How can medicines be managed for Parkinson’s disease patients with swallowing difficulties?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
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Background

Parkinson’s disease (PD) is a progressive neurodegenerative disorder that affects 1 in 500 people in the UK (1). Symptoms include bradykinesia, rigidity, tremor and postural instability (2). PD medications play an important role in the management of symptoms. It is crucial not to stop PD medications for any significant length of time as there is a risk of neuroleptic malignant like syndrome (Parkinsonism hyperpyrexia syndrome) which may be fatal, as well as causing significant exacerbation of symptoms and patient distress (3).

Access to the correct medications at the right time remains a problem for people with PD when they are admitted to hospital. Reasons include drugs not being available and patients being unable to take their medications due to compromised swallow (3). This led Parkinson’s UK to initiate the “Get it on time” campaign (4). Measures that have been suggested to ensure seamless patient care include referral of all PD patients to PD specialists on admission (for planned admission this should be done in advance where possible), appropriate prescribing and ensuring easy access to PD medications (3).

PD patients with compromised swallow are one patient group that are at risk of missed doses as they may be unable to swallow their normal prescribed medications. Measures need to be put in place to ensure that these patients are managed appropriately during admission. This medicines Q&A aims to provide information regarding how to manage PD patients’ medication if they have swallowing difficulties on admission to hospital.

Answer

1. Referral of PD patients to specialists

PD patients suspected to have swallowing difficulties would need their swallow status to be assessed in the first instance and any underlying causes treated (e.g. nausea and vomiting) (4). Alternative routes would need to be considered, as appropriate, in patients who are not able to take their usual PD medicines. It is recommended that advice is sought from a PD specialist on the management of PD patients and local PD guidance consulted if available. Advice can also be sought from pharmacists on the use of alternative formulations of medicines (4).

2. How do you administer PD medication in patients who cannot swallow solid oral dosage forms?

Patients who are unable to take their solid dose medications orally may require alternative formulations or the alteration of medicines for administration through a naso-gastric (NG) tube. Information on the alteration of medicines for administration in patients with swallowing difficulties can be obtained from standard medicines information resources (5,6). The alteration of medicines would result in the medication being unlicensed (5). It is important to note that not all medications can be crushed and dispersed in water. Controlled release preparations, for example, should not be crushed (5,6). Changing to alternative formulations may result in altered bioavailability. Dispersible formulations of levodopa, for example, have a faster onset and shorter duration of action than modified release capsules (5,6). Therefore close monitoring of the patient is essential following any changes to PD medication. Pharmacists are well placed to give advice on the alteration of medications.
3. What non-oral PD medicines are available?

In patients in whom a NG tube is not suitable, insertion delayed or not tolerated, the use of non-oral preparations can provide an alternative as long as there are no specific contraindications.

Rotigotine is a dopamine agonist, available in a transdermal patch formulation that offers an alternative way of administering PD medications in patients who are nil by mouth (3,7).

Other non-oral PD medications include apomorphine subcutaneous injection or infusion and Duodopa intestinal gel. These should be instigated on the guidance of a PD specialist, however, if a patient is established on these preparations then they must be continued (4,7). Duodopa intestinal gel requires the insertion of a percutaneous endoscopic gastrostomy with jejunal tube (PEG-J) and is not suitable in an emergency situation (4).

4. How would you switch from oral PD medicines to rotigotine patch?

There have been some published studies on dose conversions between oral dopamine agonists (8,9,10). However, limited studies have proposed dose equivalence of PD medications to a rotigotine patch (3, 11-15).

The CLEOPATRA-PD double blind, double dummy randomised controlled trial investigated the efficacy of adjunct treatment with rotigotine (up to 16mg/day) compared to pramipexole (up to 4.5mg/day) or placebo in levodopa treated patients with advanced PD. The study showed similar efficacy between rotigotine and pramipexole in primary (≥30% reduction in absolute off time from baseline to end of maintenance) and secondary (which included Unified Parkinson’s Disease Rating Scale (UPDRS) II and Ill scores during on periods) endpoints (11). The responder rates and numerical differences in absolute off time reduction were however in favour of the pramipexole group. The authors therefore suggest that this may indicate a higher dose equivalence for rotigotine versus pramipexole than that reflected by the 4 to 1 ratio reached in the trial (11).

The SURE-PD randomised double blind, double dummy trial investigated the efficacy and safety of rotigotine transdermal patch versus placebo and ropinirole in early stages of PD. Patients were randomised to receive 2mg/24hrs of rotigotine patch with weekly increments of 2mg/24 hrs (maximum dose used 8mg/24hrs), ropinirole 0.25 mg three times a day with weekly increments of 0.25mg three times a day (maximum dose used 24mg/day) or placebo. The study showed the rotigotine group to be less effective than (but not inferior to) ropinirole in the mean UPDRS II and III scores during on periods (12). The rotigotine dose used in the study was 8mg/24 hours which is probably not therapeutically equivalent to high ropinirole doses of up to 24mg/24 hours (12). A post hoc analysis comparing outcomes between rotigotine doses up to 8mg/24hours with ropinirole doses up to 12mg/24 hours showed non-inferiority (i.e. equivalent outcomes) between rotigotine and ropinirole (12).

An open label multicentre study assessed the overnight switch from oral dopamine agonists to transdermal rotigotine in subjects not adequately controlled with ropinirole (up to 9mg/day), pramipexole (up to 2mg/day) or cabergoline (up to 3mg/day) (14). The approximated dose equivalence used were 1:1 ropinirole to rotigotine, 1:4 pramipexole to rotigotine, 1:2.5 cabergoline to rotigotine. The switch to rotigotine patch showed improved antiparkinsonian control as shown by reductions from baseline values in UPDRS II and III scores. The authors suggest that interpretation of the data, however, is limited by a number of factors including insufficient power of the study group and that doses of oral dopamine agonists used before the rotigotine switch was lower than that commonly used to achieve optimal antiparkinsonian benefit. Therefore, exact dose equivalence using the approximated dose equivalence ratio used in the study cannot be assumed with the doses tested in the study (14).

Available studies propose dose equivalences for individual dopaminergic therapy, however PD patients can be on various classes and doses of PD medications (16). To facilitate comparison a number of authors suggest that a levodopa equivalent daily dose (LEDD) can be calculated for various PD medications (3,13,16,17). There have been various formula used for calculating LEDDs based on clinical trials, summary of product characteristics and clinical experience (3,13,16,17). Brennan and Genever published an article on the management of PD patients, who are unable to take their normal PD medications, during surgery (3). Using data from published articles, they propose an estimated
dose equivalent table for all currently available PD medications and suggest a conversion of oral PD medications to a rotigotine patch or apomorphine depending on their adjusted LEDD (3). Practical advice is provided in an article by J Alty et al which discusses the management of PD patients who are unable to take their usual oral medications. It includes advice on a range of issues including the administration of PD medications down enteral tubes, the conversion of different drug class doses into an equivalent daily rotigotine patch, and suggests equivalent doses for individual dopamine agonists to a rotigotine patch (18).

Rotigotine patch is associated with a range of side-effects including orthostatic hypotension, impulse control disorders and other dopaminergic adverse reactions such as hallucinations, dyskinesia and peripheral oedema. It is therefore crucial that the patient goes back to their usual oral medications once their swallowing status is returned to normal (19).

5. Local guidelines

Due to the limited published evidence and variable opinion on the dose conversions reported and the different effects that PD medications can have on individual patients, there remains a lack of consensus and guidance on the dose conversions for the different PD medications used. The specialist PD team are therefore best placed to assess patient history and clinical status to decide if rotigotine patch is appropriate and give specific advice on appropriate initial doses for individual patients.

It is recognised that the PD team are not always available and therefore local guidance based on expert opinion is helpful. Such a guideline has been developed within NHS Greater Glasgow and Clyde (available on request). This provides recommendations on the use of alternative formulations in patients with swallowing difficulties or who require administration of medications via a NG tube. It includes initial dosing advice for the conversion of oral PD medications to a rotigotine patch.

Parkinson’s UK has developed a guideline and calculator to help non-specialist clinicians to control PD patient symptoms in patients who cannot take their oral medications until specialists are available. This can be accessed via www.parkinsonscalculator.com. The guideline has been endorsed by the British Geriatric Society Movement Disorder Section (20).

6. Other considerations

It is important to assess PD patients on an individual basis when changes are made to their normal PD medications (3). Patients should be monitored for response and doses should be adjusted accordingly (3). The patient’s current clinical status and past medical history should also be considered.

Summary

It is crucial that PD patients receive their medications on time as PD drugs stopped for any significant length of time may lead to neuroleptic malignant like syndrome (Parkinsonism hyperpyrexia syndrome) which may be fatal, as well as causing significant exacerbation of symptoms and patient distress (3). PD patients should be referred to PD specialists on admission to hospital as they are best placed to assess the patient and make recommendations on therapy. Alternative formulations or routes of therapy need to be considered in patients with swallowing difficulties or who are nil by mouth. Advice on this should be sought from a PD specialist or local guidance if available. Pharmacists can provide advice on the use of alternative formulations of medicines. In all cases, early referral is recommended to enable medicine administration problems to be prevented before missed doses occur.

Limitations

This Q&A provides general information to be considered in the management of patients with swallowing difficulties. The specific management of PD patients should be agreed with local PD specialists. The patient’s current clinical status and past medical history should be considered as well as contraindications, cautions and side-effects of treatments.
References


Quality Assurance

Prepared by
Yasmin Al-Din
Medicines Information
NHS Greater Glasgow and Clyde
E-mail: MedInfo@ggc.scot.nhs.uk

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Checked by
Yvonne Semple
Medicines Information
NHS Greater Glasgow and Clyde

Date of check
