this class,[8,9] and it is clear that many patients will not respond optimally to an acute course of any given treatment.[10]

Escitalopram is the most selective SRI studied to date.[11] The efficacy and tolerability of escitalopram throughout its recommended dose range (10–20 mg/day) have been established in several placebo-controlled trials.[12–14] By contrast, venlafaxine is a nonselective SRI that additionally exhibits appreciable inhibition of norepinephrine reuptake at higher doses.[15] The extended release (XR) formulation of venlafaxine has been shown to be an effective antidepressant across its recommended dose range of 75 to 225 mg/day,[16,17] with some indication that higher doses may be associated with increased efficacy.[18–20]

A recently completed randomized trial compared flexibly dosed escitalopram 10 to 20 mg/day with venlafaxine

XR 75 to 150 mg/day in a primary care setting and found the 2 compounds to be comparably effective.[21] The aim of the present study was to compare the efficacy and tolerability of escitalopram and venlafaxine XR when titrated rapidly to their highest recommended doses.

METHOD

Eight centers in the United States participated in this randomized, double-blind, fixed-dose study comparing the efficacy and safety of escitalopram 20 mg/day and venlafaxine XR 225 mg/day.

Patients

Male and female outpatients, 18 to 65 years of age, who met DSM-IV[22] criteria for major depressive disorder were eligible for the study. Patients were required to have a minimum total score of 20 on the 24-item Hamilton Rating Scale for Depression (HAM-D)[23] at both screening and baseline visits. Results of physical examinations, laboratory tests, and electrocardiograms (ECG) were required to be normal at the screening visit, or any abnormalities had to be judged clinically insignificant. Female patients of childbearing potential were required to have a negative serum β-human chorionic gonadotropin pregnancy test and to be practicing a medically accepted form of contraception. Women who were lactating were excluded from the trial.

Also excluded from the study were patients currently meeting DSM-IV criteria for primary diagnoses for any Axis I disorder other than major depressive disorder, as well as patients with a history of schizophrenia or other psychotic disorder and patients with a cognitive disorder (including mental retardation) or personality disorder of sufficient severity to interfere with their participation. Patients who met DSM-IV criteria for substance abuse or dependence within the past 6 months were ineligible to participate, as were those judged to be at risk of suicide. Patients with any clinically significant medical illness that had not been stable for at least 1 year were also excluded.

Use of a depot neuroleptic within 6 months prior to study entry was prohibited, as was use of any neuroleptic, antidepressant, or anxiolytic medication within 2 weeks (5 weeks for fluoxetine) prior to the first administration of double-blind study medication. Patients who had previously received treatment with either escitalopram or venlafaxine were not eligible to participate, nor were those who had previously failed to respond to adequate trials of 2 or more antidepressants. Concomitant use of any psychoactive drug (or any drug with a psychotropic component) was not allowed, except zolpidem or zaleplon as needed for sleep.

The study protocol was approved by the institutional review boards for the participating study centers. All participants provided written informed consent.

Study Design

Patients meeting eligibility criteria at the screening visit entered a 1-week, single-blind, placebo lead-in period. Those who continued to meet all entry criteria after 1 week were randomly assigned to receive 8 weeks of double-blind, fixed-dose treatment with either escitalopram or venlafaxine XR. The dose of study medication was titrated upward as rapidly as possible in accordance with approved labeling information,[24,25] to the target doses of escitalopram 20 mg/day or venlafaxine XR 225 mg/day. Patients randomly assigned to escitalopram treatment received 10 mg/day of escitalopram during the first week, after which the dose was increased to 20 mg/day for the remaining 7 weeks. Patients randomly assigned to receive venlafaxine XR initiated treatment at 75 mg/day for days 1 to 4, after which the dose was increased to 150 mg/day for days 5 to 8 and then increased to 225 mg/day for the remainder of the treatment period. To maintain the blind, all study medication was provided in blister packs of identically appearing capsules and administered as 2 capsules per day, to be taken in the evening, regardless of dose or treatment group. No adjustment of dosage was allowed, although medication could be taken as a single dose in the morning, if preferred. Patients unable to tolerate the assigned study medication were discontinued from the trial.

On completion of 8 weeks of double-blind treatment (or on early discontinuation from the study), patients entered a 2-week blinded down-titration period. Patients in the escitalopram 20 mg/day group had their dose decreased to 10 mg/day at the start of the down-titration period. Patients receiving venlafaxine XR had their dose decreased from 225 mg/day to 150 mg/day at the start of the down-titration period and then decreased 1 week later to 75 mg/day.

Assessments

Evaluations were conducted at screening, at baseline, and after 1, 2, 4, 6, and 8 weeks of double-blind treatment. Efficacy assessments included the Montgomery-Asberg Depression Rating Scale (MADRS),[26] the 24-item HAM-D, and the Clinical Global Impressions-Improvement scale (CGI-I)[27] and -Severity of Illness scale (CGI-S)[27] and were performed at baseline (with the exception of the CGI-I) and all subsequent visits, except at the end of the down-titration period. Anxiety symptoms were measured at baseline and at the end of weeks 2 and 8 (or on early termination) using the Hamilton Rating Scale for Anxiety (HAM-A).[28] The effects of treatment on the somatic symptoms associated with depression were assessed with the HAM-D somatic subscale,[29] consisting of HAM-D items 10 (anxiety-psychological), 11 (anxiety-somatic), 12 (somatic symptoms-gastrointestinal), 13 (somatic symptoms-general), 15 (hypochondriasis), and 17 (insight). Additionally, patient functioning was assessed at baseline and at the study endpoint (week 8 or on early termination) with 2 patient-rated questionnaires: the Center

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population

Characteristic	Escitalopram (N = 98)	Venlafaxine XR (N = 100)
Age, mean ± SD, y	37.3 ± 12.3	37.5 ± 11.6
Gender, female, %[a]	69.4	47.0
Race, white, %	77.6	73.0
Course of illness, recurrent, %	60.2	62.0
Duration of major depressive disorder, mean ± SD, y	8.5 ± 10.1	9.8 ± 10.5

[a]p < .01; escitalopram vs. venlafaxine.
Abbreviation: XR = extended release.

Table 2. Reasons for Patient Attrition

	Escitalopram (N = 98)		Venlafaxine XR (N = 100)	
Status	N	%	N	%
Completed	72	74	66	66
Withdrawn	26	27	34	34
Reason for withdrawal				
Lost to follow-up	14	14	8	8
Adverse event	4	4	16	16[a]
Consent withdrawn	2	2	6	6
Protocol violation	4	4	3	3
Other	2	2	1	1

[a]p < .01; Fisher exact test.
Abbreviation: XR = extended release.

for Epidemiological Studies-Depression Scale (CES-D)[30] and the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q).[31]

Safety assessments were conducted at every visit and comprised vital signs, body weight, use of concomitant medication, and adverse event monitoring. Patients were not queried concerning specific adverse events. Physical examination, 12-lead ECG, and laboratory tests were performed at screening and at the end of week 8 or on early termination.

Statistical Analysis

The primary efficacy variable in this study was the change from baseline to week 8 in MADRS total score, using the last-observation-carried-forward (LOCF) analysis. Secondary efficacy parameters included the change from baseline in HAM-D and HAM-D somatic subscale scores; HAM-A, CGI-S, CES-D, and Q-LES-Q scores; and CGI-I score at endpoint. Both LOCF and observed-cases (OC) analyses were performed. Additionally, 4 prospectively defined criteria of treatment response were assessed: an improvement from baseline of at least 50% in MADRS or HAM-D total score, a CGI-I score of 1 or 2, and a MADRS score of ≤ 12. Two prospectively defined criteria of remission were separately employed: MADRS score of ≤ 10 and a score on the first 17 items of the HAM-D of ≤ 7.

The change from baseline to endpoint was analyzed using an analysis of covariance (ANCOVA) model, with treatment group and study center as factors and baseline score as a covariate. For CGI-I scores, an ANCOVA model was used, with treatment group and center as factors and baseline CGI-S score as covariate.

Response and remission rates were analyzed using logistic regression with treatment group and baseline score as explanatory values. Differences between treatment groups in demographic and baseline characteristics were tested using an analysis of variance model with treatment and study center as factors for continuous variables and Cochran-Mantel-Haenszel tests controlling for center for categorical variables. The proportion of patients prematurely discontinuing from the study was analyzed using the Fisher exact test.

All statistical tests were 2-sided with a 5% significance level. All efficacy analyses were based on the intent-to-treat population (those who had received at least 1 dose of double-blind study medication and had at least 1 post-baseline MADRS assessment). All patients who received at least 1 dose of double-blind study medication were included in the safety analyses. All efficacy results presented are based on the LOCF analysis, unless otherwise indicated.

RESULTS

A total of 198 patients received at least 1 dose of double-blind treatment with escitalopram 20 mg/day (N = 98) or venlafaxine XR 225 mg/day (N = 100) and were included in all safety analyses. Efficacy analyses were performed on the intent-to-treat population, which included 97 escitalopram-treated patients and 98 venlafaxine-treated patients.

Patient Characteristics

Baseline patient characteristics of the study population are shown in Table 1. There were no differences between treatment groups, with the exception that a greater proportion of patients randomly assigned to receive escitalopram were female (69.4%) compared with the venlafaxine XR group (47.0%; p < .01). The majority of patients in both treatment groups were white and had recurrent depression. The mean duration of major depressive disorder was 8.5 years in the escitalopram group and 9.8 years in the venlafaxine XR group. Patients in both groups were moderately to severely ill at baseline with mean MADRS scores of 30.0 and 30.7 for the venlafaxine XR and escitalopram treatment groups, respectively. There were no clinically meaningful differences between treatment groups at baseline in terms of disease severity, course of illness, or duration of major depressive disorder.

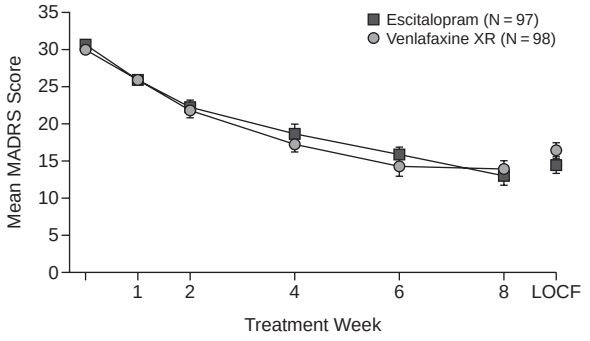
Overall, approximately 70% of patients completed the study (Table 2). The completion rates were similar for the escitalopram and venlafaxine XR treatment groups (73.5% and 66.0%, respectively), although a statistically

Table 3. Efficacy Parameters: Baseline and Change From Baseline to Endpoint Scores[a]

	Baseline		Change From Baseline to Endpoint			
			LOCF		OC	
Scale	Escitalopram (N = 97)	Venlafaxine XR (N = 98)	Escitalopram (N = 97)	Venlafaxine XR (N = 98)	Escitalopram (N = 77)	Venlafaxine XR (N = 68)
MADRS	30.7 ± 4.6	30.0 ± 5.0	–15.9 ± 10.3	–13.6 ± 9.6	–17.5 ± 9.5	–16.0 ± 8.6
HAM-D	28.6 ± 4.1[b]	27.4 ± 4.5	–14.9 ± 9.0	–12.9 ± 9.1	–16.4 ± 8.3[c]	–15.0 ± 8.1
CGI-I[d]	…	…	2.2 ± 1.0	2.4 ± 1.1	2.1 ± 0.9	2.1 ± 0.9
CGI-S	4.5 ± 0.5	4.5 ± 0.6	–1.5 ± 1.1	–1.4 ± 1.2	–1.6 ± 1.0	–1.7 ± 1.2
HAM-A	15.4 ± 4.2	15.1 ± 4.1	–6.7 ± 5.4	–6.2 ± 5.7	–7.2 ± 5.3	–7.7 ± 5.3[e]
CES-D	33.6 ± 10.5	34.3 ± 9.5	–15.1 ± 11.9	–12.8 ± 12.7	–15.2 ± 12.1[c]	–14.1 ± 12.3
Q-LES-Q[f]	43.0 ± 8.6	43.4 ± 9.0	+12.8 ± 11.4	+9.9 ± 11.1	+12.8 ± 11.8[c]	+11.4 ± 10.6
HAM-D somatic subscale	6.5 ± 1.8	6.7 ± 1.5	–3.1 ± 2.6	–2.9 ± 2.8	–3.4 ± 2.5	–3.6 ± 2.7

[a]Values shown as mean ± SD.
[b]Statistically significant difference between treatment groups (p = .045).
[c]N = 76.
[d]Values represent mean scores at endpoint. Lower mean CGI-I scores reflect greater improvement.
[e]N = 67.
[f]Positive mean change from baseline reflects improvement in quality of life.
Abbreviations: CES-D = Center for Epidemiological Studies-Depression Scale, CGI-I = Clinical Global Impressions-Improvement scale, CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, LOCF = last observation carried forward, MADRS = Montgomery-Asberg Depression Rating Scale, OC = observed cases, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, XR = extended release.

Figure 1. MADRS Total Score by Visit (observed cases) and at Endpoint (LOCF) in Patients Treated With Escitalopram 20 mg/day or Venlafaxine XR 225 mg/day



Abbreviations: LOCF = last observation carried forward, MADRS = Montgomery-Asberg Depression Rating Scale, XR = extended release.

significantly greater proportion of venlafaxine-treated patients (16% vs. 4%; p < .01) withdrew from the study prematurely as the result of an adverse event. No other reason for early termination was statistically significantly different between the 2 treatment groups. Of interest is that no patient in either treatment group withdrew from treatment due to lack of efficacy.

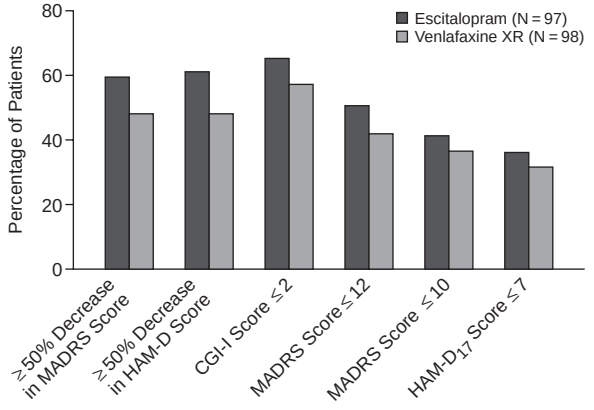
Efficacy Analyses

Baseline scores and changes from baseline to endpoint for primary and secondary efficacy parameters are shown in Table 3. There were no statistically significant differences between groups in baseline scores for these outcome measures, with the exception of the HAM-D (p = .045). On all measures, treatment with both escitalopram and venlafaxine XR resulted in clinically meaningful improvements over baseline values. On the primary efficacy measure of change from baseline in MADRS total score (LOCF), treatment with escitalopram resulted in a mean change at endpoint of –15.9 compared with –13.6 for venlafaxine XR (Figure 1). Similarly, escitalopram and venlafaxine XR treatments led to mean changes in HAM-D scores from baseline to endpoint (LOCF) of –14.9 and –12.9, respectively. Observed-cases values were qualitatively similar, with mean changes from baseline to week 8 in MADRS scores of –17.5 and –16.0 for the escitalopram and venlafaxine XR groups, respectively. Mean changes from baseline to week 8 in OC values for HAM-D total scores were –16.4 and –15.0 for the escitalopram and venlafaxine XR groups, respectively. The mean changes in the HAM-D somatic subscale (LOCF) were –3.1 for escitalopram and –2.9 for venlafaxine XR. None of the differences between treatment groups was statistically significant.

Response and remission rates at endpoint, for each response and remission definition, were as follows: ≥ 50% decrease in MADRS score, 58.8% escitalopram, 48.0% venlafaxine; ≥ 50% decrease in HAM-D score, 61% escitalopram, 48% venlafaxine; CGI-I score ≤ 2, 65% escitalopram, 57% venlafaxine; MADRS score ≤ 12, 50.5% escitalopram, 41.8% venlafaxine; MADRS score ≤ 10, 41.2% escitalopram, 36.7% venlafaxine; and $HAM\text{-}D_{17}$ score ≤ 7, 36.1% escitalopram, 31.6% venlafaxine (Figure 2). These differences were not statistically significant.

Post hoc analyses were performed on the change from baseline in MADRS scores to account for the baseline imbalance with respect to sex. Addition of sex as a covariate to the ANCOVA model resulted in borderline significance in favor of escitalopram (p = .052), due to greater improvement in men in the escitalopram group (–20.4) rela-

Figure 2. Response and Remission Rates at Endpoint (LOCF) for Patients Treated With Escitalopram 20 mg/day or Venlafaxine XR 225 mg/day



Abbreviations: CGI-I = Clinical Global Impressions-Improvement scale, HAM-D = Hamilton Rating Scale for Depression, LOCF = last observation carried forward, MADRS = Montgomery-Asberg Depression Rating Scale, XR = extended release.

tive to the venlafaxine group (–13.4). The corresponding changes in women were –13.9 and –13.7, respectively. Thus, the higher proportion of women in the escitalopram group relative to the venlafaxine XR group did not favor escitalopram with respect to efficacy.

Safety Analyses

Adverse events led to the premature discontinuation of 16% of venlafaxine XR–treated patients and 4% of escitalopram-treated patients ($p < .01$). The overall incidence of adverse event reports was 85% for the venlafaxine XR treatment group and 68% for the escitalopram treatment group. The most frequent treatment-emergent adverse events, occurring in at least 10% of patients in either treatment group, are shown in Table 4. Nausea occurred significantly more frequently in venlafaxine XR–treated patients than in escitalopram-treated patients. Headache was the only common adverse event reported numerically more frequently among escitalopram-treated patients (15.3%) than venlafaxine XR–treated patients (14.0%). Mean changes in vital signs were significantly higher for venlafaxine XR–treated patients than for escitalopram-treated patients (Table 5).

DISCUSSION

There has been much speculation concerning the relationship between the selectivity of SRIs and their clinical risk-to-benefit profiles.[20,32,33] The present trial assessed the efficacy and tolerability of escitalopram, the most selective of the available SRIs, and venlafaxine XR at a dose that is widely acknowledged to inhibit noradrenergic as well as serotonergic reuptake.[15]

Table 4. Most Frequent Adverse Events (% of patients) Occurring in ≥ 10% of Patients in Either Treatment Group

Adverse Event	Escitalopram (N = 98)	Venlafaxine XR (N = 100)
Nausea	6.1	24.0[a]
Ejaculation disorder[b]	6.7	22.6
Somnolence	9.2	17.0
Dry mouth	12.2	16.0
Headache	15.3	14.0
Sweating increased	5.1	11.0

[a]$p < .05$; Fisher exact test.
[b]As a percentage of male patients (escitalopram, N = 30; venlafaxine XR, N = 53).
Abbreviation: XR = extended release.

Table 5. Changes in Vital Sign Parameters Following Treatment With Escitalopram or Venlafaxine XR

Parameter	Escitalopram, Mean ± SD	Venlafaxine XR, Mean ± SD
Systolic blood pressure (supine), mm Hg		
Baseline	119.2 ± 14.6	121.3 ± 13.1
Endpoint – baseline	–0.4 ± 11.4	3.7 ± 10.6[a]
Diastolic blood pressure (supine), mm Hg		
Baseline	70.7 ± 9.0	74.0 ± 9.3
Endpoint – baseline	0.4 ± 8.6	2.3 ± 9.1[a]
Pulse (supine), bpm		
Baseline	70.1 ± 11.1	71.0 ± 11.2
Endpoint – baseline	–1.8 ± 10.4	3.8 ± 10.3[a]
Ventricular heart rate, bpm[b]		
Screen	65.1 ± 9.0	66.0 ± 9.5
Week 8 – screen	1.0 ± 8.2	7.1 ± 10.7[a]

[a]$p < .05$; analysis of covariance model using baseline vital sign as baseline covariate and center and treatment as main effects.
[b]As measured by electrocardiogram leads.
Abbreviation: XR = extended release.

Both escitalopram and venlafaxine XR led to improvements in depressive symptoms following an acute treatment course. Furthermore, escitalopram was at least as effective as venlafaxine XR on outcome measures that included assessments of anxiety, quality of life, somatic symptoms, and severity of symptoms. Observed-cases analyses of efficacy measures at endpoint were consistent with LOCF outcomes. Therefore, the higher discontinuation rate due to adverse events did not mask a superior efficacy outcome for the venlafaxine XR treatment group.

Escitalopram was better tolerated than venlafaxine XR, as indicated by several findings. Four times as many venlafaxine XR–treated as escitalopram-treated patients discontinued study treatment prematurely because of adverse events, a difference that was statistically significant. The venlafaxine XR treatment group had a notably higher incidence of treatment-emergent adverse events than the escitalopram treatment group overall. Furthermore, the incidence of the most frequent adverse events was greater for venlafaxine XR treatment than for escitalopram treatment (and in the case of nausea, the differ-

ence was statistically significant). The higher rates of adverse events such as nausea and ejaculation disorder associated with venlafaxine XR treatment relative to escitalopram treatment in the current study are consistent with previously reported individual results for these compounds.[12–14,16,17,24,25]

In the United States, the approved dose ranges for escitalopram and venlafaxine XR are 10 to 20 mg/day and 75 to 225 mg/day, respectively. A previous report compared flexibly dosed escitalopram 10 to 20 mg/day and venlafaxine XR 75 to 150 mg/day and found the 2 agents to be comparably effective.[21] In that trial, adverse event rates (for the most commonly reported events) were generally lower for escitalopram than for venlafaxine XR, despite the use of lower doses of venlafaxine XR.

In our trial, escitalopram and venlafaxine XR were titrated as rapidly as recommended in labeling information and reached their maximum doses within a day of each other. Since maximum dose was reached at approximately the same time, the potential bias of treating earlier or for longer duration with the maximum dose of one drug versus the other was minimized. However, this methodology imposes other limitations. First, it is possible that longer intervals between titration steps, or flexible dosing, would have led to improved tolerability among venlafaxine-treated patients. In flexible-dose trials of venlafaxine XR in which patients were allowed 4 weeks to be up-titrated to 225 mg/day, discontinuation rates due to adverse events for venlafaxine-treated patients were 6%[17] and 11%,[16] compared with 16% in the current trial. In contrast, it is notable that in the current trial rapidity of titration did not similarly limit the tolerability of escitalopram 20 mg/day. A second limitation is that the titration scheme in this study led to an overall doubling of the escitalopram dose (10–20 mg/day) but a trebling of the venlafaxine XR dose (75–225 mg/day). This is a source of imbalance that is inherent in the recommended dose ranges for escitalopram and venlafaxine XR.

Three further factors must be considered with regard to interpretation of the efficacy findings. First, a placebo treatment arm was not included in this trial, so it is not possible to determine whether the extent of improvement produced by either escitalopram or venlafaxine XR would be statistically superior to placebo treatment. However, the proportions of patients meeting prospectively defined criteria for response and remission were consistent with results from previously reported placebo-controlled trials with each agent.[13,14,17,18] Second, there was a statistically significant imbalance in the proportion of women in the 2 treatment groups; however, this imbalance did not bias the efficacy results in favor of escitalopram. Third, the inability to detect statistically significant differences might be attributable to the small sample size. The data that are suggestive of superior efficacy of venlafaxine over other SRIs were based on a pooled analysis to increase the overall sample size.[32,33] Future prospective trials to determine whether one compound is indeed more effective than another will benefit from inclusion of a placebo group and will need to be powered appropriately to detect differences that are both statistically and clinically significant.

In conclusion, this study fails to support the hypothesis that the nonselective inhibition of monoaminergic reuptake leads to improved efficacy compared with selective inhibition of serotonergic reuptake, since escitalopram was at least as effective as venlafaxine XR at their highest recommended doses. Moreover, the nonselectivity of venlafaxine appeared to be associated with poorer tolerability.

Drug names: escitalopram (Lexapro), fluoxetine (Prozac and others), venlafaxine (Effexor), zaleplon (Sonata), zolpidem (Ambien).

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