Differential effects of venlafaxine compared to selective serotonin reuptake inhibitors (SSRIs) in the treatment of MDD according to baseline severity - A Meta-Analysis

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Abstract

Objectives: Prior meta-analyses have suggested superior efficacy of venlafaxine compared to SSRIs. In this meta-analysis we compared the efficacy of venlafaxine and SSRIs in patients with MDD classified according to baseline severity.

Methods: Data from 31 venlafaxine studies were pooled and remission rates defined as a HAMD-D<30 were analysed. Subjects were divided into two groups based on their baseline HAM-D<30 total score (30 vs. >30). Fisher’s exact test was used to compare the treatment effects on the remission rates for each subgroup. All of the analyses were based on the intent-to-treat patients. LOCF and completer analyses were performed using standardized measurements.

Results: 1836 patients with a baseline HAM-D-D<30 could be identified. The LOCF analysis revealed, that the OR is 1.93 (95% CI 1.25, 2.97), p = 0.003 and the NNT is 13. Data from 954 patients with a baseline HAM-D-D>30 were available. The LOCF analysis revealed, that the OR is 1.55 (95% CI 1.10, 2.18), p = 0.015 and the NNT is 11.

Conclusion: This analysis demonstrates that venlafaxine is superior to SSRIs in both the mild/moderate depression and severe depression in achieving remission. However, the magnitude of superiority was higher in the subgroup of patients with a baseline HAM-D-D<30 suggesting a pronounced clinical benefit for the treatment of severely depressed patients.

Introduction

Results of pooled analysis of relevant clinical trials suggest, that Venlafaxine is associated with higher remission rates than SSRIs. A recent meta-analysis (Nemeroff et al. 2008) showed a difference in remission rates of 6% in favor of venlafaxine suggesting a modest clinical advantage compared to SSRIs. Little data are available which analyse the clinical benefits on the remission rates for each severity group of the disease. Due to generic competition by several classes of antidepressants (e.g. SSRIs) and national/international guidelines venlafaxine is widely used as second or third line therapy. Results of studies in treatment resistant depression demonstrated the efficacy of venlafaxine in depressed patients after failure of SSRIs (Baldomero et al. 2005, Thase et al. 2006).

The purpose of this meta-analysis was to extend the findings of a previous meta-analysis (Nemeroff et al. 2008) comparing the efficacy of venlafaxine and SSRIs in patients with MDD classified according to baseline severity. Similarly to the previous report this analysis was performed on an all-inclusive set of Wyeth-sponsored studies, for which individual patient data were available.

Methods

The data of the recent meta-analysis (Nemeroff et al. 2008) were used for the subanalysis shown here. Individual patients were included only if data were obtained from all studies completed by Wyeth Pharmaceuticals comparing venlafaxine and an SSRI in the treatment of major depressive disorder (i.e. January 2005). From the reported 34 randomized controlled double-blind trials we could be used for this analysis, showing. Further details concerning individual study characteristics (i.e. design, drug, dosage) and exclusion criteria were described by Nemeroff et al. 2008.

Twenty studies used venlafaxine immediate release (IR) and 11 studies used venlafaxine extended release (ER). The SR comparison was flutekine (B studies), paroxetine (B studies), sertraline (B studies), clomipramin (D studies) and fluoxetine (B studies). Nine studies also included a placebo control group. Only Venlafaxine and SSRI (as a group) patients were included for the purpose of this analysis.

All analyses were based on the pooled data of the intent to treat (ITT) population. The ITT population included all randomized subjects who had a HAM-D-D evaluation, received at least one dose of study medication and had not left one-on-one therapy assessment of HAM-D-D.

Primary endpoint was the remission rate after 8 weeks of treatment, a remission defined as a HAM-D-D<7. For the observed analyses (LOCF) data were included of patients completing at least 8 weeks and showing values for that time point. LOCF analysis was carried out by carrying forward the last observed value in case of missing data at week 8.

Subjects were divided into two subgroups based on their baseline HAM-D-D total score. Patients with HAM-D-D<30 were considered as severely depressed and patients with HAM-D-D<30 were considered as mildly to moderately depressed patients.

Fisher’s exact test was used to compare treatment effects between venlafaxine and SSRIs on the remission rates for each subgroup. No multiple comparison adjustment was made. For all studies included, a combined total effect size was computed as a raw odds ratio with 95% confidence interval. NNTs (numbers needed to treat) were calculated to estimate clinical significance of differences.

Results

The 6592 patients of the ITT population (intent to treat) were divided into two subgroups following severity of depression at baseline before treatment, (6592 (venlafaxine: n=3900; SSRIs: n=2692). Patients with mild to moderate depression (baseline HAM-D-D<30). Remission rates of venlafaxine were significantly superior to those of SSRIs treated patients in a group in both severity groups (Figure 1). In LOCF analysis remission rates with venlafaxine and SSRIs were generally higher for patients with mild to moderate depression (4.6% vs. 2.4%) than in patients with mild to moderate depression (5.9% vs. 3.3%). Results of LOCF analysis are very similar (Figure 1).

Comparison of groups was characterized with further statistics (Table 1). For patients with mild to moderate depression: In LOCF analysis, odds ratio (OR) was 1.31 (95% confidence interval CI 1.18-1.46), p < 0.001 and a number needed to treat (NNT) of 11. OC analysis showed an OR of 1.93 (95% CI 1.25-2.97), p = 0.003 and NNT was 7.

Conclusion

This analysis demonstrates that venlafaxine is superior to SSRIs as a class in both the mild/moderate and severe depression in achieving remission. However, the magnitude of superiority was higher in the subgroup of patients with a baseline HAM-D-D<30 suggesting a pronounced clinical benefit for the treatment of severely depressed patients.

Literature


Treatement effects of Venlafaxine on work activity compared to SSRIs in the treatment of MDD according to Baseline severity

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Abstract

Objectives: In this meta-analysis we compared the effects of venlafaxine and SSRIs on work activity in major depressive disorder (MDD) patients classified according to baseline severity.

Methods: Data from the work and activity item 7 of the HAMD of 31 pooled studies comparing venlafaxine with SSRIs were used. Subjects were divided into two groups based on their baseline HAMD total score distribution and the proportions of patients achieving full work function were summarized for both LOCF and Completers at week 8. Fisher’s exact test was used to compare the treatment effect.

Results: 10945 patients, with a baseline HAMD > 30 were included. The OR for all subjects achieving full work functionality was 1.22 (95%CI 1.08, 1.36), p<0.001 for both LOCF and Completers. The OR for subjects with a baseline HAMD > 20 was 1.13 (95%CI 1.05, 1.22), p=0.009 for LOCF and 1.14 (95%CI 1.05, 1.25), p=0.001 for completers. Conclusion: This analysis demonstrates that venlafaxine is superior to SSRIs in improving work functionality in both mild/moderate and even more pronounced in severe depression. These results emphasize the impact of the treatment with venlafaxine on patients returning to normal social life.

Introduction

The prevalence of major depression in working people (Eaton et al. 1995) causes a considerable work impairment (Kessler et al. 1997). Treatment with antidepressants can reduce depression symptom severity and restore occupational function (Finkelstein et al. 2002), defined as response or remission of depression and the consequent work impairment. A recent meta-analysis (Nemeroff et al. 2008) showed a difference of remission rates in favour of the serotonin-norepinephrine reuptake inhibitor venlafaxine versus selective serotonin reuptake inhibitors (SSRIs) as a class. Several meta-analyses showed a 6 - 8% difference in remission rates in favour of venlafaxine compared to SSRIs (Smith et al. 2012). However, the clinical relevance of these findings has been controversially discussed. Remission is associated with improved quality of life and work activity. Little data are available which investigate the impact of antidepressant therapy on work functionality by randomized controlled trials. Therefore, this analysis used data from the Work and Activity item 7 of the HAMD 17 (Nemeroff et al. 2008) as well as other studies comparing venlafaxine with SSRIs (Smith et al. 2012). Since remission of work activity was defined as a score of 0 in item 7 of HAMD 17, further analyses were carried out with patients showing already at baseline impairment of work activity (item 7 score 1 or more). This analysis demonstrates that venlafaxine is superior to SSRIs in improving work functionality in both mild/moderate and even more pronounced in severe depression. These results emphasize the impact of the treatment with venlafaxine on patients returning to normal social life.

Methods

The data of the recent meta-analysis (Nemeroff et al. 2008) were used for the subanalysis shown here. Individual patient data were obtained from all studies completed by Wyeth Pharmaceuticals comparing venlafaxine and an SSRI in the treatment of MDD (HAMD17: 17 items Hamilton depression scale). The other antidepressants were defined as non-selective serotonin reuptake inhibitors (SNRIs). Twenty studies used venlafaxine immediate release (IR) and 11 studies used venlafaxine extended release (ER). The SSRIs were fluoxetine (18%), paroxetine (13%), citalopram (12%), selective serotonin reuptake inhibitors (SSRIs) and selective serotonin-norepinephrine reuptake inhibitors (SNRIs) (37%). Data were analyzed for both subgroups separately. The baseline group was defined as an item 7 score of 1 or more. This analysis included patients achieving full work functionality showed an item 7 score of 0 and were defined as patients with full work functionality. Since remission of work activity was defined as a score of 0 in item 7 of HAMD 17, further analyses were carried out with patients showing already at baseline impairment of work activity (item 7 score 1 or more). This analysis demonstrates that venlafaxine is superior to SSRIs in improving work functionality in both mild/moderate and even more pronounced in severe depression. These results emphasize the impact of the treatment with venlafaxine on patients returning to normal social life.

Results

In this meta-analysis we compared the effects of venlafaxine and SSRIs on work activity in MDD patients classified according to baseline severity. The 56% of patients of the ITT population (intent to treat) were divided into two subgroups following severity of depression at baseline before treatment, HAMD 17 (venlafaxine: n=229, SSRI: n=297) patients showing a baseline HAMD-17 < 30 and HAMD 17 (venlafaxine: n=229, SSRI: n=297) patients showing a baseline HAMD-17 ≥ 30. Remission was defined for item 7 of HAMD (work and activity) by reaching a score of 0 (no impairment) at week 8.

Conclusion

Given the substantial work impairment associated with MDD, evaluating antidepressant treatment in terms of return to work functioning is important. This analysis was possible to define a remission for the HAMD-17 item 7 (work and activity). A significant superiority could be demonstrated for venlafaxine vs. SSRIs for the item scores concerning item 7. A smaller proportion in the investigated population started treatment without a baseline impairment in work and activity. Analyses only for patients with impairment in item 7 at baseline contributed results of the total population. Superseding could be shown in item 7 in the pool of patients with impairment in item 7 at baseline. The results were only shown for patients with mild to moderate depression (below HAMD 30). No difference in item 7 score was found for patients with mild and moderate depression: the odds ratio (OR) for remission of work activity item 7 was 2.58, p=0.032 for completers. The OR for subjects with work impairment at baseline was 1.19 (95%CI 1.11, 1.26), p<0.001 for both LOCF and Completers. With regard to the population of patients with impairment of work activity already at baseline, an OR of 1.20 (95%CI 1.10 - 1.30), p = 0.002 was found in LOCF analysis and of 1.36 (95%CI 1.25 - 1.48), p = 0.008 in OC analysis. Since remission of work activity was defined as a score of 0 in item 7 of HAMD 17, further analyses were carried out with patients showing already at baseline impairment of work activity (item 7 score 1 or more). This analysis demonstrates that venlafaxine is superior to SSRIs as a class in improving work functionality in both mild/moderate and even more pronounced in severe depression. These results emphasize the impact of the treatment with venlafaxine on patients returning to normal social life.

Literature


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