Alleviation of painful physical symptoms in depressed patients will increase remission

Depression is a chronic disease consisting of emotional/psychological and painful symptoms. Emotional symptoms have been shown to respond to currently available antidepressants; however, painful symptoms may not be as responsive. It was hypothesised that resolution of both psychological and painful symptoms of depression would predict a higher percentage of patients achieving remission.

Method

Efficacy data were pooled from two identical, but independent, nine-week randomised, double-blind clinical trials of duloxetine 60mg qd and placebo. All patients met diagnostic criteria for DSM-IV major depressive disorder, which was confirmed by the Mini-International Neuropsychiatric Interview. Efficacy measures included the 17-item Hamilton Rating Scale for Depression (HAM-D-17) total score, the HAM-D-17 Maier subscale, the Clinical Global Impressions-Severity of Illness (COI-S) scale, the Patient Global Impression of Improvement (POI-I) scale, the Somatic Symptom Inventory, the Quality of Life in Depression Scale, and Visual Analogue Scales (VAS) for pain.

Results

Duloxetine-treated patients demonstrated significantly greater improvement in overall pain, back pain, and shoulder pain at week nine compared with patients receiving placebo. When treatment effects were pooled over all visits, patients receiving duloxetine, 60mg qd, exhibited significantly greater improvement than placebo-treated patients in five of the six assessed VAS pain measures. Approximately 50% of the improvement in overall pain was independent of improvement in HAM-D-17 total score. Assuming the same level of improvement in core emotional symptoms of depression, improvement in overall pain severity was associated with higher estimated probabilities of remission.

Discussion

In the present analyses of pooled data, duloxetine was significantly superior to placebo in reducing the severity of painful physical symptoms in depressed patients. Similar findings were reported from the individual studies included in the pooled analyses. Data were pooled to provide the most reliable estimates for both the magnitude of the treatment effect and the proportion of the treatment outcome that were due to a direct effect on pain vs secondary effects resulting from improvements in depression.

As evidenced by the path analysis, approximately half of duloxetine's total effect on pain was a direct effect and approximately half was an indirect effect attributable to improvement in depression. The primary hypothesis of the present investigation was that alleviation of painful physical symptoms was associated with higher remission rates. Although it is difficult to address this question with a prospectively defined study, these post hoc analyses provide compelling evidence that, independent of changes in the core emotional symptoms of depression, alleviation of painful symptoms was associated with greater probabilities of remission.

It has been suggested that antidepressants that inhibit the reuptake of both 5-HT and norepinephrine demonstrate greater efficacy than those acting upon a single neurotransmitter on the basis of several clinical trials in which dual reuptake medications, or combinations of selective 5-HT and norepinephrine inhibitors, demonstrated efficacy superior to that of SSRI comparators.

In previous studies of duloxetine, the estimated probabilities of remission ranged from 43-57%. It has been postulated that duloxetine's dual reuptake mechanism of action may be responsible for its ability to address both emotional and painful symptoms of depression and thereby achieve high rates of remission. The current results underscore the importance of effectively addressing the painful symptoms frequently associated with major depressive disorder (MDD) and support the notion that treatment of both psychological and somatic/physical aspects of MDD may be associated with higher rates of remission.

On some VAS pain measures (back pain, shoulder pain), duloxetine-treated patients exhibited significantly greater reductions in pain severity, compared with placebo, after only one week of treatment, while overall pain severity showed significant improvement over placebo at week two and maintained this advantage to endpoint.

Conclusions

Treatment with duloxetine, 60mg qd, significantly reduced pain compared with placebo. Improvements in pain severity were attributable equally to the direct effect of duloxetine and to associated changes in depression severity.

Improvement in painful physical symptoms was associated with higher remission rates even after accounting for improvement in core emotional symptoms.

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