Management of medication in patients with Parkinson's disease who are nil-by-mouth

Introduction

Parkinson's disease affects approximately 200 in every 100 000 patients in London (Schrag et al, 2000). These individuals experience increased rates of emergency admissions to hospital secondary to falls, fractures, impaired mobility, infections, psychiatric disturbances and cardiovascular disease. The duration of their hospital stay is frequently prolonged compared to patients who do not have Parkinson's disease (Woodford and Walker, 2005). In addition, significant numbers of patients with Parkinson's disease are admitted for elective surgery.

Abrupt cessation of Parkinson's disease medication leads to clinical complications. A case series revealed that 74% had their medication stopped, omitted or inappropriately prescribed during admission (Magadalinou et al, 2007). Of these, 61% consequently suffered adverse clinical sequelae, including eight serious clinical incidents and one transfer to intensive care. Concerns were raised regarding the ability of medical and nursing staff to recognize and manage complications effectively. This review highlights the potential adverse effects of stopping medications in patients with Parkinson's disease who are placed nil-by-mouth on admission to hospital, and how to prevent these from occurring.

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Clinical implications of altered dosing regimens in patients with Parkinson's disease

Unfamiliarity in managing patients with Parkinson's disease among medical and nursing staff results in missed doses, especially in the nil-by-mouth scenario. A qualitative study examining patient and carer perceptions of the management of Parkinson's disease postoperatively noted that problems exist not only in the context of nil-by-mouth patients, but with parkinsonian patients as a whole (Barber et al, 2001). Patients and relatives commented that staff required regular reminders to provide anti-parkinsonian medication. The timing of medication was often incorrect in hospital, culminating in symptom deterioration.

A further study of surgical inpatients confirmed an increase in complications when Parkinson's disease medications were omitted (Derry et al, 2010). The most common were neuropsychiatric (confusion, hallucination and agitation), motor deterioration, falls and renal impairment. (Renal impairment is usually the result of reduced fluid intake secondary to poor swallow as a consequence of reduced Parkinson's disease medications.) These issues have been highlighted as essential aspects of Parkinson's disease management by the National Institute for Clinical Excellence and the Parkinson's Disease UK 'Get it On Time' campaign, which promotes the delivery of medication 'on time, every time' (National Patient Safety Agency, 2010).

Missed doses can also precipitate the 'parkinsonism-hyperpyrexia' syndrome (Jones and Hindle, 2011). This is an uncommon but potentially fatal presentation consisting of rigidity, hyperpyrexia and stupor, which may be difficult to distinguish from neuroleptic malignant syndrome. It can result from missed doses, but also can be caused by infection or anaemia. Sustained unresponsiveness to dopamine or dopaminergic agonists is typical, and the pitfall is in interpreting this as treatment failure. Management of this should be considered in supportive measures including rehydration with intravenous fluids, dopaminergic drug replacement and prompt recognition and management of any further complications.

Surgical admissions

Patients being admitted for elective surgery should be encouraged to consult their movement disorder team before admission. A multidisciplinary approach involving GPs, consultants, pharmacists and specialist nurses is essential to plan for the nil-by-mouth period. The pre-admission clinic can be useful in addressing these issues. This will ensure that specific medications which are not routinely held by pharmacy are acquired ahead of time to prevent delays. Patients kept nil-by-mouth should remain so for the minimum amount of time possible and alternative methods of delivering medication considered. This involves planning ahead for the pre-, peri- and postoperative periods.

If surgery is unplanned, suggestions from the appropriate teams should be sought or, preferably, a hospital protocol followed. Medication should be continued until the time of anaesthetic induction, with careful consideration given to placing patients with Parkinson's disease as high priority on operating lists because of the risks associated with a prolonged period nil-by-mouth. Use of loco-regional techniques may be preferable to general anaesthesia, but even for patients in the latter group it may be appropriate to allow oral anti-Parkinson's disease medications pre-operatively with small sips of water. In exceptional circumstances, enteral medication can be administered intraoperatively, even in patients under general anaesthesia. Postoperatively, early assessment of the patient by the team in charge should be undertaken, with particular emphasis on the patient's ability to absorb enteral medications to expedite restarting regular medications at the earliest opportunity.

Careful consideration should be given to the choice of anaesthetic and induction agents. Propofol can temporarily suppress tremor but exacerbate dyskinesia. In dysphagic patients, anticholinergic agents increase saliva viscosity, impairing swallowing further. In all admissions for patients with Parkinson's disease, extreme caution should be exercised with regards to antiemetics. Centrally-acting dopamine antagonists (namely prochlorperazine and metoclopromide) exacerbate parkinsonism; for this reason, domperidone (in suppository form when nil-by-mouth), cyclizine or ondansetron are favourable alternatives (Brennan and Genever, 2010). Importantly, similar considerations apply to anti-dopaminergic antipsychotic medications, such as haloperidol.

Alternative routes of administration of anti-Parkinsonian medication

Enteral

The maintenance of timing and delivery of anti-Parkinson's disease medication is critical to minimizing clinical deterioration. Traditional oral L-dopa formulations such as co-beneldopa (Madopar) and co-careldopa (Sinemet) induce fewer fluctuations in plasma L-dopa concentrations than standard forms of the drugs, and are available in capsule, tablet, controlled release and soluble formulations. It is noteworthy that the aforementioned drugs are brand names and many hospitals will use a generic version of these. It is therefore imperative to include the drug name and not just the brand when prescribing as occasionally doses may be missed when supply problems exist for specific brands.

Novel therapies have also combined L-dopa/carbidopa and entacapone into a single combined tablet (Stalevo), reducing the overall number of tablets that patients with Parkinson's disease need to take (Lyons and Pahwa, 2006). Combined tablets, however, are taken at more frequent intervals (every 3–4 hours to maintain L-dopa steady state), which makes prevention of prolonged periods nil-by-mouth even more critical when managing patients on these agents. The alternative slower release preparations are also generally not crushable, which poses problems and may require short-term conversion to immediate release agents given more frequently during the nil-by-mouth period.

Some preparations are buccally absorbed (Johnston et al, 2005). Orally disintegrating carbidopa tablets (Parcopa) have been developed and are convenient and easy to use (Nausieda et al, 2005). They can be administered without water and may become extremely valuable for patients with advanced dysphagia and risk of aspiration. A transmucosal preparation of selegiline (Zydis) is also available (Poston and Waters, 2007). This freeze-dried tablet dissolves on the tongue and can potentially offer a more convenient and fast-acting route for those unable to take medication. Again, it is important to consider the availability of the above as many hospitals do not stock these routinely and they may need to be ordered in advance for preoperative patients.

Finally, in dysphagic patients kept acutely nil-by-mouth, a nasogastric or nasojejunal tube can provide a temporary route for drug administration. Referral for percutaneous endoscopic gastrostomy or jejunostomy feeding is rare and should only be considered if the oral route will be unsuitable for a prolonged time and no alternative options are available. This route of administration requires crushable or dispersible medication preparations. In specially selected cases, levodopa intestinal gel (Duodopa) via a modified percutanous endoscopic gastrostomy tube is available for end-stage disease but has associated motor complications (MacMahon and MacMahon, 2012), in addition to being very expensive.

Parenteral

Apomorphine has been used extensively in Europe for many years as an anti-parkinsonian agent. In the UK, movement disorders specialist teams will initiate a therapeutic trial, given subcutaneously in a bolus dosing regimen. The dose is then titrated and converted into a subcutaneous infusion depending on patient response and tolerability. Most hospitals have local protocols for its dosing and administration, and hence liaison with pharmacy is essential before prescribing. Apomorphine requires a shared care arrangement with primary care to be continued as an outpatient. It can be highly emetogenic and is therefore not ideal as an out-of-hours solution for the nil-by-mouth patient. Sourcing can also be an issue out-of-hours as it is a highly specialized treatment. If required, advice should always be sought from a Parkinson's disease specialist before initiating therapy.

Transdermal patches

Transdermal patches have been developed to administer Parkinson's disease medication and deliver the drug continuously over 24 hours. Rotigotine is a D2-like receptor selective agonist with only mild side effects reported to date. In trials, it improves parkinsonian symptoms in early disease on a scale comparable to that of dopamine agonists such as ropinirole (Johnston et al, 2005). In late stage disease, it can compensate for decreasing L-dopa dosing.

Protocol for the nil-by-mouth patient with Parkinson's disease

A rough guide adapted from the Parkinson's Disease Nurse Specialist Association website (www.pdnsa.net/) is summarized in *Figures 1* (the nil-by-mouth patient) and *2* (the dysphagic patient). Care should be taken to ensure patients do not aspirate, with sip-swallow tests performed where appropriate. Early involvement of speech and language teams should also be considered. Local guidelines and protocols should be formulated and agreed in trusts to guide general physicians while specialist assistance is pending. Flexibility in delivery of dopamine may be necessary, and direct receptor agonists such as pramipexole are available as first-line or adjuvant therapy, although specialist advice should always be sought when considering drug changes.

Conclusions

Teams responsible for patients with Parkinson's disease who need to be kept nil-by-mouth should be aware of the potential adverse effects of omitting medication. Medications should be given at set times, which are often outside of the 'normal' administration times. Clarification with nursing staff once the drug chart is complete, in order to draw attention to this, is often constructive. Nil-by-mouth periods and omitted medication times should be kept to a minimum.

Where nil-by-mouth will be maintained for prolonged periods, alternative

Figure 1. Algorithm for assessing and managing the patient with Parkinson's disease who is being kept nil-by-mouth. Adapted from Jones and Hindle (2011).

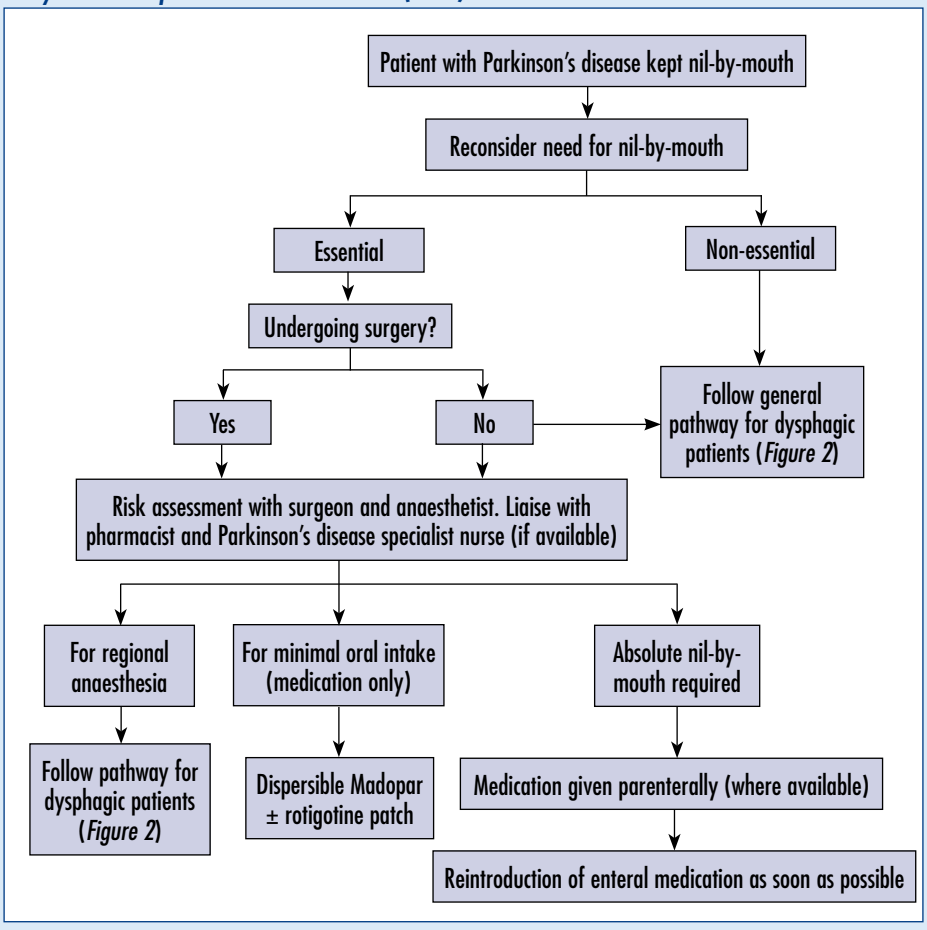
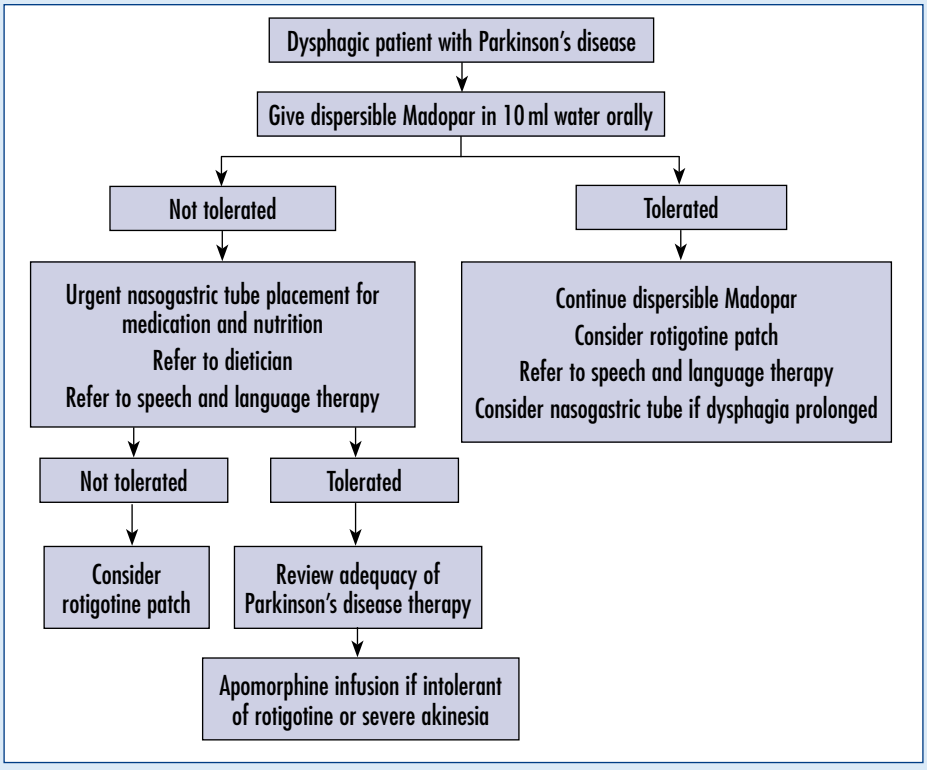


Figure 2. Algorithm for managing Parkinson's disease medication in the dysphagic patient. Adapted from Jones and Hindle (2011).



approaches do exist to administer medication. Medical and nursing staff should be aware of the potential risks and how to recognize signs of deterioration in these patients, and refer for specialist input where available. Finally, it is imperative to listen to patients and their relatives, who will be most aware of the timing of medication and any deterioration in symptoms. BJHM

Conflict of interest: none.

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KEY POINTS

- Patients with Parkinson's disease are at risk of adverse sequelae if medication is omitted, even for short periods.
- Aim to minimize the need and duration for keeping patients with Parkinson's disease nil-by-mouth, and where this is foreseeable develop a medication plan with the multidisciplinary team ahead of time.
- Alternative methods of administering Parkinson's disease medications do exist, and should be explored if necessary.
- Specialist input from a movement disorder multidisciplinary team is strongly advised.
- Hospital trusts should have or should establish a readily accessible guideline to facilitate management of such patients.

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TOP TIPS

- Be vigilant for adverse effects of missed doses of Parkinson's disease medications.
- Where a period of nil-by-mouth is foreseeable, plan ahead and involve the GP, movement disorder team and specialist nurse.
- Consider options that will avoid making the patient with Parkinson's disease nil-by-mouth.
- Alert pharmacy to periods of planned nil-by-mouth to ensure appropriate medication formulations are available for the patient.
- Regularly reassess the requirement for strict nil-by-mouth and reintroduce enteral medications as soon as possible.
- Be guided by patients and their relatives regarding timings of medications and symptomatic deterioration. Ignore them at your peril!