Studie Schwartz

Poster

REBOXETINE VERSUS VENLAFAXINE IN SEVERE MAJOR DEPRESSION

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Abstract

Approximately one-third of outpatients with major depressive disorder (MDD) meet the requirements for severe illness (symptom intensity, diagnostic subtype and/or degree of functional impairment), while patients receiving inpatient care are, by definition, more severely ill. The present study was conducted to assess the efficacy and tolerability of the selective noradrenaline reuptake inhibitor (selective NRI) reboxetine in the treatment of adults with severe MDD compared with venlafaxine.

Adult patients (18–65 years) with a confirmed diagnosis of MDD were randomised to receive either reboxetine (8–10 mg/day) or venlafaxine (225–375 mg/day) for up to 8 weeks in this double-blind, parallel-group trial. Only patients with severe symptomatology as defined by a HAM-D 17-item total score ≥25 points were included in the study. Clinical efficacy was assessed at weekly intervals using the HAM-D 17-item rating scale. Secondary measures included the Clinical Global Impression Severity (CGI-S) and Improvement (CGI-I) scales and the Social Adaptation Self-evaluation Scale (SASS). Response to treatment was defined as a ≥50% decrease in the HAM-D 17-item total score and remission was defined as a HAM-D 17-item total score of ≤8 points. Adverse events were recorded by direct observation and spontaneous reporting.

The mean HAM-D 17-item total score decreased markedly from baseline to Week 8 in both treatment groups (reboxetine 28.6 ±3.1 to 13.4 ±8.1; venlafaxine 28.8 ±2.8 to 12.2 ±7.7). After 8 weeks of treatment, 56% of patients treated with reboxetine were classed as responders compared with 54% of patients in the venlafaxine group. Twenty-four per cent of patients in each treatment group were classed as being in remission after 8 weeks of treatment. A week-by-week analysis of remission rates revealed that by Week 4, a markedly greater proportion of patients treated with reboxetine achieved symptomatic remission compared with those in the venlafaxine group, although by Week 8 remission rates were comparable. Marked improvements were also seen on the secondary efficacy measures.

The results of the present study demonstrate that reboxetine 8–10 mg/day is as effective as venlafaxine 225–375 mg/day in the treatment of severe MDD in adults and is well tolerated.

Introduction

Approximately one-third of outpatients with major depressive disorder (MDD) are classified as severely ill based on symptom intensity, diagnostic subtype and/or degree of functional impairment [1]. Severely depressed patients tend to have a longer duration of illness and a lower probability of spontaneous remission [2]. Moreover, approximately 80% of patients with severe illness experience suicide ideation [3].

Although many antidepressants are available for the treatment of MDD, effective treatment of the more severely depressed patient is often more challenging. Some studies have shown that antidepressants with a more noradrenergic mechanism of action (reboxetine, venlafaxine, mirtazapine) are particularly effective in treating severe depression.

Reboxetine is a selective noradrenaline reuptake inhibitor (selective NRI) that is effective and well tolerated in the treatment of MDD [4]. Moreover, reboxetine has been shown to be effective in the treatment of severely depressed hospitalised patients [5].

The aim of this study was to compare the efficacy and tolerability of reboxetine with high doses of venlafaxine in patients with severe MDD.

Methods

- Male and female patients (aged 18–65 years) with a confirmed diagnosis of MDD (DSM-IV) and severe symptomatology (defined by a HAM-D 17-item total score ≥25) were randomised to receive either reboxetine or venlafaxine for 8 weeks in a multinational, double-blind, parallel-group study.
- Patients randomised to the reboxetine treatment group received an initial dose of 8 mg/day with an optional increase to 10 mg/day from Day 29. Patients randomised to the venlafaxine treatment group received 75 mg on Day 1, 150 mg on Day 2 and 225 mg on Day 3. The dose of venlafaxine could be increased to 300 mg/day on Day 29 and to 375 mg/day on Day 30 at the investigator's discretion.
- Patients with a history or current symptoms of bipolar disorder, dysthymia, schizophrenia or delerium, a diagnosis of obsessive-compulsive disorder or with a high risk of suicide were excluded from the study. Patients receiving antidepressive agents, monoamine oxidase inhibitors, fluoxetine, amphetamines or α- or β-adrenergic agonists underwent a wash-out period of 4–14 days prior to the start of the study.
- Clinical efficacy was assessed after 1, 2, 4 and 8 weeks of treatment using the HAM-D 17-item rating scale. Response to treatment was defined as a ≥50% decrease in HAM-D 17-item total score and remission was defined as a HAM-D 17-item total score of ≤8 points.
- Adverse events were recorded by direct observation and spontaneous reporting.

Results

Patient and clinical outcome

- A total of 167 patients with a confirmed diagnosis of severe MDD were recruited to the study and received either reboxetine (n=80) or venlafaxine (n=87) for 8 weeks. Patient demographics are presented in Table 1.

Table 1. Patient demographics and baseline assessment score

	Reboxetine (n=80)	Venlafaxine (n=87)
Patient (male/female)	23/57	29/58
Mean age, years [range]	41.9 [19–65]	42.2 [19–66]
Presence of		
Single major depressive episode	32 (40.0%)	33 (37.9%)
≥2 major depressive episodes	48 (60.0%)	54 (62.1%)
Melancholic features	75 (93.8%)	79 (90.8%)
Mean HAM-D total score [range][a]	28.2 [22–35]	28.4 [25–37]

[a]HAM-D, Hamilton psychiatric 17-item rating scale for depression

- Mean HAM-D 17-item scores decreased markedly in both treatment groups during 8 weeks of treatment (Figure 1). Among patients treated with reboxetine, mean total scores decreased from 28.2 ±3.1 at baseline to 13.4 ±8.1 at Week 8, while among patients treated with venlafaxine mean total scores decreased from 28.4 ±2.7 to 12.2 ±7.7.

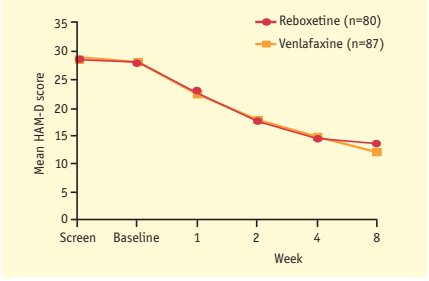

Figure 1. Mean change in HAM-D 17-item score in adult patients with severe depression following 8 weeks of treatment with reboxetine (8–10 mg/day) or venlafaxine (225–375 mg/day).

- Approximately 10% of patients in both groups responded to treatment (≥50% in HAM-D total score from baseline) within 1 week of starting therapy (Figure 2). After 8 weeks of treatment, 56.2% of patients receiving reboxetine and 55.1% of patients receiving venlafaxine had responded to treatment (Figure 2).

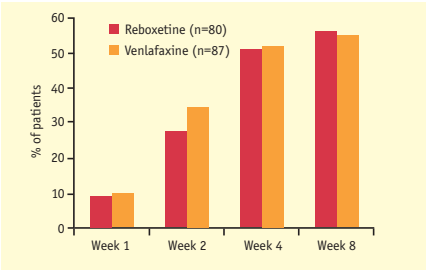

Figure 2. Per cent of patients responding to treatment (≥50% reduction in HAM-D 17-item score) with reboxetine (8–10 mg/day) or venlafaxine (225–375 mg/day).

- After 4 weeks of treatment, a greater proportion of patients treated with reboxetine were considered to be in remission (HAM-D 17-item score ≤8) compared with those treated with venlafaxine (17.5% vs 12.0%, respectively; Figure 3). After 8 weeks of treatment, the proportion of patients in remission was similar in both treatment groups (reboxetine, 24.7%; venlaflaxine, 24.1%).

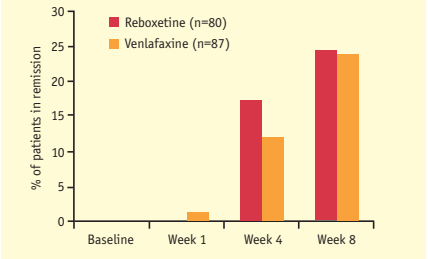

Figure 3. Per cent of patients in remission (HAM-D 17-item score ≤8) before and after 1, 4 or 8 weeks of treatment with reboxetine (8–10 mg/day) or venlafaxine (225–375 mg/day).

Tolerability

- The most frequently reported adverse events (≥5% incidence) among reboxetine-treated patients were dry mouth (16.7%), increased sweating (12.1%), headache (7.6%), anxiety (7.6%), constipation (6.1%) and insomnia (6.1%). Among patients treated with venlafaxine, the most frequently reported adverse events were constipation (19.0%), dry mouth (14.3%), increased sweating (11.1%), nausea (9.5%), headache (6.3%) and insomnia (6.3%). Six patients in the reboxetine group and 7 in the venlafaxine group withdrew from the study due to adverse events.

Conclusions

- Reboxetine, a selective NRI, is as effective as high doses of venlafaxine in the treatment of patients with severe MDD as defined by a HAM-D 17-item total score ≥25.
- Reboxetine may be more effective than venlafaxine in helping patients achieve early remission of depressive symptoms.
- Both reboxetine and venlafaxine were well tolerated.

References

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