Unraveling depression in Parkinson’s disease

Depression is a common psychiatric non-motor symptom occurring in Parkinson’s disease (PD) and negatively affecting patients’ quality of life and disability [1]. There is large variability in depression prevalence rates and this is related to overlap with motor features, difficulties in the evaluation of cognitively impaired patients and lack of scales specifically designed and validated for PD. In a prospective study, Hughes et al. [2] reported that presence of depression and dementia were important predictors of mortality in PD subjects followed for over 11 years. In a cohort of 114 PD patients, Weintraub et al. [3] found that depression and cognitive impairment were associated with altered functional ability, in addition to psychosis, age, PD duration, apathy, sleepiness, and motor impairment. Nuti et al. [4] reported in a population of 90 PD subjects that depression and dysthymia (diagnosed according to DSM-IV criteria) were present in 40% of cases with associated generalized anxiety (11%) and panic disorder (30%). Finally, Chaudhuri et al. [5] used a specific questionnaire (NMS Quest) to assess non-motor symptoms and reported that sadness was present in 44.7% of PD versus 26% controls.

Despite the relevance of depression in PD, there is little evidence for efficacy and safety of antidepressant therapies and trials assessing effectiveness of individual drugs are mostly open-label, non-randomized, and limited to small patient cohorts [6]. A Cochrane review published in 2003 on the treatment of depression in PD found only three randomized controlled trials on antidepressant medications for a total of 106 patients [7]. The authors concluded that available data on the effectiveness of antidepressant therapies in PD were insufficient and no recommendation was possible for their use.

This may explain why depression in PD is undertreated, at least according to some recent large surveys. The Parkinson Study Group collected data on 23,000 PD patients in the USA and found that 26% was on treatment with antidepressant drugs [8]. A recent register-based study in Denmark showed that among 22,827 patients on anti-Parkinson medications, 19.9% were taking antidepressants [9]. Similarly, a cross-sectional epidemiologic study on non-motor symptoms conducted in selected movement disorder centers in Italy (PRIAMO) revealed that only 169 of 1072 PD patients (15.8%) were treated for depression [10].

Moreover, serotonin reuptake inhibitors (SSRIs) that are frequently used to treat depression have been reported to occasionally worsen parkinsonism. Among SSRIs sertraline is characterized by a low selectivity for serotonin relative to dopamine reuptake, suggesting a favorable efficacy profile. One recent randomized study showed that sertraline treatment in PD is safe and unlike the tricyclic antidepressant amitriptyline improves quality of life, particularly activities of daily living, mobility, and stigma [11].

In the current issue of the journal, Kulisevsky et al. [12] report the results of a 6-month prospective evaluation of sertraline therapy in a large cohort of 310 depressed PD patients at various disease stages and recruited from over 50 Spanish movement disorder centers. Interestingly, the authors found that sertraline treatment not only improved depression but also resulted in motor benefit as expressed by changes in both total Unified Parkinson’s disease Rating Scale (UPDRS) and sub-scores including motor. Only a few patients noticed increase of tremor amplitude. The study is important given the large number of included subjects. However, patients were not randomized and neurologists were allowed changes in dopaminergic therapy during the observation period making interpretation of the results somehow controversial.

Nonetheless, these findings are complementary to those of a randomized study showing that pramipexole, a dopamine agonist with high affinity for D3 receptors, improved both mood and mobility in a cohort of PD patients on stable levodopa monotherapy [13].

Some considerations should now be drawn: first, depression has gained clinical relevance in PD and application of a revised version of UPDRS along with specific questionnaires and scales will help recognition of affected patients. Secondly, depression affects quality of life and patient self-perception of motor function and this further emphasizes the need for treatment. Thirdly, SSRIs and in particular sertraline have now demonstrated good safety and tolerability for clinical use and they may be considered first line in treating PD depression. Dopamine agonists are also likely to be beneficial and pramipexole is currently evaluated in a double-blind multicentre study. Finally, effectiveness and safety should be confirmed in placebo-controlled trials. Placebo effect is large in depression and particularly in PD. A recent study of rotigotine patch in advanced PD reported a 35% responder rate to placebo (vs. 67% to pramipexole and 59.7% to rotigotine) [14]. Therefore, further studies are warranted to fill this important gap, ensure best medical therapy to patients and provide class I evidence of efficacy for antidepressants in PD.
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References