TREATMENT OF PARKINSON'S DISEASE DEMENTIA

T. van Laar¹, P.P. De Deyn², D. Aarsland³,⁴

¹Department of Neurology, University Medical Center Groningen, Groningen, The Netherlands, ²Department of Neurology, General Hospital Middelheim and Institute Born-Bunge, University of Antwerp, Antwerpen, Belgium, ³Stavanger University Hospital, Stavanger, ⁴AHUS University Hospital, Lørenskog, Norway

Introduction: Significant cholinergic defects exist in patients with Parkinson's disease dementia (PDD) which may be treated with cholinesterase inhibitors (ChEIs). Evidence of striatal-glutamatergic activity in Parkinsonism has led to investigation of the N-methyl D-aspartate receptor antagonist memantine.

Aims: To report the current scope of efficacy, tolerability and safety data available from studies conducted with ChEIs or memantine in PDD.

Methods: A systematic search of literature indexed by PubMed (supplemented using ClinicalTrials.gov) during the past 10 years was conducted, using combinations of the terms: cholinesterase inhibitor; Parkinson's disease; dementia; cognitive impairment; rivastigmine; donepezil; galantamine; memantine.

Results: Studies retrieved were mostly small (< 40 patients), exclusive of three large randomized controlled trials (RCT). Smaller studies often lacked wide-ranging outcome-measures and/or longer study duration, with highly variable treatment outcomes, often lacking significance. A small memantine RCT (n=72) showed significant differences versus placebo on ADCS-CGIC, whilst a larger RCT (n=199) lacked significant findings in PDD, warranting further study. One large ChEI RCT in PDD was conducted with donepezil. Results are currently unavailable publically, although preliminary data suggests that donepezil lacked statistically significant effects versus placebo on one of two primary outcome-measures. Another large ChEI RCT showed significant improvements with rivastigmine-treatment versus placebo on ADAS-cog (p< 0.001), ADCS-CGIC (p< 0.007) and secondary efficacy outcomes.

Conclusions: Numerous small studies suggest potentially efficacious drugs for PDD treatment. However, large RCT of rivastigmine-treatment for PDD published beneficial effects across multiple symptom domains. Consequently, rivastigmine is currently the only approved ChEI for the symptomatic treatment of mild-to-moderate PDD.