Parkinson's Disease and how you can make a difference with medication

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Royal Hallamshire Hospital
What Treatment

- No treatment all
- Complementary Therapy
- Tablets
- Injections
- Patches
- surgery
Drugs to treat PD

- Levodopa dose timing becomes critical as the condition progresses
- Dopamine agonists
- Amantadine
- COMT inhibitors e.g. entacapone slows the destruction of L-dopa, tolcapone.
- MAO-B inhibitors e.g. selegeline reduces break down of dopamine in the brain, rasageline
- Anticholinergics eg Benzhexol

The main treatment for PD is medication which work by replacing or mimicking the actions of dopamine
Introduction to dopamine and its receptors

Dopamine synthesis

Dopamine vesicles

Pre-synaptic membrane

Dopamine release

Synaptic cleft

Neurone

Catechol-O-methyltransferase

Monoamine oxidase

Dopamine inactivation

Post-synaptic membrane

Dopamine receptors D₁, D₂, D₃, D₄, D₅

transmitted

Image adapted from B R Thanvi, post grad. 80. p453
**Sinemet/Madopar/Stalevo**

- **Action:** Increases the level of Dopamine in the brain
- **Effect:** Reduces slowness, rigidity, and less so tremor

- Sinemet is levodopa and carbidopa
- Madopar is levodopa and benzeride
- Stalevo is levodopa and cabidopa and entacapone
- All medications have a range of doses and forms
- Eg dispersible madopar – also standard and CR
Long Term Problems

- Dyskinesia (involuntary movement)
- Wearing off
Wearing-off pattern

A typical day

PD medication

‘on’ time

‘off’ time

Symptoms alleviated

Symptoms return

Wearing-off period

Medication starts to work

Time

Taken from European Parkinson’s Disease Association Publication
Factors associated with the development of motor complications:
- Duration of therapy
- Dose
- Severity of disease
- Pulsatile stimulation with immediate-release preparations

Psychiatric
- Confusion
- Visual hallucinations
- Delusions
- Illusions

Response fluctuations
- End-of-dose deterioration (wearing-off)
- Unpredictable ‘on’/’off’ switching

Involuntary movements
- Peak dose dyskinesia
- Diphasic dyskinesia
- Dystonia

Levodopa long-term side effects
Action of Dopamine Agonists

- Mimics the action of dopamine
- Improves slowness, stiffness, and tremor
- No effect on balance and walking problems
Tablets that mimic dopamine (Dopamine Agonists)

- Pramipexole–Mirapexin tablet
- Bromocriptine–Parlodel tablet
- Ropinerole–Requip tablet
- Apomorphine–APO–go (injection)
- Rotigotine–transdermal treatment–patch
Apomorphine

• A highly potent D1 and D2 agonist that also acts on D3 receptors but has no opioid properties

• Used to treat disabling motor fluctuations that persist despite ongoing treatment with L-dopa and/or DAs

• Administered either by patient self-injection, or by infusion

• **Dose:** Dependant on patient response following an apomorphine challenge
Gastrointestinal:
- Nausea vomiting, loss of appetite

Psychiatric / nervous system:
- Confusion, hallucinations
- Pathological gambling, increased libido and hypersexuality have been reported

Cardiovascular:
- Postural hypotension

Ergot related effects
- Fibrotic and serosal inflammatory disorders such as:
  - Plueritis
  - Plueral effusion
  - Cardiac valvulopathy – involving one or more valves (aortic, mitral and tricuspid)
  - Retroperitoneal fibrosis

Gastrointestinal:
- Nausea vomiting, loss of appetite

General:
- Somnolence
- Leg oedema
DAs: Sleep Related Side Effects

- All DAs have, to varying degrees, been associated with somnolence and episodes of sudden onset of sleep (SOOS)

- There have been reports of SOOS happening during daily activities, including driving or operating machinery, without awareness or warning signs, though these remains uncommon

- The DVLA has stated that the risk of SOOS is low and taking PD drugs should not lead to an automatic cessation of driving
Ergot-derived dopamine agonists have been associated with fibrotic reactions – lung, cardiac and retroperitoneal fibrosis. Generally only Bromocriptine is the only medication used in this class at Sheffield.

Patients should have appropriate baseline investigations on an annual basis:

- Chest x ray, bloods for renal function test and erythrocyte sedimentation rate and echocardiogram.
- Observe for persistent cough, chest pain, cardiac failure, abdominal pain / tenderness
Impulse Control Disorder

- A person’s inability to resist a temptation or impulse
- More likely to happen in those with a previous history of novelty seeking or risk – taking behaviors
- Compulsive behaviors have been reported as a side effect with levodopa and dopamine agonists
- Behaviors can include:
  - Pathological gambling
  - Hypersexuality
  - Compulsive eating
  - Compulsive shopping
  - Punding
- It is important that this is discussed with the patient and if symptoms are experienced, help should be sought from a Parkinson’s Disease Nurse Specialist or Consultant
**COMT Inhibitors**
**Cathcol-O-methyltransferase**

- **Includes drugs**: entacapone (Comtess), tolcapone (Tasmar), Stalevo(levodopa+entacapone)

- **Work by**: blocking a dopamine digesting enzyme to increase dopamine levels
Uses of COMT inhibitors

- Used to lessen “wearing off” of levodopa and help movement fluctuations

- **Side effects:** nausea and dyskinesia

- Tolcapone can cause liver problems so needs regular blood tests
COMT Inhibitor side effects

Psychiatric
• Insomnia
• Hallucinations
• Confusion

Nervous system
• Dyskinesia

Renal / urinary:
• Urine discolouration

Gastrointestinal:
• Nausea
• Diarrhoea
• Abdominal pain
• Vomiting
• Constipation
• Anorexia

General:
• Sweating
Drugs that prolong dopamine availability – MAO-B inhibitors

- Monoamine oxidase is an enzyme that breaks down dopamine in the brain. These drugs can either be used alone or with Levodopa to reduce breakdown and increase the effects of Levodopa.
  - **Includes drugs**: Rasagiline, Selegiline, and Zelapar
  - Not to be taken with SSRI’s or related antidepressants
Selegiline

- Clinically active by inhibiting dopamine metabolism in brain
- May be neuroprotective
- Selective MAO-B inhibitor
- Side effects: insomnia, hallucinations, nausea (rarely)
- Potential interactions with tricyclics and SSRI antidepressants
- **Dose**: 5 mg at breakfast and lunch or 10mg at breakfast
- Zelapar 1.25mg once a day
MAOB side effects

Psychiatric / nervous system
- Depression
- Vertigo
- Hallucinations

Cardiovascular
- Hypotension

Gastrointestinal:
- Dyspepsia
- Nausea
Anticholinergics

• Dopaminergic depletion is thought to lead to cholinergic overactivity
• Initially used in the 1950s
• Effective mainly for tremor and rigidity
• Common agents:
  – Benzhexol
  – Orphenadrine
• Side effects include:
  – Dry mouth, sedation, neuro psychiatric complications, constipation, urinary retention
• Dose:
  – Benzhexol: 0.5 – 1mg daily usually at bedtime, gradually increased; max. 6 mg daily
  – Orphenadrine: 150 mg daily in divided doses, increased gradually; max. 400 mg daily
Amantadine (antiviral)

- **Action:**
  Improves dyskinesias

- **Side effects:**
  Constipation, skin rashes, ankle swelling and nausea

- **Use:**
  To be taken with levodopa (sinemet or Madopar)
Drug Management

- Patient choice is important
- Referral to a specialist for diagnosis and long-term treatment
- Access to a PD nurse specialist
- Importance of patient education to ensure concordance
- General ease of use
- Regular monitoring either by telephone or nurse led clinic
- Avoid complex formulations if possible
- Anti parkinsonian medication should be gradually withdrawn to avoid Neuroleptic Malignant Syndrome
Drug classes in Parkinson’s

- **Levodopa**
- **MAO-B inhibitors**
  - Monoamine oxidase B inhibitors
- **Anticholinergics**
- **DAs**
  - Dopamine agonists
- **COMTs**
  - Catechol-O-methyltransferase inhibitors
Anti-Emetics not to be taken by those who have PD( for nausea and vomiting

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<thead>
<tr>
<th>Trade name</th>
<th>Generic name</th>
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<tbody>
<tr>
<td>Maxalon</td>
<td>Metoclopramide</td>
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<tr>
<td>Stemital</td>
<td>Prochlorperazine</td>
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The only safe treatment for nausea and sickness for those who have PD is Domperidone

Also  Hyoscine patch can cause paranoia and hallucinations advice not to use with PD
The more commonly known drugs that are not recommended to be taken by those who have PD

- **Antipsychotic drugs**

<table>
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<tr>
<td>Haldol</td>
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<td>Melleril</td>
<td>Thioridazine</td>
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<td>Risperidol</td>
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<td>Stelazine</td>
<td>Trifluoperazine</td>
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<td>Largactil</td>
<td>Chlopromazine</td>
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<td>Olanzapine</td>
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drugs for PD

ALL EXACERBATE HALLUCINATIONS AND PSYCHOSIS
“Anti-parkinsonian medication should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (e.g. gastroenteritis, abdominal surgery) to avoid the potential for acute akinesia or neuroleptic malignant syndrome.
“In view of the risks of sudden changes in anti-parkinsonian medication, people with PD who are admitted to hospital or to care homes should have their medication:
- given at the appropriate times, which in some cases may mean allowing self medication
- adjusted by, or adjusted only after discussion with a specialist in the management of PD”
Reducing harm from omitted and delayed medicines in hospital (Feb 2010)

1 Identify a list of critical medicines where timeliness of medication is crucial, this list should include medicines for Parkinson’s disease.....

2 Ensure medicine management procedures include guidance on the importance of prescribing, supplying and administering critical medicines, timeliness issues and what to do when a medication has been omitted or delayed.
3. Review and where necessary, make changes to systems for the supply of urgent medicines within and out of hours to minimise risk.

4. Review incident reports regularly and carry out an annual audit of omitted and delayed critical medicines. Ensure that system improvements to reduce harm from omitted and delayed medicines are made. This information should be included in the annual medication safety report.

5. Make all staff aware (by wide distribution of the RRR) that omission or delay of critical medicines for inpatients or on discharge from hospital, are patient safety incidents and should be reported.
The symptoms and progression of PD is unique in each individual

- It has taken a long time for the specialist and patient to establish the drug regime

- Once the medication regime has been disrupted the person may take days, weeks, months to recover and some never do!

- Other factors are loss of dignity and independence for the patient, may need to go into care so massive financial implications.
Please listen to the carer/patient they are experts in managing the PD symptoms. They may advice what not to prescribe e.g. Opoid analgesia. Listen to them and value their expertise.

Is self medication an option?

Please inform the Parkinson's Nurse Specialist service of admission.

Extension 0114 2711704
Useful reference

- The Professional’s Guide to Parkinson’s Disease code B 126
  Free from PD UK
  0207963 9332 / Email campaigns@parkinsons.org.uk