Dopaminergic Therapy in Parkinson's

The purpose of this factsheet is to rationalise the dopaminergic therapy options in Parkinson's

Table 1: Initial Therapy Options

Levodopa

(+DOPA Decarboxylase Inhibitor, DDI)

- The 'gold standard'
- Good degree of symptom control
- Initiate at a low dose in the elderly and titrate upwards
- ADRs: GI, CV, Psychiatric, sleep disorders incl. sudden onset of sleep
- Cautions: Severe renal or hepatic disease, severe pulmonary or CV disease
- Dietary protein can affect absorption
- Oral iron can affect absorption

Co-beneldopa capsules

- Levodopa+benserazide (DDI)
- 62.5mg, 125mg, 250mg
- Initiate 62.5mg tds. Elderly: 62.5mg od-bd

Co-careldopa tablets

- Levodopa+carbidopa (DDI)
- 62.5mg, 119mg, 125mg, 250mg
- Initiate 62.5mg tds. Elderly: 62.5mg od-bd

Dispersible and MR versions

- Dispersible co-beneldopa tablets may be useful as a 'rescue' dose. They may also be useful in preference to levodopa liquid specials
- Modified release co-beneldopa/co-careldopa may be useful for nocturnal akinesia

Non-Ergot Dopamine Agonist

- Moderate degree of symptom control
- Less dyskinesia than levodopa but similar motor fluctuations
- ADRs: Fatigue, nausea, constipation, peripheral oedema, impulse control disorders, sleep disorders inc SOS, hypotensive reactions, hallucinations
- Cautions: Severe CV disease, major psychotic disorders, postural hypotension

Ropinrole (IR/MR tablets)

- Avoid if eGFR <30ml/min/1.73m^2
- Avoid in hepatic impairment
- IR preparation: Initiate 250mcg tds
- MR version **Ippinia XL** available if preferred - Initiate 2mg once daily

Pramipexole (IR/MR tablets)

- Care: Express doses and strengths in terms of pramipexole base
- Adjust dose in renal impairment - avoid MR version if eGFR <30ml/min/1.73m^2
- MR version available if preferred but high cost - use only if **Ippinia XL** not appropriate
- IR preparation: Initiate 88mcg tds
- MR version: Initiate 260mcg once daily

Rotigotine patches

- Avoid in severe hepatic impairment
- Initiate 2mg patch once daily
- Rotate patch sites, avoid same area for 14 days

Monoamine Oxidase Type B Inhibitor

- Low/moderate degree of symptom control
- Fewer motor complications than dopamine agonists (DAs)in early treatment
- Less effect on cognition decline than DAs
- ADRs: GI, CV, sleep disturbances
- Cautions: Antidepressants, pethidine, GI/duodenal ulceration (selegiline), CV disease, psychotic disorders
- No good evidence of neuroprotection
- No dietary restrictions (tyramine) necessary at licensed doses

Selegiline tablet/oral lyphilisate

- Initiate 5mg tablet in the morning
- Do not take at night due to amphetamine-like metabolites. Alerting effect may be useful in patients with daytime somnolence
- Oral lyphilisate (Zelapar) useful for patients with swallowing difficulties. 1.25mg oral lyphilisate equivalent to 10mg tablet
- Zelapar has negligible amphetamine-like metabolites
- Caution: Severe renal or hepatic impairment

Rasagiline tablets

- Initiate 1mg tablet once daily
- No amphetamine-like metabolites
- Caution: Hepatic impairment

Other options: Anticholinergics & Amantadine

Anticholinergics: Trihexyphenidyl, Orphenadrine

- Sometimes used in younger patients where tremor predominates
- ADRs limit effective use in older patients

Amantadine

- Sometimes used for dyskinesias and/or adjunctive treatment of motor symptoms
- Initially 100mg daily for one week then 100mg twice daily. Max daily dose 400mg.
- Not to be taken after midday due to alerting effects and potential sleep disruption.
- Reduce dose based on renal function
- ADRs: Insomnia, agitation, psychoses, hallucinations, peripheral oedema

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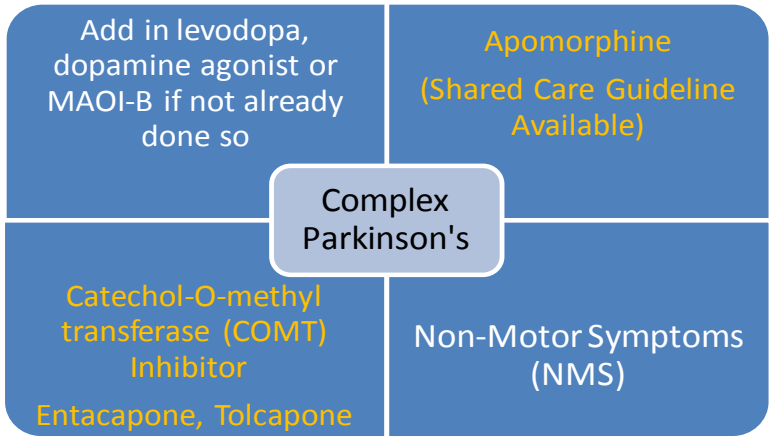
Table 2: Options in Complex Parkinson's where there is inadequate symptom control with initial therapies



Non-Motor Symptoms

- Don't overlook the management of NMS which can have the greatest impact on QoL than the motor symptoms
- Common NMS include constipation (50%), anxiety (40%), REM Sleep Behaviour Disorder (37%), depression (37%), excessive daytime sleepiness (33%), fatigue, pain, sexual dysfunction, bladder problems, cognitive impairment, psychoses, smell/taste disturbance

Entacapone

- Co-prescribe with levodopa+DOPA Decarboxylase inhibitor for 'end of dose' motor fluctuations
- Must be taken at the same time as levodopa doses
- 200mg with each dose of levodopa up to max. 2g (10 tabs) daily
- Avoid in hepatic impairment
- ADRs: Nausea, vomiting, abdominal pain, reddish-brown discolouration of urine
- Combination product **Sastravi/**Stalevo available

Tolcapone

- Only use if entacapone is inappropriate/ineffective
- Intensive LFT requirements.
- Patients should be told how to recognise signs of liver disorder
- Caution if eGFR <30ml/min/1.73m^2
- Avoid in hepatic impairment
- 100mg 3 times daily, leave 6 hours between each dose. Max 200mg 3 times a day in exceptional circumstances
- Continue beyond 3 weeks only if substantial improvement

Key Prescribing Points

- Be vigilant for impulse control disorders, especially with dopamine agonists (6-14% of patients)
- Parkinson's regimens can be complex. Contact the patient's nominated nurse specialist or consultant for advice on changes
- Be aware especially of the use of IR and MR forms of levodopa when prescribing. Often patients will have IR levodopa during the day and an MR preparation at night
- Avoid abrupt withdrawal of dopaminergic medication or 'drug holidays'. This can potentially result in neuroleptic malignant s yndrome
- Patients taking selegiline or rasagiline with antidepressants should be aware of the symptoms of serotonin syndrome
- If patients present with acute deterioration in their Parkinson's, refer to the 'Acute Deterioration' Pathway - check for acute illness; UTI, constipation or problems with medication taking.
- All people with Parkinson's who drive should be advised to inform the DVLA and their car insurer of their condition

References

- NICE (2006): Parkinson's disease: Diagnosis and management in primary and secondary care .https://www.nice.org.uk/guidance/cg035
- BMJ (2014): Initial management of Parkinson's disease
- TN (2015): Meta-analyses on prevalence of selected non-motor symptoms before and after diagnosis