Dementia with Lewy Bodies

The treatment of DLB can be challenging. The mainstays of pharmacologic treatment include the acetylcholinesterase inhibitors (AChEIs) and judicious use of the atypical neuroleptics and levodopa (l-dopa).

AChEIs have recently been shown to have efficacy in the treatment of DLB. Given the profound cholinergic deficit of DLB, which is greater than that in AD, these medications are pharmacologically rational therapy.

Rivastigmine has been reported to have both efficacy and safety in the treatment of DLB. A double-blind, randomized, placebo-controlled trial (RCT) demonstrated improvements in neuropsychiatric symptoms, including hallucinations and delusions. As well, there were benefits on cognitive outcomes, including a series of computerized attentional tests. There was a striking loss of clinical benefit with short withdrawal of the medication.

Donepezil has also been reported to show efficacy in the treatment of DLB, however there are not yet any RCTs with this agent. The available observational studies have reported that donepezil also has an effect on cognition (increasing or stabilizing scores on tests of cognition) and on neuropsychiatric symptoms, including hallucinations and delusions.

There are no published reports on the use of galantamine in the treatment of DLB.

Atypical neuroleptics.

Neuroleptics are used in the treatment of DLB because of the frequency and severity of neuropsychiatric symptoms. While many of these symptoms can often be ameliorated by the use of AChEIs, they often still require adjunct treatment. This is especially true if the patient requires dopaminergic agents for his or her parkinsonian symptoms. DLB patients have an exceptional sensitivity to neuroleptics, especially the older, atypical neuroleptics. This supersensitivity can result not only in a worsening of their parkinsonian features, but also in sedation, falls, neuroleptic malignant syndrome and death. Because of this sensitivity, treatment of hallucinations and other psychotic symptoms with neuroleptics is generally limited to situations where such symptoms are interfering
with the care or well-being of the patient. Even then, treatment is approached cautiously. The current preferred atypical neuroleptic for this situation is quetiapine, though hard evidence for this preference is still limited. Fernandez et al\(^8\) studied 11 patients with DLB using a retrospective chart review. Quetiapine was well tolerated, with a 90% response rate for psychosis. Motor decline was noted in 27% of subjects.

There have been two studies evaluating olanzapine in the treatment of DLB, with conflicting results. Walker et al\(^9\) found that the majority of their patients were either unable to tolerate even minimal doses of olanzapine, or experienced no benefit with the medication. Cummings et al\(^10\) with a slightly larger study group in a placebo-controlled study, found benefit for olanzapine. The best dose was found to be 5 mg/day.

Risperidone has also had mixed results in the treatment of DLB. While some investigators have found it useful in controlling psychotic and behavioral symptoms,\(^11\) others have found that the adverse effects outweigh the benefits.\(^12-14\)

**L-Dopa.** There have been no formal studies evaluating the effects of L-dopa in patients with DLB, however it is used clinically to treat the parkinsonian symptoms of this disease. Caution must be exercised in its use to not exacerbate psychotic symptoms. However, in many instances, it can be safely instituted with the target symptoms being motor parkinsonism and not the associated dementia.

**Combination therapy.** There have been a few case reports detailing successes with combination therapy in DLB. The combinations include risperidone and donepezil,\(^15\) and L-dopa and 

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There are a number of RCTs with placebo control being performed.

**Atypical neuroleptics.** There are no large-scale, blinded, placebo-controlled studies using atypical neuroleptics in PDD. Again, as in DLB, caution must be exercised when using these agents, as PDD patients are extremely sensitive to the extrapyramidal side effects of these medications.

**Alzheimer’s Disease with Parkinsonism.** There are currently no reports in the literature looking at the pharmacologic treatment of parkinsonism in Alzheimer’s disease, however recent study reports have indicated that ACHEIs are safe and well tolerated in more advanced AD including in patients with motor parkinsonism.

**Conclusions**

The Parkinsonian dementias are a challenging therapeutic problem, however recent research findings have informed clinicians of new treatment options. DLB has deep cholinergic deficits for which symptomatic benefits can be obtained with acetylcholinesterase inhibitors. The utility of ACHEIs for PDD is not yet determined but preliminary reports are encouraging. For more advanced AD where Parkinsonian features are encountered ACHEIs can still be efficacious therapy and are generally well tolerated without increasing motor Parkinsonism. The use of neuroleptics in the Parkinsonian dementias must be very judicious.
References


