Palliative care in Parkinson’s disease

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Objectives

• Background and Pathology
• Clinical features of Parkinsonism
• Medical management
• Common symptoms and their management
• Disease trajectory and markers of progression
• Advance care planning
• Management in the last days of life
Parkinson’s disease
Parkinson’s disease

- UK prevalence of 127,000 (Parkinson’s disease)¹
- Projected increase to >160,000 by 2020
- Male (55%) > Female (45%)
- Approx. 2% prevalence >80yrs²
- Mention on death certificate 7,600 (2008)³
- Mortality 2 to 5 x age matched population⁴
Aetiology
Pathology

- Mechanism of neurodegeneration not fully understood
- Neuronal loss in the substantia nigra
- Dopamine depletion
- Presence of Lewy bodies
Possible risk factors

- Older age
- Family history
- Males
- Non-smokers
- Low caffeine
- Repeated head trauma
- Rural living / agricultural work
Clinical features

Bradykinesia
- Reduced dexterity
- Reduced arm swing
- Shuffling / festinant gait
- Freezing

Tremor
- ‘Pill rolling’
- Resting tremor
- Worsened by stress / anxiety

Rigidity
- Asymmetric increased tone
- ‘Lead pipe’ Vs ‘Cog-wheel’
- May contribute to pain

Postural instability
- May be a later feature
- May be exacerbated by orthostatic hypotension
- Risk of recurrent falls
### Non-motor symptoms / signs

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Symptom</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Fatigue</td>
<td>Dysphagia</td>
</tr>
<tr>
<td>Siallorhoea</td>
<td>Bladder Symptoms</td>
<td>Sweating</td>
</tr>
<tr>
<td>Hyposmia</td>
<td>Constipation</td>
<td>Sleep disorders</td>
</tr>
<tr>
<td>Quiet speech</td>
<td>Sexual dysfunction</td>
<td>Autonomic dysfunction</td>
</tr>
<tr>
<td>Nausea</td>
<td>Restless legs</td>
<td>Swallowing problems</td>
</tr>
</tbody>
</table>

### Neuropsychiatric features

- Depression
- Anxiety
- Apathy
- Hallucinations / psychosis
- Cognitive impairment
Dementia

• In PD, 5 to 6 x rate for age-matched controls
• Cognitive impairment at some point in disease in up to 80%
• Dementia with Lewy Bodies – onset before or within 1yr of Parkinsonian symptoms
• May benefit from cholinesterase inhibitors
  – Rivastigmine
  – Donepezil
Parkinson’s disease and related disorders

Clinical subtypes:
- Tremor dominant
- Akinetic rigid
- Postural instability / gait disturbance

Related disorders / differential diagnosis:
• Multiple system atrophy (MSA)
• Progressive Supranuclear Palsy (PSP)
• Corticobasal degeneration
MSA

• Features of parkinsonism, autonomic dysfunction, cerebellar ataxia

• MSA-P; Predominant parkinsonism

• MSA-C; Predominant cerebellar ataxia

• Poor response to levodopa

• Less likely to develop dementia

• Mean survival 7 to 9 yrs
PSP

Clinical features:
- Vertical supranuclear gaze palsy
- Postural instability / falls
- Dysarthria/Dysphagia
- Rigidity
- Frontal cognitive impairment

• Management largely supportive
• Rapid progression; mean survival 5 to 7 years
Parkinson’s disease - management

- Medical treatments
- Surgical (in selected patient group)
- MDT support:
  - Parkinson’s disease CNS; education + ongoing advice
  - Physio
  - OT
  - SALT
  - Palliative care team
  - Social worker
  - Neuro-rehab team
Medical management

• NICE guidance
  – Consider treatment when symptomatic + functional disability
  – No universally accepted 1st line therapy
    – L-DOPA
    – Dopamine agonist
    – MAO-B inhibitor

• Limited evidence for disease-modifying effects with any current PD therapy\textsuperscript{5}
### LEVODOPA

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbidopa and levodopa (Co-careldopa) DUODOPA  (Intestinal gel)</td>
<td>abbvie</td>
<td>100ml per cassette containing 2000mg levodopa and 500mg carbidopa monohydrate</td>
</tr>
<tr>
<td>Levodopa and benserazide (Co-beneldopa) MADOPAR</td>
<td>Roche</td>
<td>50mg/12.5mg 100mg/25mg 200mg/50mg CR 100mg/25mg (dispersible) 50mg/12.5mg (dispersible) 100mg/25mg (dispersible)</td>
</tr>
<tr>
<td>Levodopa and carbidopa (Co-careldopa) SINEMET</td>
<td>MSD</td>
<td>25mg/100mg 12.5mg/50mg 25mg/250mg 10mg/100mg CR 50mg/200mg Half-CR 25mg/100mg</td>
</tr>
<tr>
<td>Levodopa, carbidopa and entacapone STALEVO</td>
<td>Orion Pharma</td>
<td>50mg 75mg 100mg 125mg 150mg 175mg 200mg</td>
</tr>
<tr>
<td>Carbidopa and levodopa (Co-careldopa) LECADO</td>
<td>SANDOZ</td>
<td>100/25mg 200/50mg</td>
</tr>
<tr>
<td>Carbidopa and levodopa (Co-careldopa) CARMET</td>
<td>TEVA</td>
<td>25/100mg 50/200mg</td>
</tr>
</tbody>
</table>

Co-careldopa also available in generic form.
Levodopa limitations

- Limited/variable effect on:
  - Tremor
  - Postural instability
  - Non-motor symptoms
- Reduced efficacy over time
- No definitive evidence that treatment with levodopa reduces mortality\(^7\)
Drugs which reduce dopamine breakdown:

- **Selegiline, rasagiline** - inhibit dopamine breakdown by monoamine oxidase B (MAOB) enzyme inhibition

- **Entacapone, tolcapone** - inhibit dopamine breakdown by catechol-O-methyltransferase (COMT) enzyme inhibition
Dopamine agonists

- Pramipexole (e.g. Mirapexin®)
- Ropinirole (e.g. Requip®)
- Bromocriptine (e.g. Parlodel®)
- Cabergoline (e.g. Cabaser®)

Oral medications

- Rotigotine patch (e.g. Neupro®)
- Apomorphine - via subcutaneous injections / pump (e.g. APO-go®)

Non-oral medications
Drugs for Parkinson's disease can turn patients into gamblers, sex addicts and compulsive shoppers

- Impulsive and compulsive behaviour is common with dopamine agonists
- Dopamine agonist drugs were 277 times more likely to result in a report of specific impulse control symptoms than other drugs, report found
- Up to 14% of patients develop changes in behaviour when taking them

By ANNA HODGEKISS FOR MAILONLINE

Other drug therapies

Amantadine – Glutamate antagonist, stimulates dopamine release

Non-motor symptoms:
- Analgesia
- Laxatives
- SSRIs
- Cognitive impairment – Cholinesterase inhibitors
Deep brain stimulation
- **Diagnosis**
  - Investigation, early specialist referral, confirm diagnosis
  - MDT assessment, information giving
  - Consider drug treatment
  - Duration: ≈ 1.6 yrs

- **Maintenance**
  - Focus on maintenance of function + self care
  - Regular assessment of motor and non-motor symptoms
  - Physio / OT / SALT input
  - Duration: ≈ 5.9 yrs

- **Complex**
  - Increasing motor fluctuations, falls
  - Frequent review of complex drug regimes + adverse effects
  - Consider adjuvant treatments
  - Duration: ≈ 4.9 yrs

- **Palliative**
  - Reduced response to medications – review regime/rationalise
  - Consider palliative care input
  - Implications of cognitive impairment
  - Duration: ≈ 2.2 yrs

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MacMahon & Thomas (1998)
Advance care planning?

Diagnosis
≈ 1.6 yrs
- Investigation, early specialist referral, confirm diagnosis
- MDT assessment, information giving
- Consider drug treatment

Maintenance
≈ 5.9 yrs
- Focus on maintenance of function + self care
- Regular assessment of motor and non-motor symptoms
- Physio / OT / SALT input

Complex
≈ 4.9 yrs
- Increasing motor fluctuations, falls
- Frequent review of complex drug regimes + adverse effects
- Consider adjuvant treatments

Palliative
≈ 2.2 yrs
- Reduced response to medications – review regime/rationalise
- Consider palliative care input
- Implications of cognitive impairment

MacMahon & Thomas (1998)
Prognostic indicators

• Drug regime becoming less effective
• Reduced functional status / increased support needs for ADLs
• Increased motor fluctuations
• Reduced mobility, falls
• Neuropsychiatric sequelae of Parkinson’s disease

‘Frailty’ markers⁹
• Declining performance status
• >3 of:
  • Weakness
  • Slowed walking
  • Reduced physical activity
  • Weight loss
  • Fatigue/Exhaustion
  • Depression
  • Inability to tolerate adequate dopaminergic therapy
  • Unsuitable for surgery
  • Advanced comorbidities
The palliative phase

Physical:
- Increased motor fluctuations
- Pain
- Nausea
- Breathlessness
- Reduced oral intake / swallowing
- Reduced mobility
- ?Rationalise medication regime

Involve specialist / PD CNS:

Prioritise Levodopa preparations > Dopamine agonists > MAO-B > amantadine / others (discontinue first)
## Place of death in PD

**Table 4: ‘Underlying’ cause of death from neurodegenerative diseases by place of death, males, England, 2002 to 2008 (total for all years shown)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Hospital</th>
<th>Hospice</th>
<th>Nursing home</th>
<th>Old people’s home</th>
<th>Own residence</th>
<th>Elsewhere</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>n</td>
<td>n</td>
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<tr>
<td>Parkinson's disease</td>
<td>8,473</td>
<td>53</td>
<td>84</td>
<td>1</td>
<td>4,063</td>
<td>2,013</td>
<td>1,411</td>
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<tr>
<td>Motor neurone disease</td>
<td>2,463</td>
<td>50</td>
<td>614</td>
<td>12</td>
<td>343</td>
<td>99</td>
<td>1,399</td>
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<tr>
<td>Multiple sclerosis</td>
<td>1,291</td>
<td>58</td>
<td>56</td>
<td>3</td>
<td>340</td>
<td>108</td>
<td>356</td>
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<tr>
<td>Huntington's disease</td>
<td>270</td>
<td>44</td>
<td>16</td>
<td>3</td>
<td>181</td>
<td>47</td>
<td>74</td>
</tr>
<tr>
<td>Multiple system degeneration</td>
<td>135</td>
<td>51</td>
<td>15</td>
<td>6</td>
<td>34</td>
<td>14</td>
<td>65</td>
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<tr>
<td>Progressive supranuclear palsy</td>
<td>360</td>
<td>46</td>
<td>40</td>
<td>5</td>
<td>181</td>
<td>67</td>
<td>135</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>12,992</strong></td>
<td><strong>52</strong></td>
<td><strong>825</strong></td>
<td><strong>3</strong></td>
<td><strong>5,142</strong></td>
<td><strong>2,348</strong></td>
<td><strong>3,440</strong></td>
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</tbody>
</table>

*Source: Office for National Statistics, annual mortality extracts, and unpublished MND and PSP reclassified deaths*
Advance care planning

“People with PD and their carers should be given the opportunity to discuss end-of-life issues with appropriate healthcare professionals.”

– NICE CG 35: Parkinson’s disease
A qualitative study of the views of health professionals

Current practice:

• Advance care planning (ACP) not consistently taking place
• Disease course more widely discussed than specific ACP
• ACP often takes place late in disease
• Approach showed significant variation between teams
• A range of tools are in use
Barriers to ACP in Parkinson’s disease

• Variable prognosis and disease course

• Barriers amongst professionals
  • Insufficient training / experience
  • Lack of confidence

• Blocking by patient/relatives

• “Not enough time”

• Lack of resources to guide ACP?

• Cognitive impairment
ACP considerations in Parkinson’s

- Preferred priorities for care
- Preferred place of care (in advancing disease)
- Who should be involved in care
- Practical management of physical disability
- CPR decisions
- Preferred place of death
- Artificial nutrition
  - Specifically PEG/RIG
- Artificial hydration
- Limits to escalation of treatment
  - Antibiotic treatment
  - Hospitalisation in the event of acute illness
- Advance decisions to refuse treatment/advance directives
- Lasting power of attorney
- Other legal issues on an individual basis (financial, wills etc.)
- Potential for difficulties in communication
- Implications of cognitive impairment
PREPARING FOR END OF LIFE

A practical and emotional guide

http://www.parkinsons.org.uk/content/preparing-end-life-booklet
<table>
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<td>How will my condition progress?</td>
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<td>Could I die from Parkinson's?</td>
<td>5</td>
</tr>
<tr>
<td>How might my symptoms progress?</td>
<td>5</td>
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<tr>
<td>Why should I think about end of life issues?</td>
<td>6</td>
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<td>Arranging the right care</td>
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<td>What is palliative care?</td>
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<td>Who provides palliative care?</td>
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<tr>
<td>Involving my family</td>
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<td>When should I start thinking about palliative care?</td>
<td>9</td>
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<tr>
<td>Preparing for end of life</td>
<td>10</td>
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<tr>
<td>Talking to people close to you</td>
<td>10</td>
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<tr>
<td>Talking to children</td>
<td>10</td>
</tr>
<tr>
<td>Making your wishes known</td>
<td>11</td>
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<tr>
<td>Looking after your affairs</td>
<td>11</td>
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<tr>
<td>Making a Will</td>
<td>12</td>
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<tr>
<td>Power of Attorney</td>
<td>14</td>
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<tr>
<td>Losing the capacity to make decisions</td>
<td>16</td>
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<td>Making an Advance Decision</td>
<td>18</td>
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<td>Brain donation for Parkinson’s research</td>
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<td>Where to get emotional support</td>
<td>22</td>
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<tr>
<td>Counselling</td>
<td>22</td>
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<tr>
<td>Where is counselling available?</td>
<td>22</td>
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<td>Information and support centres</td>
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<td>Parkinson’s UK local groups</td>
<td>23</td>
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<tr>
<td>Religious and spiritual support</td>
<td>24</td>
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<tr>
<td>Online support</td>
<td>24</td>
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<tr>
<td>What to do when someone dies: information for family and friends</td>
<td>25</td>
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<tr>
<td>How to register a death</td>
<td>25</td>
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<tr>
<td>Who do I need to inform?</td>
<td>26</td>
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<td>How do I arrange a funeral?</td>
<td>26</td>
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<tr>
<td>How do I cope with bereavement?</td>
<td>27</td>
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<tr>
<td>More information and support</td>
<td>29</td>
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<tr>
<td>Parkinson’s nurses</td>
<td>29</td>
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<td>Information and support from Parkinson’s UK</td>
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<td>Parkinson’s UK Brain Bank</td>
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<tr>
<td>Useful contacts</td>
<td>30</td>
</tr>
<tr>
<td>Checklist for important documents and information</td>
<td>35</td>
</tr>
</tbody>
</table>
The role of palliative care

“Palliative care should be incorporated into the care of patients with Parkinson’s disease”

– NSF for long term conditions
– NICE guidance
– GSF guidance
– NCPC
– British Movement Disorders Society
– Parkinson’s UK

How, when, what and by whom?

Little evidence though models have been proposed
End of life care

• Exclude reversible causes
  - “Off” phase with significant rigidity / bradykinesia may be mistaken for terminal phase
  - Ensure no recent discontinuation / omission of usual anti-parkinsonian meds

• Continue usual medications if able
  – Consider different preparations e.g. dispersible
  – Consider non-oral alternatives
Specific considerations in PD

• Non-oral anti-parkinsonian medications at the end of life
• Nausea
• Pain
• Agitation
• Constipation
A senior clinician identifies that a patient with Parkinsonism is approaching the end of life.

- Is the patient able to reliably swallow PD medications? **NO**
  - NO: Contact Parkinson’s specialist team, continue apomorphine/rotigotine/Duodopa if already prescribed.
  - YES: Maintain current regime as far as possible.
- Does the patient have an enteral feeding tube already in place? **NO**
  - NO: Consider placement of an NG tube - if appropriate, depending on the clinical condition of the patient.
  - YES: Consider use of a rotigotine patch. See section 6.1 below.
- Has the medication regime been modified to optimise the oral route? **YES**
  - NO: Regime should be reviewed by the Parkinson’s specialist team as soon as possible. Advice on formulations and compatibility of medications should be sought from pharmacy where necessary. See also sections 5.4 and 5.7 for further information on rationalising anti-parkinsonian medications.
  - YES: Consider other medications for effective end of life symptom control are prescribed.

![Diagram](image)
A senior clinician identifies that a patient with Parkinsonism is approaching the end of life.

Is the patient able to reliably swallow PD medications?

- NO
  - Maintain current regime as far as possible

- YES
  - Does the patient have an enteral feeding tube already in place?
    - NO
      - Convert to medications suitable for NG/PEG/RIG administration as described in section 5.7
    - YES
      - Has the medication regime been modified to optimise the oral route?
        - NO
          - Consider use of dispersible preparations. Some tablets may be crushed and given with fluids, thickened if necessary
        - YES
          - On occasions it may be appropriate to give oral medications to patients even when swallowing is unreliable - is this an option? (see below)

Contact Parkinson’s specialist team, continue apomorphine/rotigotine/Duodopa if already prescribed.

On occasions it may be appropriate to give oral medications to patients even when swallowing is unreliable - is this an option? (see below)

This should be a risk/benefit decision made by the multidisciplinary team in conjunction with the patient and/or their representative. Rationale and decision-making process should be clearly documented in the notes.

Regimes should be reviewed by the Parkinson’s specialist team as soon as possible. Advice on formulations and compatibility of medications should be sought from pharmacy where necessary. See also sections 5.4 and 5.7 for further information on rationalising anti-parkinsonian medications.
Has the medication regime been modified to optimise the oral route?

- **NO**
  - Consider use of dispersible preparations. Some tablets may be crushed and given with fluids, thickened if necessary.

- **YES**
  - On occasions it may be appropriate to give oral medications to patients even when swallowing is unreliable - is this an option? (see below)

Contact Parkinson's specialist team, continue apomorphine/rotigotine/Duodopa if already prescribed

- **YES**
  - This should be a risk/benefit decision made by the multidisciplinary team in conjunction with the patient and/or their representative. Rationale and decision-making process should be clearly documented in the notes.

- **NO**
  - Consider medications via a non-oral route
    - **NO**
      - Consider use of a rotigotine patch
        - See section 5.1 below
    - **OR**
      - Consider placement of an NG tube
        - If appropriate depending on the clinical condition of the patient

Ensure other medications for effective end of life symptom control are prescribed

Apomorphine should only be newly commenced following specialist input
For patients who already have NG/ PEG / RIG...

<table>
<thead>
<tr>
<th>Current anti-parkinsonian medication</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-careldopa tablets (e.g. Sinemet®)</td>
<td>Use equivalent dose Madopar® dispersible tablets</td>
</tr>
<tr>
<td>Co-beneldopa capsules (e.g. Madopar®)</td>
<td>Use equivalent dose Madopar® dispersible tablets</td>
</tr>
<tr>
<td>Stalevo® tablets</td>
<td>Use equivalent dose Madopar® dispersible tablets</td>
</tr>
<tr>
<td>Pramipexole tablets (Mirapexin®)</td>
<td>Tablets can be crushed</td>
</tr>
<tr>
<td>Pramipexole m/r tablets (Mirapexin® Prolonged Release)</td>
<td>Use equivalent dose of standard release pramipexole tablets and crush</td>
</tr>
<tr>
<td>Ropinirole (Requip®) tablets</td>
<td>Tablets can be crushed</td>
</tr>
<tr>
<td>Ropinirole m/r tablets (Requip® XL)</td>
<td>Use equivalent dose of standard release Requip® tablets and crush</td>
</tr>
</tbody>
</table>
• Consider an **increase** in rotigotine dose if patients are more rigid than usual, or symptoms of parkinsonism deteriorate.

• Consider a **reduction** in rotigotine dose if patients experience hallucinations, agitation or other adverse effects
Nausea and vomiting

- Avoid dopamine antagonists; haloperidol, metoclopramide
- Anti-cholinergics may worsen confusion

Domperidone
Ondansetron
Other symptoms

• Pain
  – Musculoskeletal
  – Dystonic
  – Neuropathic
  – Poorly understood central mechanisms

• Simple analgesia
• Opioids – though may not be responsive
• Neuropathic agents
• Passive movements
• TENS
• Complementary therapies
Other symptoms

• Agitation / hallucinations
  – Review dopaminergic therapies
  – Clozapine
  – Quetiapine
  – Benzodiazepines

• Constipation
  – Review exacerbating meds
  – Consider tablet burden
  – Stimulant +/- softener +/- PR supps/enemas
Summary

• Significant variation in disease course and prognosis
• Potentially high symptom burden from motor and/or non-motor symptoms
• Advance care planning – challenging but important
• Options for non-oral medications at the end of life
• Importance of MDT and liaison with PD specialists
References

Thank you