

Duloxetine in elderly patients with depression

Improvement in cognition, painful symptoms and mood

Cognitive impairment is common in patients with depression. Verbal learning, memory tests, working memory, focussed attention and decision making may all be impaired. In the elderly, major depressive disorder is common, but in addition to its association with depression, the aetiology of cognitive impairment is complex and includes cerebrovascular and Alzheimer's-type neurodegenerative changes. Cognitive impairment may precede depression, and some elderly patients with depression may have neurodegenerative changes that are precursors to dementia.

Physical disability and pain are also common comorbidities in elderly patients with depression. Pain may affect up to 65% of patients and is associated with worse outcomes and greater healthcare utilization.

An ideal antidepressant for treating depression in elderly patients would improve not only mood, but also cognitive function and painful physical symptoms, and it should be well tolerated in a population of patients who may be already taking a variety of other medications.

Abnormalities in both serotonin and noradrenalin (NA) pathways have been shown to play a role in the pain associated with depression and may be contributory factors in cognitive defects. Duloxetine is a potent dual re-uptake inhibitor of serotonin and NA, which has been shown to be effective in treating depression and in alleviating painful physical symptoms associated with depression.

To examine the effect of duloxetine on cognition and pain in elderly patients with depression, Raskin and colleagues randomly assigned 311 elderly outpatients, mean age 73 years, with recurrent major depressive disorder to duloxetine 60 mg/day (n=207) or placebo (n=104) for 8 weeks.

The primary outcome measure was composite cognitive test scores based on four different tests assessing aspects of verbal learning and memory, attention, executive function and working memory. Secondary measures included the Geriatric Depression Scale (GDS), Hamilton Depression Scale (HAM-D), Visual Analogue Scale (VAS) for pain and the Clinical Global Impression (CGI) severity scale.

Compared to the patients receiving placebo, composite cognitive scores were significantly improved in all patients receiving duloxetine. The difference was most marked in patients with severe depression at baseline (HAM-D ≥ 24), in whom cognitive function worsened during the 8 weeks of treatment with placebo, but improved with duloxetine. The improvement in composite scores was mainly due to improvements in the verbal learning and memory test, whereas the scores were not significantly different for the other tests.

Patients receiving duloxetine also had significantly greater improvements in the GDS starting at week 1 and in the HAM-D Total and CGI scores, beginning at week 4 and week 2, respectively. There was a significant effect of baseline depression severity on the outcome, with a greater advantage of duloxetine over placebo in patients with more severe depression compared to those with less severe depression. The proportion of patients with a HAM-D response ($\geq 50\%$ decrease in HAM-D score) and HAM-D remission (HAM-D Total score ≤ 7 at endpoint) was higher in the duloxetine group compared to the placebo group.

In addition, compared to placebo, patients receiving duloxetine had significantly better improvements in VAS scores for back pain and amount of time in pain while awake.

Duloxetine was well tolerated. A similar proportion of patients withdrew for any reason in the duloxetine and placebo groups (21.7% and 23.1%, respectively) and due to adverse events (9.7% and 8.7%, respectively). Blood pressure and pulse changes were modest and did not differ between groups. Sustained hypertension occurred in 0.5% of the duloxetine-treated patients and in 1.0% of patients receiving placebo.

The results of this study demonstrate that improvement in mood with duloxetine 60 mg daily in elderly patients with depression is associated with an improvement in cognition and in physical pain scores. Previous studies have shown that alternative antidepressants (paroxetine and nortriptyline) do not routinely improve cognition in such patients. It is speculated that the dual effect of duloxetine on serotonin and NA may be responsible for the beneficial effects on cognition and path analysis in this study suggested that improvement in composite cognitive scores was a direct effect of treatment, rather than consequent to improvement in mood.

Unlike other antidepressants that have not shown robust antidepressant efficacy in elderly patients, the rates of response and remission in this study were comparable to those observed in studies of the general adult population. Furthermore the tolerability profile of duloxetine in these elderly patients was similar to that observed in previous studies, with no more patients discontinuing treatment than in the placebo group.

Duloxetine may represent a new treatment option for older patients with recurrent depressive disorder.

Reference

Raskin J, Wiltse CG, Siegal A, et al. Efficacy of duloxetine on cognition, depression and pain in elderly patients with major depressive disorder: An 8-week, double-blind, placebo-controlled trial. *Am J Psychiatry* 2007; 164: 900-909.