

# Treating pain in depression is associated with higher rates of remission

Painful physical symptoms are present in up to three out of every four patients with major depressive disorder (MDD). These symptoms include headaches, stomach pain, neck and back pain, diffuse musculoskeletal pain and vague poorly localised pains. They are important for a number of reasons. Firstly, they confound the diagnosis of MDD. A recent multinational survey reported that 69% of patients who were diagnosed with depression in primary care facilities presented with pain as their only complaint. Secondly, where these symptoms are not adequately addressed during treatment for MDD, residual painful symptoms have been shown to be predictive of a poor outcome in the long-term. Conversely, Fava has shown that addressing these painful symptoms during treatment for depression results in higher remission rates.<sup>1</sup>

Duloxetine is a potent dual reuptake inhibitor of serotonin (5-HT) and noradrenaline (NA). Experimental evidence has shown that both 5-HT and NA exert analgesic effects via descending pain pathways, and dual reuptake inhibition (for example, with tricyclic antidepressants) has been shown to provide superior analgesic effects compared to drugs that act only on a single neurotransmitter. Duloxetine has been shown to alleviate painful symptoms associated with depression.

To examine the association between pain relief and remission rate, Fava and colleagues pooled data from 2 identical randomised, placebo-controlled, double-blind studies of duloxetine 60 mg once daily in the treatment of adults with MDD.<sup>1</sup> Treatment was continued for up to 9 weeks and 495 patients were included in the efficacy analysis.

Compared to placebo, patients who received duloxetine recorded significantly greater reductions in pain scores for overall pain, back pain, shoulder pain, pain while awake and interference with daily activities. The improvement in pain with duloxetine was greater than that expected from relief of depressive symptoms alone. In a path analysis, approximately half of duloxetine's total effect on overall pain was independent of its effect on depression, whereas 49.4% was an indirect effect mediated by improvement in mood. After accounting for changes in the core emotional symptoms of depression, greater improvement in pain scores was independently associated with a higher estimated probability of remission. Because greater improvement in emotional symptoms also

increases the chance of remission, the improvements in pain and in core emotional symptoms act synergistically to increase the chance of remission. The concept of a synergistic relationship, rather than that of one outcome driving the other, was supported by the observation that correlations of early changes in pain with subsequent improvements in depression scores were of approximately the same magnitude as correlations of early changes in depression scores with subsequent changes in pain.

The remission rate for pain responders ( $\geq 50\%$  improvement in pain scores) was double that of pain non-responders (36.2% vs. 17.8%;  $p > 0.001$ ) and, compared to patients who did not enter remission, those who did enter remission had significantly lower pain scores at week 1 and every subsequent follow-up visit. Early pain response, particularly within the first 2 weeks of treatment, was also associated with a significantly higher probability of remission, regardless of the change in emotional symptoms scores during that time. Both improvement in mood and improvement in pain scores were associated with improvements in measures of quality of life.

The results of this analysis highlight the importance of diagnosing pain associated with depression and treating it effectively. Because pain occurs so commonly in depressed patients, but the association is not always recognised, and because many patients may not specifically complain of pain, patients who are diagnosed with depression should be asked whether they are experiencing painful symptoms. Conversely, patients whose main complaint is pain, in conjunction with investigation for an organic cause, should also be assessed for depression.

By inhibiting both the re-uptake of 5-HT and NA, duloxetine addresses both the emotional and painful physical symptoms of depression and this dual activity is associated with a higher likelihood of remission.

## Reference

1. Fava M, Mallinckrodt CH, Detke MJ, et al. The effect of duloxetine on painful physical symptoms in depressed patients: Do improvements in these symptoms result in higher remission rates. *J Clin Psychiatry* 2004; 65: 521-530.