Emergency Room Treatment of Psychosis

OVERVIEW

The term Lewy body dementias (LBD) represents two clinical entities – dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD). While the temporal sequence of symptoms is different in DLB and PDD, individuals with Lewy body dementias have a progressive dementia plus any combination of the following symptoms: hallucinations, Parkinsonism, fluctuating cognitive abilities, REM behavior disorder and severe sensitivity to neuroleptics. Because DLB and PDD have essentially the same symptoms and treatment issues, we will use LBD as an umbrella term representing both clinical entities.

Visual hallucinations occur in up to 80 % of patients with LBD (and are considered a Core feature of DLB). If hallucinations are not frightening to the patient, even if they are considered bothersome by the family, drug therapy may not be needed. The goal of addressing behavioral disturbances in LBD is to ensure the safety of the patient and others. If long term treatment with cholinesterase inhibitors is ineffective, or more acute symptom control of behavior is required, it may be difficult to avoid a cautious trial of an atypical antipsychotic. The clinician should warn both the caregiver and patient of the possibility of a severe sensitivity reaction which occurs in an estimated 25-50% of patients administered antipsychotic drugs in the usual dose range. This is characterized by worsening cognition, sedation, increased or possibly irreversible acute onset parkinsonism, or symptoms resembling neuroleptic malignant syndrome, which can be fatal. **Typical antipsychotics should be avoided. Injectable administration which avoids first pass metabolism is likely to be particularly hazardous.**

There is no consistent evidence that any particular atypical antipsychotic is safer than others in LBD and efficacy is not established for any of them. **A survey of clinicians experienced in managing LBD found a significant preference for quetiapine and trial data suggests that clozapine might be used for control of psychotic symptoms such as hallucinations and delusions in the non-acute situation.** If any antipsychotic is administered to a person with LBD it is suggested that dosing starts low, that the patient is regularly examined for the emergence of side effects including parkinsonism, sedation, increased confusion or autonomic dysfunction and that referral is made as soon as possible to a specialist experienced in treating LBD (usually a geriatric psychiatrist, neurologist or geriatrician).

Key Considerations to Take BEFORE Treating Behavioral Disturbances in LBD

1. The first line measure in treating problematic behaviors such as hallucinations should be to evaluate for physical ailments that may be provoking behavioral disturbances (fecal impaction, pain, decubitus ulcers, urinary tract infection, bronchitis/pneumonitis, etc.).
2. Avoidance of or reduction of doses of other medications that can potentially cause agitation should also be attempted, such as OTC sleep agents and bladder-control medications, and reducing dopaminergic drugs used to treat Parkinson's disease, if clinically indicated.
3. Benzodiazepines are better avoided given their risk of sedation, increasing risk of falls, and paradoxical agitation.
4. If pharmacologic treatment of hallucinations, delusions or agitated behavior is needed, **traditional antipsychotics (e.g. haloperidol) should be avoided.**
5. When other medications are needed urgently to modify behaviors, they should be used for the shortest duration possible, and the clinician should warn both the caregiver and patient of the possibility of a severe sensitivity reaction.

TREATMENT OPTIONS

Although no evidence-based guidelines exist to guide specific pharmacotherapy for hallucinations and behavioral symptoms in LBD, the following background literature review is provided for reference and guidance.

AChEI for behavioral symptoms

Cholinergic deficits appear to be related to psychosis in LBD, which correlates with low CHAT activity and increased muscarinic receptor binding. Visual hallucinations may be predictors of a good response to cholinesterase inhibitors (AChEIs), including donepezil, rivastigmine and galantamine .

A meta-analysis of 6 large trials in AD showed a small but significant benefit of AChEI treatment in decreasing neuropyschiatric symptoms. There also appears to be a differential effect of AChEI on different psychiatric symptoms, with psychosis and anxiety being the most consistently responsive.

A few reports are available for behavioral improvement with the use of the AChEI rivastigmine in LBD. In a large multicenter trial, rivastigmine resulted in improvement by 30% from baseline in psychiatric symptoms. In a recent case control study of rivastigmine, treatment was associated with reduction in

total behavioral scores, hallucinations and sleep disturbance compared to AD. There were lower rates of apathy, anxiety, delusions and hallucinations in the treatment group compared to controls.

Medication Generic Name (Brand Name)	**Starting Dose**	**Suggested Titrating Schedule**	**Typical Therapeutic Range**
donepezil	5 mg every morning	Increase to 10 mg every morning 4 weeks later	5 mg every morning to 10 mg every morning
rivastigmine	1.5 mg every morning and evening; with meals	Increase in 1.5 mg increments for both doses every 4 to 6 weeks, maximum 6 mg every morning and evening. (The insert recommendation indicates titrating in 2-4 week increments, but 2 weeks may be too rapid for many LBD patients.)	1.5 mg every morning and evening to 6.0 mg every morning and evening
rivastigmine patch	4.6 mg/24 hr	Change to 9.5 mg/24 hr 4 weeks later	4.6 mg/24 hr 9.5 mg/24 hr
galantamine	8 mg every morning	Increase in 8 mg increments every 4 weeks, maximum 24 mg every morning	8 mg every morning to 24 mg every morning

b. Antipsychotics

Severe neuroleptic sensitivity affects up to 50% of the LBD patients who are treated with traditional antipsychotic medications, and is characterized by worsening cognition, sedation, increased or possibly irreversible acute onset parkinsonism, or symptoms resembling neuroleptic malignant syndrome, which can be fatal.

AChEIs are a long term treatment strategy, and benefits are not observed immediately. In situations where psychotic symptoms pose a significant safety risk to the patient, caregiver or family, it may be difficult to avoid a cautious trial of an atypical antipsychotic.

The management of psychosis in DLB has been mostly based on results of trials in AD and follows the general guidelines of pharmacotherapy in geriatric populations. According to the FDA, "in analyses of seventeen placebo-controlled studies of four drugs in this class (atypical antipsychotics), the rate of death for those elderly patients with dementia was about 1.6 to 1.7 times that of placebo. Although the causes of death were varied, most deaths seemed to be either heart-related (such as heart failure or sudden death) or from infections (pneumonia)."

In addition, some recommendations for the use of antipsychotics in DLB are based on studies in PD which has similar synuclein-based pathology. This may be misleading given the extreme sensitivity of some DLB patients to even low doses of antipsychotics, producing sedation, parkinsonism and autonomic dysfunction with significantly increased morbidity and mortality. Conversely, the use of antipsychotics in AD may also mislead physicians to assume patients with LBD would respond to antipsychotics the same as AD patients.

The FDA's 'black box warning' and the risks of sensitivity reactions indicates that these drugs are not approved for the routine treatment of mild to moderate behavioral symptoms in elderly patients with dementia. Physicians should discuss the risks and benefits of these types of medications, so that LBD patients and caregivers can consider issues of quality of life against the risks associated with them.

NOTE: ***Typical antipsychotics (such as haloperidol) and atypical antipsychotics with relatively strong D2 receptor antagonism (such as olanzapine and risperidone) should be avoided due to the risk of neuroleptic malignant syndrome, parkinsonism, somnolence and orthostatic hypotension.***

A survey of clinicians experienced in managing LBD found a preference for quetiapine and trial data suggests that clozapine might be used for control of psychotic symptoms in the non-acute situation. (The American Academy of Neurology, in 2006, endorsed the use of quetiapine for psychotic symptoms in PD, with clozapine as the second line choice.)

Quetiapine has become a popular treatment of psychosis in LBD given the low incidence of motor deterioration and its ability to control visual hallucinations with low doses. Efficacy and tolerability has been documented in both PD and DLB, however most data is from unblinded, open-label studies.

Clozapine has been demonstrated to be effective for PD psychosis in two randomized clinical trials on different continents. However, due to the potentially fatal adverse event of agranulocytosis in 1-2% blood monitoring is required, it is not first line.

Medication	**Starting Dose**	**Suggested Titrating Schedule**	**Typical Therapeutic Range**
quetiapine	25 mg before bed	Increase in 25 mg increments every 3 days	25 mg before bed to 100 mg every morning / 400 mg every night
clozapine	12.5 mg before bed	Increase in 12.5-mg increments every 2 to 3 days	12.5 mg before bed to 50 mg three times daily

To learn more about LBD, visit www.lbda.org

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