Parkinson's disease on acute admissions - ICU Clinical Guideline

Reference no.: CG-ICU/2020/3540

Aim:

The aim of this guidance is to help healthcare professionals in the care of patients with Parkinson's disease whilst in Intensive care.

Introduction:

Parkinson's disease is one of the most common neurological conditions, estimated to affect around 250 people per 100 000 in the UK.1 PD was first described by James Parkinson, which carries his name in 1817 as a "shaking palsy." People with Parkinson's disease classically present with motor symptoms including bradykinesia, rigidity, rest tremor, and postural instability; however, non-motor symptoms may also be prominent, including depression, cognitive impairment, and autonomic disturbances. Parkinsonism is a broad term for conditions that are phenotypically similar to patients with PD. The 2 major neuropathologic findings in Parkinson disease are loss of pigmented dopaminergic neurons of the substantia nigra pars compacta and the presence of Lewy bodies and Lewy neurites.

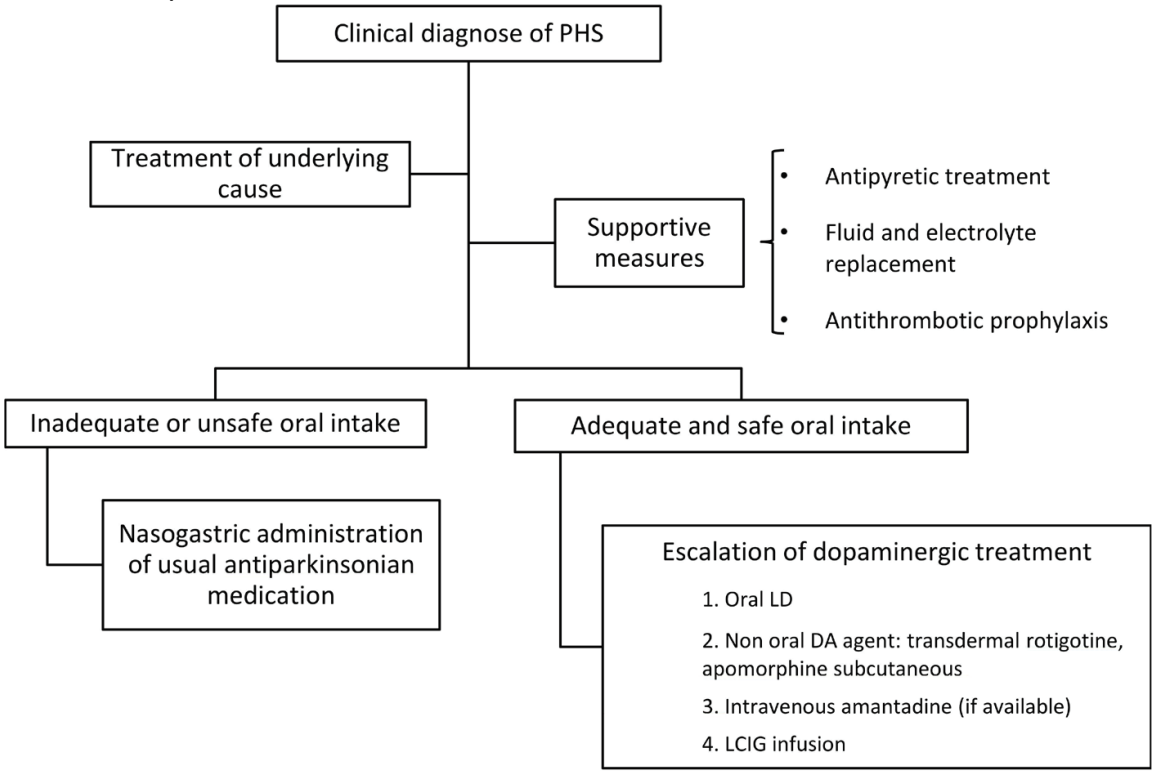
Parkinsonism-hyperpyrexia syndrome

Omissions or delay of regular medication in the perioperative state or ICU can lead to worsened PD symptoms, chest wall rigidity complicating ventilator management, and a severe hyperpyrexia, rigid, encephalopathic state termed parkinsonism-hyperpyrexia syndrome, a severe complication with an incidence of 0.3% and mortality of 4%.
It is important that the administration of a patients Parkinson's medication is not delayed. They may develop hyperthermia and elevated serum muscle enzymes, following muscle damage from marked rigidity. Some patients develop dysautonomic features, such as tachycardia, unstable blood pressure and diaphoresis, resembling the clinical picture of neuroleptic malignant syndrome.[1]
Systemic complications may develop as the akinesia rapidly progresses, including aspiration pneumonia from decreased level of consciousness and rigidity; acute renal failure from rhabdomyolysis and dehydration; and thrombotic events such as deep vein thrombosis, pulmonary thromboembolism or (in severe cases) disseminated intravascular coagulation.
Alongside this it becomes harder for the patient to communicate and voice their needs to staff. When a patient misses their Parkinson's medication it can affect their mobility as it can cause them pain and distress, and this leads to an increase risk of falls and staff pressures.

Table 1. Precipitant factors of severe off and the parkinsonism-hyperpyrexia syndrome.
Adapted from Pract Neurol: first published as 10.1136/practneurol-2018-002075 on 19 August 2019

Dopaminergic treatment related	Non-dopaminergic treatment related
Abrupt withdrawal or medication switch	**Concurrent conditions:**
Decrease of absorption:	Infection
• Enteral and parenteral nutrition with high protein diet	Trauma
• Gastrointestinal problems (severe constipation, paralytic ileus)	Stress
Dosage reduction:	Dehydration
• Loss of compliance	Excessively hot weather
• Psychiatric problems (confusion, hallucinations)	
• Severe dyskinesia	
• Postoperative period	
Addition of dopaminergic blocker	

PD patients are also sensitive to antipsychotic particularly sensitive to antidopaminergic agents such as (e.g., haloperidol) and antiemetics metoclopramide, promethazine and prochlorperazine. Even after small doses of antipsychotics, PD patients can become severely rigid, or akinetic-mute due to severe axial and limb rigidity. and antiemetic medications, which can exacerbate rigidity and aspiration. Elderly patients with PD are more sensitive to sedative medications and more susceptible to develop post-operative or ICU delirium, which has increased morbidity and mortality.



PHS: parkinsonism-hyperpyrexia syndrome, LCIG: levodopa/carbidopa intestinal gel, DA: dopamine agonist, LD: levodopa

Figure 1 Management of parkinsonism-hyperpyrexia syndrome. Adapted from Pract Neurol: first published as 10.1136/practneurol-2018-002075 on 19 August 2019

Dyskinesia-hyperpyrexia syndrome
Levodopa-induced dyskinesias can be severe and occasionally even life-threatening, presenting as a dyskinetic storm (also known as dyskinesia-hyperpyrexia syndrome).[13]

Serotonin syndrome
Serotonin syndrome is a rare but preventable adverse effect of serotonergic agonist treatment; it culminates in a hyperserotonergic status due to overstimulation of postsynaptic serotonin (5-HT or 5- hydroxytryptamine) receptor in the central nervous system. The syndrome can be potentially induced by drugs frequently used in Parkinson's disease treatment, including MAO inhibitors (selegiline, rasagiline and safinamide), selective-serotonin reuptake inhibitors, tricyclic antidepressants and opiates.

Table 2. Parkinsonism-hyperpyrexia and serotonin syndromes. Adapted from Pract Neurol: first published as 10.1136/practneurol-2018-002075 on 19 August 2019

Parkinsonism-hyperpyrexia syndrome	**Serotonin syndrome**
Muscle rigidity, prominent akinesia	Tremor, myoclonus, akathisia hypertonicity
Altered mental status Hyperthermia Rhabdomyolysis	
Trigger factors	
Infection, trauma, medication changes	Drug combinations: MAO inhibitor, SSRI, tricyclic antidepressant, opioids
Treatment	
Escalating dopaminergic treatment	Stopping the causative drug
Supportive intensive care management	

Medicines Management:

It is important to obtain an accurate drug history so the patients Parkinson's medications can be prescribed as soon as possible to avoid missing doses. When prescribing the patients Parkinson's medication ensure that they are prescribed according to the times that they are usually taken and not changed to suit the hospital drug rounds.

Dopamine antagonists should not be prescribed unless the patient has been assessed by the dementia team or neurologist e.g. Metoclopramide, Prochlorperazine and Promethazine. If the patient is showing signs of nausea and vomiting then alternative drugs like Domperidone and Cyclizine can be prescribed.

If a patient is confused or agitated then the drug of choice for acute agitation is

Lorazepam (0.5-1mg prn). In dementia patients with PD a low dose Haloperidol can be prescribed for agitation (please refer to the dementia guidelines). The response should be reviewed regularly to ensure movement/ swallowing is not adversely affected.
When reviewing a patient, it is important to:

- treat infections,
- correct any electrolyte imbalances,
- ascertain whether there have been any recent changes to their medications.
- determine whether the patient has constipation.

This is usually sufficient for a patient to return to their baseline without adjusting their Parkinson's medication.

Swallowing difficulties:

If the patient has swallowing difficulties an urgent assessment by a Speech and Language Therapist (SALT) is required. Depending on the result of the SALT assessment the route or formulation of the medication may need to be changed. An NG tube should be considered as soon as possible to ensure that doses are not missed. Please contact pharmacy for further advice. The table below may be able to guide you with this.

Nil by Mouth (NBM) patients:

If a patient is NBM and an NG tube has been inserted certain medications can be administered through the NG tube. This method is often unlicensed and should only be used if there is no other way for the patient to take their medication. The following tables outlines how to administer Parkinson's medication via a NG tube.

Patients with Parkinson's undergoing surgery

Many Parkinson's patient undergo surgery for conditions that are not related to their Parkinson's. It is important to know how long the postoperative period will last without being able to take oral medication. In case of a major intervention, especially abdominal surgery with inherent difficulties of gastrointestinal absorption it is crucial to consider alternative administration routes of dopaminergic medication, such as dispersible preparations, nasogastric administration, transdermal dopamine agonist and apomorphine. When prompt dopamine replacement is required, higher dose of rotigotine (more than 16 mg/24 hours) and immediate release of pramipexole through nasogastric tube should be considered or at least discussed with the specialist pharmacist and Stroke consultant.

Table 3. Motor and non-motor symptoms of Parkinson's disease and their anaesthetic implications. Adapted from https://associationofanaesthetists-publications.onlinelibrary.wiley.com.

Symptoms	Anaesthetic implications
Motor	
Tremor	Motion artefacts on monitoring (e.g. pulse oximetry, electrocardiography)
	Difficult intravenous access in ipsilateral limb
	Interference with patient-controlled analgesia
Rigidity	Difficulty in positioning for surgery and regional anaesthesia
	Potential difficult airway; difficult awake fibreoptic intubation
	Restrictive lung disease if chest rigidity
Bradykinesia	Slower postoperative functional recovery
Postural instability, falls	Associated injury and fractures from falls; need for fall prevention
	Slower postoperative functional recovery
Bulbar dysfunction	Pulmonary aspiration, dysphagia
	Retained secretions
	Laryngospasm
Motor fluctuations, dyskinesia	
	Require optimal timing of medication during peri-operative period
	Interfere with procedures that require immobility
Non-motor	
Autonomic dysfunction	Labile blood pressure and orthostatic hypotension
	May be worsened with other anaesthetic drugs and fluid status
	Delayed gastric emptying, ileus; worsened with surgery, bed rest, opioids and poor enteral intake
	Urinary dysfunction
	Altered temperature regulation
Cognitive impairment	Postoperative neurocognitive disorders
	Delayed emergence
Psychiatric disorders	Drug interactions between antidepressants, anxiolytics and antipsychotics with anaesthetic and analgesic medications.
	Postoperative delirium, acute psychosis, depression and anxiety
Pain	Drug interactions between analgesics and Parkinson's disease medication
	Co-existing chronic pain-related Parkinson's disease
Sleep disturbances	Worsened with hospital environment, sedative medication
Other	Fatigue, hyposmia, visual dysfunction and personality changes

Table 4: How to administer medication to Nil by mouth Patient

Medication	Formulation's available	Method of administration/ alternative
Madopar (co-beneldopa)	Dispersible tablets, capsules, modified release capsules	Convert capsules to the equivalent dispersible tablet dose. Dispersible tablets can be given through the NG tube.
Sinemet(co-careldopa)	Tablets, modified release tablets	The normal tablets can be dispersed in water and given in the enteral tube. Alternatively convert to the equivalent dispersible co-beneldopa dose, contact pharmacy for help with this.
Entacapone (Comtess)	Tablets	Can be dispersed in water and given through the enteral tube.*
Stalevo (combination of co-beneldopa/ entacapone)	Tablets	Tablet can be crushed and mixed with water
Cabergoline	Tablet	Crush and mix with water
Selegiline	Tablet, , liquid	Use liquid as first choice through an NG tube. Alternatively tablets can be dispersed in water.
Amantadine	Capsule, liquid	First choice is use the liquid. Second choice is to open the capsules and mix the content with water to administer through the enteral tube.
Ropinirole	Tablet, modified release tablet	Normal ropinirole tablets can be crushed and mixed with water to administer through an enteral tube. Convert the dose given in 24 hours of modified release tablets to normal release tablets that are given three times a day.
Pramipexole	Tablet, modified release tablet	Convert the dose given in 24 hours of modified release tablets to normal release tablets that are given three times a day. Normal tablets can be crushed and mixed with water for administration.

*Entacapone does not completely disperse in water, therefore when administering it though the enteral tube it is important to flush the tube thoroughly. It may also stain the tube orange (5).

Converting to the Rotigotine patch

If the NG route is not available and the patient is having swallowing difficulties then the Parkinson's medication can be converted to the Rotigotine patch. The Rotigotine patch is available in 2mg, 4mg, 6mg and 8mg strengths. It is important to remember that the patches cannot be cut, therefore the maximum available dose of Rotigotine patch available is 16mg/24hr. Higher doses of Rotigotine should only be initiated at the advice of Dr P Das (Stroke consultant)(6-7).

The patch must be applied to dry non-irritated skin and the area where it is applied must be rotated. The same area should not be used for at least 14 days. Each patient should be assessed individually and dose adjustments made accordingly. If a patient is showing signs of increased stiffness and moving more slowly, the dose of the patch should be increased and the patient should be reviewed daily. Alternatively, if the patient is confused and appears to be hallucinating then the dose of Rotigotine should be decreased following by daily reviews (6-7).

The adverse reactions associated with using the Rotigotine patch are an increased risk of impulse control disorders. This includes pathological gambling, binge eating and hypersexuality. It is also important to monitor the patient for any signs of nausea, dizziness, hallucinations, aggression and abnormal behaviour. If the patient shows signs of any adverse reactions the dose of the Rotigotine patch should be decreased until the symptoms have settled (6-7).

It is important to remember that when the patient's condition has improved and their usual regime of Parkinson's medications has been restarted the Rotigotine patch should be discontinued. This is because there is a risk of tardive dyskinesia (increased movement). Both Rotigotine and levodopa can be used together in Parkinson's disease but this treatment should only be commenced after a discussion with Dr P Das (stroke consultant).

The conversion to Rotigotine patch is dependent on the total daily levodopa that the patient is taking. For example if a patient is on Madopar 62.5mg BD the total daily levodopa would be 100mg. The total daily dopa-decarboxylase inhibitor would be 25mg. However the amount of dopa-decarboxylase inhibitor taken is irrelevant to the conversion. In this case the equivalent Rotigotine patch is 2mg/24 hours.

Table 5: Converting levodopa to Rotigotine (when taking only levodopa)

Total Daily Levodopa	**Rotigotine patch equivalent**	**Starting Rotigotine patch**
100mg	2mg/24 hours	2mg/24 hours
150mg	4mg /24 hours	4mg/24 hours
200mg	6mg /24hours	4mg/24 hours
300mg	8mg /24 hours	4mg/24 hours
400mg	10mg /24hours	6mg/24 hours
450mg	12mg /24 hours	6mg/24 hours
600mg	16mg /24 hours	8mg/24 hours *
600mg	16mg /24 hours	8mg/24 hours *
800mg	16mg /24 hours	8mg/24 hours *

*Please note that higher doses of the Rotigotine patch should only be started with the advice of Dr Das.

Table 6: Converting Stalveo to Rotigotine

Current Stalveo regime	Rotigotine patch equivalent	Staring Rotigotine patch
Stalveo 50/12.5/200 TDS	6mg/24 hrs	4mg/24 hours
Stalveo 100/25/200 TDS	10mg/24 hrs	4mg/ 24 hours
Stalveo 100/25/200 QDS	14mg/24 hrs	6mg/24 hours
Stalveo 150/37.5/200 TDS	16mg/24 hrs	8mg/24 hours*

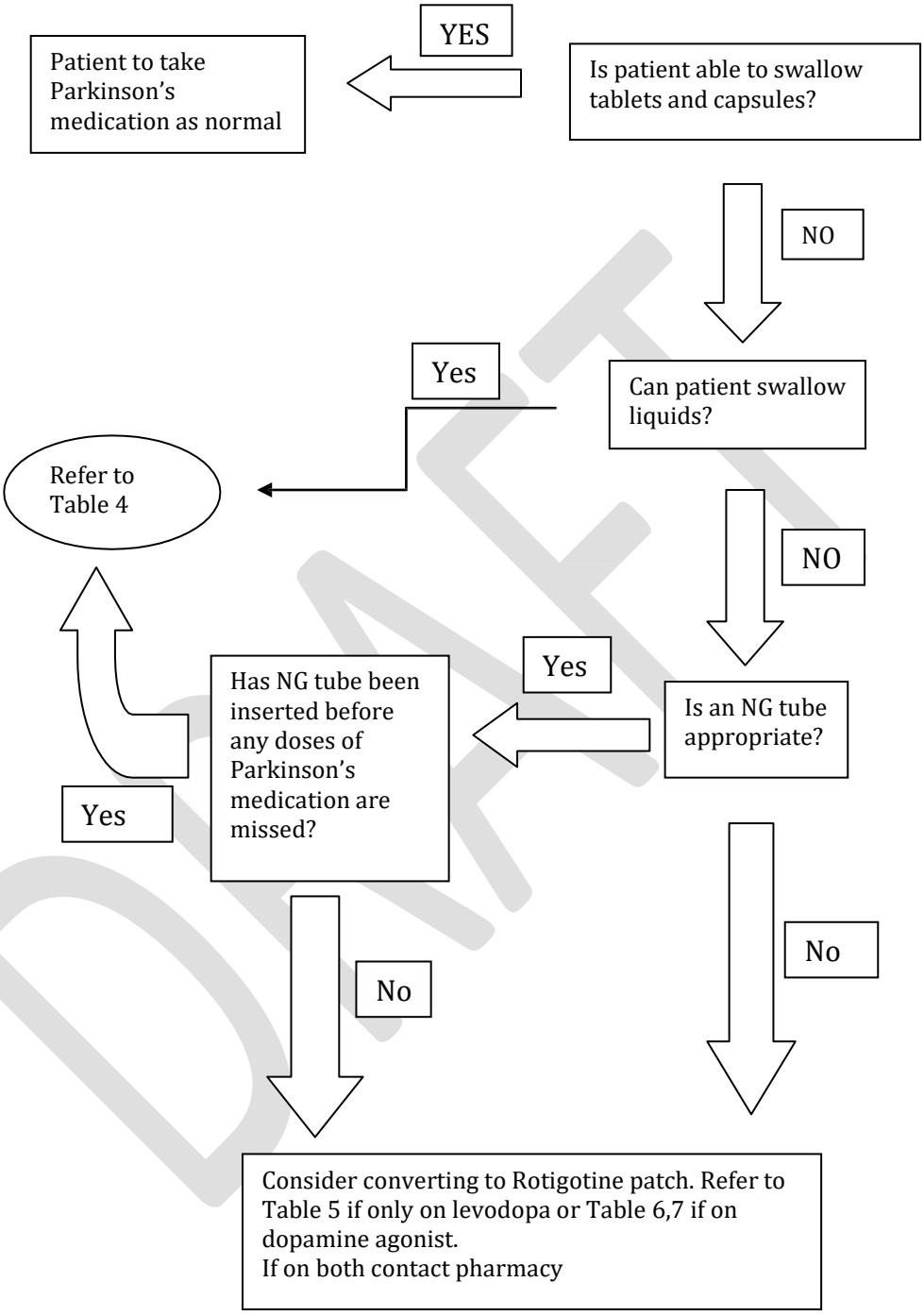
* Please note that higher doses of the Rotigotine patch should only be started with the advice of Dr Das.

Table 7: Switching oral dopamine agonist to Rotigotine patch

Pramipexole (salt content)	Ropinirole Standard release (Requip)	Ropinirole Modified release (Requip XL)	Rotigotine transdermal patch	Starting Rotigotine patch
0.125mg TDS	Starter pack	NA	2mg/24 hours	2mg/24 hours
0.25mg TDS	1mg TDS	4mg/day	4mg/24 hours	4 mg/24 hours
0.5mg TDS	2mg TDS	6mg/day	6mg/24 hours	4mg/24 hours
0.75mg TDS	3mg TDS	8mg/day	8mg/24 hours	4mg/24 hours
1mg TDS	4mg TDS	12mg/day	10-12mg/24 hours	6mg/24 hours
1.25mg TDS	6mg TDS	16mg/day	14mg/24hours	6mg/24 hours
1.5mg TDS	8mg TDS	24mg/day	16mg/24 hours	8mg/24 hours*

* Please note that higher doses of the Rotigotine patch should only be started with the advice of Dr Das

Figure 2: Outlining Clinical Management of Parkinson's Disease



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