Pramipexole shows promise for treating depression in patients with Parkinson's disease

May 9 2010

Pramipexole, a dopamine agonist, improves depressive symptoms in patients with Parkinson's disease (PD), and has the potential to become an important antidepressant treatment for these patients. The Article published Online First, and in the June issue of the *Lancet Neurology*, is the first trial to show the direct benefits of a dopamine agonist on depression in patients with Parkinson's disease.

Depression is common in patients with PD, with about 35% of patients experiencing depressive symptoms. Yet few trials have been done to evaluate antidepressant treatments in PD. Depression in PD might be related to dysfunction in dopaminergic pathways. Previous studies have shown that dopamine agonists such as pramipexole, which counteract the decline in the production of dopamine in the brain, are effective at reducing major depression in patients without PD, and might have the potential to improve depressive symptoms in PD patients.

To provide more evidence, Paolo Barone from the University of Naples, Italy and international colleagues did a randomised trial to investigate the safety and efficacy of pramipexole for depressive symptoms in patients with mild-to-moderate PD.

296 patients from 76 centres in 12 European countries and South Africa were randomly assigned to 12 weeks of pramipexole (144 patients) or placebo (152 patients). Scores on scales measuring depression (Beck

depression inventory [BDI] and geriatric depression scale [GDS-15]; with higher scores indicating more severe depression]) and functioning (unified Parkinson's disease rating scale [UPDRS]) were recorded at regular intervals up to the end of treatment.

Overall, pramipexole significantly improved depressive symptoms compared with placebo. Over 12 weeks, BDI scores in the pramipexole group decreased by 5•9 compared with 4•0 in the placebo group. GDS-15 scores improved by a mean of 2•5 in the pramipexole group vs 1•7 in the placebo group. Additionally, compared with patients in the placebo group, patients in the pramipexole group experienced significantly greater improvements in motor symptoms and activities of daily living.

Path analysis* showed that the effect of pramipexole treatment on depressive symptoms was largely independent of its effect on motor symptoms—the direct antidepressant effect accounted for nearly 80%, with the remaining 20% resulting from improvement in motor symptoms.

Adverse events were more common in patients being treated with pramipexole (73%) than with placebo (67%), the most common being nausea, headache, dizziness, and somnolence (drowsiness). There was no difference in numbers of patients experiencing serious adverse events between the two groups.

The authors say: "These results suggest that specific stimulation of dopaminergic pathways as provided by pramipexole should be considered in the management of patients with PD and clinically-significant depressive symptoms."

They conclude: "Further evaluation of pramipexole as an antidepressant in PD patients with more advanced disease is warranted…and direct

comparisons between antidepressants and dopamine agonists like pramipexole are needed to compare the effects of these two drug classes on depressive symptoms in patients with PD."

In an accompanying Comment, Hubert Fernandez from the University of Florida, USA and Marcello Merello from FLENI,** Argentina say; "Future studies are needed to determine whether dopamine agonists are as efficacious as other therapies for depression in patients with Parkinson's disease. For now, however, evidence of a positive effect of one drug on both motor and non-motor domains is an important addition to the treatment armamentarium against Parkinson's disease."

Provided by Lancet