

Management of Lewy body dementia Summary sheets



Cognitive symptoms

General Principles

- Establish the presence of significant cognitive difficulties warranting treatment. Impairments in cognition can fluctuate and may relate to:
 - memory**
 - attention**
 - executive functioning**
 - visuoperceptual abilities**
 - disorganised speech/communication.**
- Evidence of cognitive difficulties should be obtained from reports by the **patient** and an informed **carer**, and from the results of **formal cognitive testing**.
- Cognitive **fluctuations**, whilst intrinsic to LBD, may also be a feature of **delirium**. Therefore, exclusion of the latter is important.
- Other factors causing or aggravating cognitive decline should also be excluded.
- Non-pharmacological approaches** to managing cognitive impairments include cognitive stimulation, use of memory aids, increased social interaction and stimulation, and exercise.

Cholinesterase Inhibitors

- Choice will be influenced by previous experience, ease of administration, dose titration regime and side effect profile.
- Donepezil and rivastigmine are similarly effective in DLB.
- There is more evidence for the benefits/effectiveness of rivastigmine in PDD.
- There is less evidence for the use of galantamine in LBD.
- Before starting Cholinesterase Inhibitors (ChEIs)
 - Check for clinically significant cardiovascular disease, particularly orthostatic hypotension, syncope or pre-syncope or cardiac dysrhythmia / conduction disturbance or bradycardia.
 - Consider carrying out an ECG before ChEI, particularly if there is a history of cardiac issues and/or autonomic dysfunction.
 - Cardiology referral should be made in cases of uncertainty including decisions regarding fitting of pacemakers.
- Cholinesterase inhibitors are best **titrated to the maximum tolerated dose** and maintained at this level. For example:
 - Donepezil:** 5mg once daily for 4-6 weeks, increased to 10mg daily if no significant side effects occur.
 - Rivastigmine (oral):** 1.5 mg twice daily for 4 weeks, increased to 3 mg twice daily ideally. Dose can be increased up to 4.5 mg twice daily going up to 6 mg twice daily if no significant side effects occur.
 - Rivastigmine patch:** 4.6 mg/24 hours for 4 weeks, increased to 9.5mg/24 hours with a further increase to 13.3 mg/24hours if no significant side effects. May have advantages in patients with swallowing difficulties, gastrointestinal side-effects in response to oral agents, compliance issues, or if there is a history of significant response variation to oral dosing.
 - Galantamine:** 8mg/day increased to the initial maintenance dose of 16mg/day after a minimum of 4-6 weeks. A further increase of 24mg/day of galantamine can be attempted after 4 weeks at 16mg/day if no significant side effects occur.
- Assessing response and deciding about continuation:
 - Global and behavioural/psychiatric baseline symptoms should be documented.
 - Assess outcome after 3-6 months on maximum tolerated dose (be aware that some patients may take longer to respond). Once optimised, treatment should be continued for as long as the patient/carer/clinician consensus is that there are positive benefits.
 - If/when discontinued, ChEIs should be withdrawn gradually as there are reports of a rebound worsening of symptoms.
 - Strategies for non-response or poor tolerance to one ChEI include switching to another ChEI.
- Adverse effects**
 - Gastrointestinal symptoms
 - Postural hypotension
 - Urinary frequency
 - Hyper-salivation
 - Watering eyes
 - Runny nose
 - Worsening of extrapyramidal motor symptoms, particularly fine tremor.
- Adverse effects may improve with dose reduction.**

Memantine

- Consider as:**
 - monotherapy if cholinesterase inhibitors are not tolerated or contra-indicated.
 - in combination with cholinesterase inhibitors, particularly if the effectiveness of the cholinesterase inhibitor is limited or is declining, or the disease is becoming more severe.
- Dose and titration**
 - Start at 5 mg daily and increase by 5 mg per week to a maximum of 20 mg daily if tolerated.
 - In patients with an estimated glomerular filtration rate (eGFR) of <50ml/min, dose adjustments maybe required.
- Adverse effects**
 - Side effects of memantine include gastrointestinal symptoms, confusion, somnolence, hypertension and dizziness.
 - Be cautious in prescribing memantine to individuals with a history of **seizures**, or poor **renal function**.
 - May enhance the effects of **dopaminergics/selegiline**, and be toxic when given with **amantadine**.
- Assessing response and deciding about continuation**
 - Record **baseline cognitive** performance using a preferred scale.
 - Global and behavioural / psychiatric baseline** symptoms should also be documented.
 - Assess outcome after **3-6 months** on maximum tolerated dose (be aware that some patients may take longer to respond). Cognitive, global and other domain assessments may be used to support this.
 - Once optimised, treatment should be continued for as long as the patient/carer/clinician **consensus is that there are positive risk/benefits**.
 - Due to the progressive nature of LBD it is likely that global/behavioural/cognitive measures will eventually fall below baseline levels but this alone should not be taken as lack of continuing response.

Neuropsychiatric symptoms

General Principles

- Establish the **presence, severity and impact** of significant neuropsychiatric symptoms warranting treatment. These may include **visual hallucinations, hallucinations in other modalities, delusions and apathy**.

- Obtain **collateral history** for symptoms from reports of the patient and an informed carer. Systematic **rating scales** may be helpful.
- Other factors causing or aggravating** mood and behaviour disturbance should be excluded e.g. physical illness, pain or discomfort, environmental precipitants, agitation & aggression, depression & anxiety.

Cholinesterase Inhibitor use

- Consider as a first line treatment.
- Choice will be influenced by previous experience, ease of administration, dose titration regime and side effect profile.
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- There is more evidence for the benefits/effectiveness of rivastigmine in PDD.
- There is less evidence for the use of galantamine in LBD.
- Before starting Cholinesterase Inhibitors (ChEIs)
 - Check for clinically significant cardiovascular disease, particularly orthostatic hypotension, syncope or pre-syncope or cardiac dysrhythmia / conduction disturbance or bradycardia.
 - Consider carrying out an ECG before ChEI, particularly if there is a history of cardiac issues and/or autonomic dysfunction.
 - Cardiology referral should be made in cases of uncertainty including decisions regarding fitting of pacemakers.
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 - Rivastigmine patch:** Dosing and titration is typically 4.6 mg/24 hours for 4 weeks, increased to 9.5 mg/24 hours with a further increase to 13.3 mg/24hours if no significant side effects. May have advantages in patients with swallowing difficulties, gastrointestinal side-effects in response to oral agents, compliance issues, or if there is a history of significant response variation to oral dosing.
 - Galantamine:** 8mg/day increased to the initial maintenance dose of 16mg/day after a minimum of 4-6 weeks. A further increase of 24mg/day of galantamine can be attempted after 4 weeks at 16mg/day if no significant side effects occur.
- Assessing response and deciding about continuation:**
 - Global and behavioural / psychiatric baseline symptoms should be documented.
 - Assess outcome after 3-6 months on maximum tolerated dose (although some patients neuropsychiatric symptom improvement may be judged earlier). Once optimised treatment should be continued for as long as the patient/carer/clinician consensus is that there are positive benefits.
 - If/when discontinued, ChEIs should be withdrawn gradually as there are reports of a rebound worsening of symptoms.
 - Strategies for non-response or poor tolerance to one ChEI include switching to another ChEI.
- Adverse effects** include gastrointestinal symptoms, postural hypotension, urinary frequency, hyper-salivation, watering eyes, runny nose and worsening of extrapyramidal motor symptoms, particularly fine tremor. Adverse effects may improve with dose reduction.

Antipsychotic use

- There should be a full discussion with the person with dementia and/or carers about the possible benefits and risks of antipsychotic treatment. This should be recorded in medical notes.
- Watch for severe antipsychotic sensitivity reactions.
- Be aware of the significant mortality and morbidity associated with the use of antipsychotics in dementia and Parkinson's disease.**
- Identify target symptoms and monitor these regularly.
- Watch for worsening of cognition and more subtle deteriorations in motor function.
- The choice of antipsychotic should be made after an individual risk-benefit analysis.
 - Clozapine, which is effective in PD psychosis, may also help in LBD, although the evidence is lacking.
 - There is no evidence to favour any individual anti-psychotic drug in LBD although atypicals and low potency agents such as quetiapine appear to have the least side effects.
- The lowest possible dose should be initiated and then titrated upwards.
- Treatment should be time limited and regularly reviewed.

Specific symptoms

- Visual hallucinations**
 - Not all visual hallucinations need treating as in some the hallucinations may be regarded neutrally or sometimes even comforting/pleasurable.
 - Simple explanation of visual symptoms as a consequence of impaired visual processing may allay fears and avoid the need for medication.
 - Interventions such as removing cushions, patterned curtains and other stimuli that might precipitate visual misinterpretations can be helpful, as is provision of good lighting.
 - ChEI are a first line pharmacological treatment for visual hallucinations in LBD. If these are ineffective a trial of an antipsychotic agent may need to be considered.
- Delusions**
 - Delusions of misidentification, jealousy and paranoia can occur.
 - They are often associated with visual hallucinations and may improve with ChEI (first line) and antipsychotics (second line).
- Apathy**
 - Providing adequate environmental stimulation may help reduce apathy and it may also improve with a ChEI. There is no evidence to support the use of psychostimulants.
- Depression and Anxiety**
 - Consider use of social interventions to enhance mood.
 - Avoid antidepressants with significant anti-cholinergic side effects such as tricyclics.
 - Evidence for antidepressant drug efficacy and tolerability in LBD is limited. Selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors have an evidence base in Parkinson's disease.
 - Whilst there is no evidence base, ChEI may help some particularly if there is an apathy component.
- Agitation and Aggression**
 - Often multi-factorial in cause: identify the relevant antecedent and perpetuating factors and treat as appropriate.
 - Sometimes, if driven by hallucinatory and other psychotic symptoms, agitation and aggression may improve when these are treated with a ChEI first line; anti-psychotics second line.
 - There is currently no evidence for efficacy of other medications in treating agitation or aggression in LBD.

Motor symptoms

Dementia with Lewy bodies

Parkinson's disease dementia

General Principles

- Establish the **presence of significant motor difficulties** which are impairing function and warrant treatment.
- **Exclude other factors** which may be a cause of a worsening of motor function e.g. cholinesterase inhibitor or antipsychotic use, osteoarthritis.
- Be aware that parkinsonian symptoms **may be less treatment-responsive** in DLB than in Parkinson's disease.



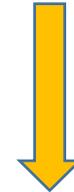
Treatment

- The preferred pharmacological treatment of parkinsonism in LBD is **levodopa monotherapy**.
- Use the **minimal levodopa dose** required for benefit.
- Either **co-careldopa** (carbidopa/levodopa) or co-beneldopa (levodopa/benserazide hydrochloride) may be used.
- Start low, and increase dose slowly: typical initiation doses are lower than in Parkinson's disease (e.g. 50mg (expressed as levodopa) taken 1-3 times daily).
- Monitor closely for **side effects**, including psychosis, postural hypotension, sedation, postural hypotension, nausea and vomiting.
- Zonisamide 25mg to 50 mg once a day as an adjunct to levodopa may have some motor benefits in PD and DLB.
- Consider **speech and language therapy** referral for motor related speech and swallowing problems.

- Physiotherapy may help with freezing of gait, gait re-education, improvement in balance, power and flexibility, enhanced mobility decrease the risk of falls and improve functional independence.
- In LBD cognitive impairment and other comorbid symptoms can diminish engagement with therapy but outcomes may still be positive.
- Occupational therapy assessment and home adaptations can help reduce the impact of motor difficulties and reduce falls risk.
- Given increased falls risk in LBD vitamin D supplementation should be considered if appropriate.

General Principles

- The **general principles are similar** to those for DLB but PDD patients will usually already have been on one or more anti-parkinsonian agents.
- Management decisions are therefore typically around **dose reduction/cessation or optimisation**.



Treatment

- A gradual and systematic **simplification of the antiparkinsonian drug regimen** is often necessary to balance neuropsychiatric symptoms vs. motor benefits.
- Where anti-parkinsonian drug regimes are being altered, this should be done in **close collaboration with the original prescriber** of the medicines where possible.
- **Withdraw (in following order) one at a time:**
 - anticholinergic drugs
 - amantadine
 - selegiline
 - dopamine agonists and
 - catechol-O-methyltransferase inhibitors.

Urinary Dysfunction

- **Non-pharmacological (first line) treatment of urinary incontinence**
 - **Regular, prompted, voiding** with use of incontinence pads may be helpful.
 - Consider **referral** to an incontinence nurse and/or urology if symptoms are particularly troublesome or have never been previously investigated.
- **Pharmacological treatment of urinary incontinence**
 - **Avoidance or reduction in diuretics** may help if no contraindications.
 - Be aware that cholinesterase inhibitors can precipitate urgency and urge incontinence.
 - **Avoid: Bladder anticholinergics** particularly the use of agents which have a significant centrally acting effect such as oxybutynin and tolterodine.
 - Intravesical botulinum toxin may have a positive effect on neurogenic detrusor overactivity in those intolerant of anticholinergics.
 - Mirabegron, a β_3 adrenergic agonist (25-50 mg per day) may be an alternative to anticholinergics for bladder overactivity.

Male sexual dysfunction

- The use of phosphodiesterase-5 inhibitors such as sildenafil can be considered for erectile dysfunction; prescribe with caution if the patient has postural / orthostatic hypotension.

Excessive sweating

- Wear loose fitting/natural fibre clothing and use natural light cotton bedding if there are significant night sweats. Antiperspirants can help some.
- Avoid foods and situations which trigger sweating e.g. alcohol, spicy foods, hot rooms.
- Ensure adequate fluid intake to replace losses.
- Alteration to the dopamine replacement regimen may sometimes help if associated with "OFF" motor state.

Constipation

- Check there has been no significant changes in bowel habits (such as per rectum bleeding, weight loss and/or anaemia) which may indicate other causes.
- Give advice on fluid and fibre intake, as well as exercise.
- If possible avoid constipating medications (e.g. opiates and some anti-parkinsonian drugs).
- Stool softeners can be helpful if stools are very hard.
- Mild suppositories such as glycerine may help also bowel emptying.
- Laxatives can be used, if required e.g.
 - Senna (7.5-15 mg at night)
 - Bisacodyl (5-10 mg at night)
 - Sodium docusate (50-400 mg in divided doses each day)
 - Bulk forming / osmotic laxatives e.g. macrogol.
- Lubiprostone is a second line treatment: 24 mcg twice daily.

Sialorrhoea

- Speech and language therapist input can be helpful.
- Use of sugar free chewing gum or boiled sweets may help some.
- Anticholinergics should not be used if possible.
- Botulinum toxin injections to salivary glands is an effective treatment.
- Clonidine 150 mcg per day is an alternative option, but can aggravate orthostatic hypotension and precipitate daytime somnolence.
- Glycopyrrolate 1–2 mg twice or three-times daily is a second line option.

Gastroparesis

- Be aware that dopaminergic medications can exacerbate gastroparesis.
- Advise the patient to have small and frequent meals and drink during meals. Avoidance of high fat foods may also help as well as walking after meals.
- Domperidone (10-20 mg three times daily) has been used to treat gastroparesis but there are significant concerns with regard to cardiotoxicity and the risk of QTc prolongation. If risk of QTc prolongation will need ECG before starting and after one week of treatment. If prescribed longer term will need regular review.
- Avoid using metoclopramide given its central dopamine antagonist effect.
- Giving levodopa in solution may help with patients with significant motor fluctuations and delayed gastric emptying.
- Alternatively, for some patients with delayed gastric emptying, their motor fluctuations may be improved through jejunal administration of levodopa.

Orthostatic hypotension

- Medications (e.g. levodopa, dopamine agonists, antihypertensives, antidepressants, alpha-adrenergic blockers, sildenafil), dehydration, cardiac disease, fever and anaemia may cause or exacerbate orthostatic hypotension.
- Orthostatic hypotension may manifest at particular times e.g. at mealtimes, when taking alcohol, in early morning, during defecation or micturition, and/or with physical activity.
- If there is **significant dizziness, falls or episodes of loss of consciousness, consider a referral** to a falls/ syncope clinic.
- **Non-pharmacological principles (first line)**
 - Advise the patient to stand slowly
 - Raising the head of the bed may help with morning orthostatic hypotension.
 - Slight increases in salt intake may help some
 - Consider use of compression hosiery
 - Increase fluid intake – usual advice is 2 litres, in total, daily.
- Potential **pharmacological therapies**
 - Fludrocortisone (50-300 mcg/ day). Titrate slowly and monitor electrolytes
 - Midodrine (2.5-10 mg bd). Monitor hepatic and renal function (needs specialist to initiate)
 - Note: these medications for orthostatic hypotension may cause severe supine hypertension and thus regular monitoring of blood pressure is needed.

Sleep disturbances

Excessive daytime sleepiness

- Document the frequency and occurrence of daytime sleepiness. Sleep scales may be helpful.
- Give advice on sleep hygiene and treat any sleep disturbances.
- Exclude physical and medication causes.
- There are no specific pharmacological interventions but cholinesterase inhibitors may improve sleepiness in some. Psychostimulants, if used, should be prescribed by a specialist experienced in their use.

Restless legs syndrome (RLS)

- Be aware may be due to other factors e.g. anaemia, diabetes or renal dysfunction. **In particular clinicians should consider checking ferritin levels** in appropriate patients, and in those with values < 50 ug/mL, to recommend oral iron replacement therapy for at least two to three months.
- Some medications e.g. antidepressants, antipsychotics and anti-emetics may exacerbate RLS.
- Regular exercise may help.
- Avoid smoking.
- **Pharmacological treatments** include:
 - Dopamine replacement therapy
 - Gabapentin

A **high degree of caution** needs to be applied if using these drugs given their potential for side effects.

Motor-related sleep disturbances

- Nocturnal extrapyramidal symptoms may be improved using long acting levodopa preparations prior to going to bed.
- Be aware though of their propensity to cause side effects e.g. neuropsychiatric.

Sleep apnoea

- Be **aware of risk factors** (overweight, male, smoker, on sedatives, alcohol use, reflux and anatomical considerations e.g. collar size >43 cm or 17 inches).
- If suspicion of sleep apnoea, consider referral to a sleep centre.
- Continuous positive airways pressure (CPAP) treatment in confirmed sleep apnoea can improve nocturnal sleep, cognition and daytime sleepiness.

REM-sleep behaviour disorder

- Consider and exclude potential mimics e.g. obstructive sleep apnoea
- **Consider non-pharmacological strategies as a first line, for example:**
 - placing bed on floor,
 - removing potentially dangerous objects and put padding around sharp/firm objects,
 - bed partners sleep separately etc.
- **Pharmacological treatments**
 - Clonazepam 250 mcg – 500 mcg (up to 1000 mcg) per day taken 30 minutes before bedtime. Be aware of side effects esp. increased risk of falls/worsening cognition.
 - Melatonin 3 mg to 12 mg per day taken before bedtime. Despite lack of evidence used by some as first line treatment given relatively benign side effect profile.
- Be aware some medications may exacerbate REM-sleep behaviour symptoms.

Insomnia & sleep fragmentation

- Advise on good **sleep hygiene:**
 - avoidance of stimulants in late afternoon/evening e.g. caffeine
 - avoid alcohol in the evening
 - establish regular pattern of sleep
 - have comfortable bedding and temperature
 - restrict daytime naps, and
 - take regular exercise.
- **Review of all medication** and avoid any drugs that may affect sleep or alertness, or may interact with other medication.
- Treat nocturia if a cause is identified. **Avoid anticholinergics** if possible.
- Melatonin 3 to 12 mg before bedtime may help some with subjective sleep disturbance.
- Zopiclone and zolpidem may be options short-term but have the potential for significant side effects.