



## CONSENSUS STATEMENT

### Perioperative management of Parkinson's disease<sup>☆,☆☆</sup>

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**Abstract** One of the particular characteristics of Parkinson's disease (PD) is the wide clinical variation as regards the treatment that can be found in the same patient. This occurs with specific treatment for PD, as well as with other drug groups that can make motor function worse. For this reason, the perioperative management of PD requires experience and above all appropriate planning. In this article, the peculiarities of PD and its treatment are reviewed, and a strategy is set out for the perioperative management of these patients.

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#### Manejo perioperatorio de la enfermedad de Parkinson

**Resumen** Una de las características singulares de la enfermedad de Parkinson (EP) es la gran variabilidad clínica en relación con el tratamiento que puede acontecer en un mismo paciente. Esto sucede tanto con el tratamiento específico para la EP como con otra serie de fármacos que pueden empeorar la función motora. Por esta razón, el manejo perioperatorio de la EP requiere experiencia y sobre todo una planificación adecuada. En este artículo se revisan las peculiaridades de la EP y su tratamiento, y se plantea una estrategia para el perioperatorio de estos pacientes.

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Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease. It affects an estimated 300 people per 100,000 inhabitants, about 120,000 people in Spain. It can occur at any age, is more infrequent in people under 40 years and its incidence increases with age. It is characterised by slowness of movement, muscle rigidity and a peculiar tremor that occurs when the patient is at rest. In recent years, there has been an increase in the number of PD patients who undergo surgery. There are no doubts about the complexity of drug therapy for PD, so special care should be paid to adverse effects and drug interactions in the perioperative period.<sup>1-6</sup> Advances in surgical and anaesthetic procedures on the one hand, and the management of PD on the other, have allowed for a safer approach. The types of surgery most often employed in these patients are urological, ophthalmological and orthopaedic surgery.<sup>2-5</sup> The present work, a consensus document among professionals in anaesthesia, general surgery and neurology with extensive experience in PD, aims to provide a strategy for the perioperative management of patients with this disease. The management of deep brain stimulation surgery has been not addressed, due to its specific characteristics.

The perioperative management of PD should include at least 2 considerations: 1 related to the disease itself and another related to the drugs used for its treatment.<sup>2,7</sup>

#### 1. The problems associated with the disease are of 2 types.

##### – Motor problems:

1. Due to lack of movement, secondary to the bradykinesia and rigidity that are characteristics of the disease and that, in times of stress such as the perioperative period, may result in complete immobility. Akinesia can lead to various types of problems: respiratory, bronchoaspirative, thrombosis such as deep phlebitis and pulmonary embolism, infection and pressure ulcers. This immobility can also lead to neuropsychiatric problems ranging from anxiety to panic attacks. This is probably the main complaint of PD patients.
2. Due to excessive movement, as may occur from shaking or dyskinesia induced by the treatment. Excessive movement can be a problem for surgeries performed with local or regional anaesthesia. Control of dyskinesia is not usually troublesome except in highly fluctuating patients. Severe tremor can be problematic when the surgical procedure requires immobility. General anaesthesia is preferred in these circumstances.
3. Respiratory disorders. Up to one-third of patients present an obstructive respiratory disorder.<sup>5</sup> To this we must add a restrictive pattern due to chest wall rigidity. Consequently, such patients may have ventilation problems.<sup>8</sup> The intrinsic laryngeal musculature and other muscles around the airway may be involved and constitute an important factor, leading to retention of secretions, atelectasis, aspiration and respiratory infections. Another possible source of complications to be addressed

is postoperative laryngospasm. Moreover, sialorrhoea, dysphagia and oesophageal dysmotility contribute to increase the risk of aspiration pneumonia. On the other hand, decrease of functional residual capacity is frequently associated and may be the cause of atelectasis and pneumonia. Lastly, it is important to remember that these patients sometimes present a sensation of dyspnoea in relation to their 'off' periods.

##### – Non-motor problems:

1. Dysautonomic manifestations. Patients may present dysautonomic disorders due to Parkinson's disease and its concomitant treatment, as well as derived from advanced age. The most common manifestations are excessive salivation, gastrointestinal disorders, seborrhoea, impaired temperature regulation, urological problems and cardiovascular disorders.

– Cardiovascular system. The most common symptom is orthostatic hypotension. Several drugs can cause an exacerbation of hypotension, including levodopa and dopaminergic agonists. Concomitant medication, particularly hypotensive drugs, should be monitored and can often be reduced or suspended in PD patients.

– Gastrointestinal function. The most common problems are sialorrhoea, dysphagia and oesophageal transit abnormalities. Intervened patients may experience a worsening of gastrointestinal complications, already common in surgery—especially abdominal surgery—suffering constipation, delayed gastric emptying and paralytic ileus.

– The urinary system is also subsidiary of complications, most notably what is known as cystocerebral syndrome, defined as the confusional syndrome which occurs as a result of acute urinary retention and bladder distension.

2. Neuropsychological manifestations. Anxiety, depression and cognitive impairment are not uncommon in PD and should be taken into account. We reiterate that anxiety associated with immobility as a result of poor management is the main complaint of PD patients undergoing surgery.

All these complications represent a greater difficulty in nursing care in the postoperative period, as well as a delay in recovery after surgery.<sup>1-6</sup>

2. Problems related to medication or its suppression. The interruption of anti-parkinsonian medication for a period longer than 6–12 h may significantly worsen PD symptoms.<sup>2,3</sup> The half-life of levodopa is short (about 90 min), while that of agonists is variable. Abrupt withdrawal of medication can cause a hyperpyrexia-parkinsonism syndrome indistinguishable from malignant neuroleptic syndrome because it is associated with rigidity, hyperpyrexia, dysautonomia and an increase in creatinase.<sup>9-11</sup> While it is a rare phenomenon, there have been documented cases that occurred several days after the suspension of dopa treatment. Another

complication that may be caused by an abrupt discontinuation of medication is the onset of akinetic crises, which in turn could lead to respiratory problems, in addition to greater anxiety in patients. On the other hand, the use of high doses of medication may trigger the onset of severe dyskinesia, which in some cases may even threaten the lives of patients.<sup>8</sup> Therefore, the management of drugs should be carried out with caution and considering that there are 2 perioperative scenarios:

– Preoperative drug management:

1. Oral levodopa. Treatment should continue until the morning of surgery. One dose with a minimal amount of water may be administered on the same morning. Although the half-life of levodopa is 90 min, its effects can last for several hours, thus facilitating perioperative mobility. After surgery, patients should resume treatment as soon as possible.
2. Dopaminergic agonists (pramipexole, ropinirole, rotigotine). Treatment may be continued until surgery. Rotigotine, being administered in the form of patches, can be continued throughout the perioperative period.
3. Selegiline and rasagiline. These are MAO-B inhibitors. They should be discontinued 3 weeks before surgery if the condition of the patient permits it. Their association with other serotonergic-acting drugs (meperidine) could trigger serotonin syndrome.
4. Amantadine. This may be continued until surgery.
5. Entacapone, tolcapone (COMT inhibitors). They may be continued until surgery.
6. Anticholinergics. These are increasingly obsolete due to their limited efficacy and multiple side effects. They should be discontinued before surgery. They may trigger confusional syndrome and interfere with various other drugs.

– Postoperative drug management:

1. Levodopa. The use of levodopa through a nasogastric tube is limited by the indication of absolute diet, common in the immediate postoperative period.<sup>12,13</sup> However, it could be used within a few hours after surgery administered through a nasogastric tube with a minimal amount of water, except in the case of abdominal surgery. In cases of dysphagia, a solution of 1–1.5 g of levodopa in 1 l of water with 1 g of vitamin C can be made and then 100 ml of this solution can be administered through a nasogastric tube every 2 h as long as the patient tolerates it.
2. Rotigotine. This is a dopaminergic agonist of receptors D1/D2/D3. It is used as a 2–4–6–8 mg transdermal patch. The usual doses are between 6 and 16 mg/day, which can be increased up to 24 mg. Various studies and cases have proven its effectiveness and feasibility in perioperative management, with no safety problems being encountered. It is an ideal drug in cases of dysphagia. Therefore, rotigotine patches are an ideal choice in the perioperative management of PD.

3. Apomorphine. This is a selective D1/D2 dopaminergic agonist, of equivalent power to that of levodopa. It is administered subcutaneously and has a peak at 3 min, with onset of effect at 6 min and the maximum at 30 min. Its half-life is similar to that of levodopa. Its side effects may include nausea, vomiting and orthostatic hypotension, which should be prevented with domperidone (20 mg/8 h, orally) or ondansetron (4–8 mg/12 h, intravenously). The dose should be individualised and can be calculated by an apomorphine test, which should be performed before the scheduled surgery.

4. Intravenous amantadine. We are awaiting the results of the study “Perioperative treatment of Parkinson patients with parenteral amantadine”, carried out between January 2008 and January 2010.

– Anaesthetics and other perioperative drugs<sup>4,8,14</sup>:

1. The anaesthetic of choice is propofol.
2. Thiopental reduces the release of dopamine at a striatal level and, although the consequences of this are unclear, it may worsen the parkinsonian condition. Ketamine would be contraindicated as it may cause an exaggerated sympathetic response.
3. Inhalation anaesthetics have complex effects on brain dopamine. Given that most patients are treated with levodopa, anaesthetics such as halothane, which sensitises the catecholaminergic action of the heart, should be avoided. Others (such as isoflurane or sevoflurane), although they are less arrhythmogenic, can induce hypotension, which may be severe in patients with dysautonomia as is the case of parkinsonian patients.
4. Non-depolarising muscle relaxants are safe; rocuronium would be the main choice in PD. Succinylcholine may be safe, although there have been reports of hyperkalemia being induced in PD patients.<sup>15</sup>
5. Phenothiazines, butyrophenones (including droperidol) and metoclopramide may worsen PD and, therefore, would be contraindicated in the perioperative management of this disease.
6. It is important not to combine drugs with serotonergic effects. It has been observed that meperidine combined with selegiline can cause serotonergic syndrome with hyperpyrexia, tremor, tachycardia and rigidity. MAOIs should be discontinued 3 weeks before surgery.
7. We must differentiate the pain associated with the surgical procedure from the pain induced by the PD itself, especially due to rigidity. The best treatment for genuinely parkinsonian pain is the dopaminergic treatment itself, with anti-parkinsonian drugs.
8. Opioids may induce rigidity and should be employed with caution.<sup>16</sup> Fentanyl can cause stiffness, while morphine at low doses can reduce dyskinesia. At high doses, it can worsen akinesia.<sup>17</sup>

## Practical approach to perioperative patients with Parkinson's disease

### General considerations

1. The same treatment that the patient was following should be maintained. It should be suspended only for the duration of absolute diet prior to surgery.
2. In premedication, 1 tablet of Sinemet or Madopar with 1 spoonful of water may be given 1 h before surgery.
3. Treatment should be restarted as soon as oral tolerance tests allow, with the same pattern being followed by the patient. In non-abdominal surgeries, treatment could start after about 2–3 h.

### Surgery requiring subsequent strict absolute diet: abdominal surgery

Rotigotine patches can be used during the time when the patient is following absolute diet. Doses should be individualised because they are not equivalent in the different stages of the disease: mild, moderate or advanced. No changes in medication are required in relation to surgery except in the cases of MAOIs, which should be discontinued 3 weeks before or when a long postoperative period is expected. In this case it is advisable to carry out an apomorphine test to determine the appropriate dosage of this drug.

There is no universally accepted conversion, but 8 mg of rotigotine would be approximately equivalent to 8 mg of ropinirole or 1.05 mg of pramipexole.

1. The conversion of levodopa cannot be more than approximate. For the purpose of perioperative management, 300 mg of levodopa could be equivalent to 8 mg of rotigotine.
2. If the patient was already receiving rotigotine, then the same dose could be maintained or even increased to 24 mg/day, according to the clinical situation.
3. Subcutaneous apomorphine can be used every 3–4 h as needed. As has been mentioned before, the apomorphine dose should be established before surgery. Apomorphine should be prescribed along with an intravenous antiemetic, such as ondansetron 4–8 mg/12 h.
4. The management is similar when emergency or unscheduled surgery is required. Serotonergic interactions should be verified if patients were being treated with MAOIs. In case of apomorphine being needed, it should be started at an approximate dose of 3 mg. General considerations should be maintained.

### Surgery requiring absolute diet for a few hours: non-abdominal surgery

The medication may be administered through a nasogastric tube with a minimum amount of water, 2 h after surgery.

### Surgery requiring subsequent admission at an intensive care unit

No additional medication is required in cases where patients are intubated and, therefore, sedated. Once they begin to wake up, the procedure should be similar to that referred for absolute diet.

### Surgery that can be performed with local or regional anaesthesia and requiring immobility of the patient for proper implementation

The typical example is ophthalmological surgery. Problems could arise from tremor or dyskinesia induced by treatment.

1. Dyskinesia can be controlled with proper programming, depending on its specific type. As these surgeries are often short, it would be possible to adjust the surgery time to the period of response to treatment. If surgery were prolonged, it would be best to plan general anaesthesia with propofol.
2. The same would hold true for patients with severe tremor, which could interfere with the execution of the surgery; general anaesthesia is preferable because the treatment of tremor is often suboptimal.
3. General anaesthesia should be of choice in most of these patients.

### Conflict of interests

The authors have no conflict of interests to declare.

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