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Perioperative Management of Parkinson's Disease^{☆,☆☆}

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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

R E S U M E N

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 about 300 individuals per 100 000 inhabitants, around 120 000 people in Spain. It may appear at any age but is less common in those under 40 years of age and its incidence increases with age. PD is characterised by slow movements, muscle stiffness and a peculiar tremor that occurs when patients are at rest. In recent years, there has been an increase in the number of patients with PD who undergo surgery. Drug treatment for PD is undoubtedly complex and therefore special care must be taken with side effects and drug interactions in the perioperative period.¹⁻⁶ Advances in surgical and anaesthetic procedures and management of PD provide a safer approach. The types of surgery most frequently performed in these patients are urological, ophthalmological and orthopaedic.²⁻⁵ This report is a consensus document between anaesthesia, general surgery and neurology practitioners with extensive experience in PD, which aims to provide a perioperative strategy for patients with this disease. The management of deep brain stimulation surgery has not been addressed due to its special characteristics.

There are at least two considerations for perioperative management of PD: one is related with the actual disease and the other with the drugs used for treatment.^{2,7}

1. There are two types of problems related to the disease

– Motor:

1. Default movement secondary to bradykinesia and stiffness characteristic of the disease, which under stressful situations such as the perioperative period, may cause complete immobility. Akinesia may lead to respiratory (bronchoaspiration) and thrombotic problems such as deep phlebitis and pulmonary embolism, infections and pressure ulcers. Moreover, this immobility may lead to neuropsychiatric problems from anxiety to panic attacks. This is probably the main complaint of patients.
2. Excess movement, which may occur due to tremors or treatment-induced dyskinesias. Excess movement may be a problem for surgery performed under local or regional anaesthesia. The control of dyskinesias is usually not problematic except in highly fluctuating patients. Severe tremors can be a serious problem when immobility is required during a surgical procedure. General anaesthesia is preferred in these circumstances.
3. Respiratory disorders. Up to one third of patients present with an obstructive respiratory disorder,⁵ in addition to a restrictive pattern due to chest wall stiffness. Consequently, these patients may have problems when to breathe.⁸ The intrinsic laryngeal muscles and other muscles surrounding the airways may be compromised and are a significant contributor to retention of secretions, atelectasis, aspiration and respiratory infections. Another possible source of complications that must be considered is postoperative laryngospasm. Moreover, sialorrhoea, dysphagia and oesophageal dysmotility contribute to increased risk of aspiration pneumonia. Moreover,

the frequently associated reduction in residual functional capacity may cause atelectasis and pneumonia. We should not forget that patients sometimes have sensations of dyspnoea related to off periods.

– Non motor:

1. Dysautonomic manifestations. Patients may have dysautonomic disorders due to Parkinson's disease, concomitant treatment and also due to age. The most frequent manifestations are excess salivation, gastrointestinal disorders, seborrhoea, impaired temperature regulation, urological problems and cardiovascular disorders.
 - Cardiovascular system. The most frequent symptom is orthostatic hypotension. Several drugs may cause an exacerbation of hypotension, including levodopa and dopaminergic agonists. Concomitant medication must be monitored, particularly the treatment for hypertension, which may often be reduced or discontinued in PD.
 - Gastrointestinal function. The most frequent problems are sialorrhoea, dysphagia and oesophageal transit abnormalities. Patients who have been operated on may experience worsening of gastrointestinal complications, which are already common in surgery (especially abdominal), presenting as constipation, delayed gastric emptying and paralytic ileus.
 - The urinary system is also vulnerable to complications, mainly the so-called cystocerebral syndrome, presenting as confusion due to acute urine retention and bladder distension.
2. Neuropsychological manifestations. Anxiety, depression and cognitive impairment are not uncommon in PD and should be considered. We reiterate that immobility-related anxiety as a result of poor management is the main cause for patients with Parkinson's disease to undergo surgery.

All of these complications involve greater difficulty in nursing care after surgery and a delayed recovery after surgery.¹⁻⁶

2. Problems related to medication or its suppression. The interruption of antiparkinsonian medication for a period longer than 6–12 h may worsen many of the symptoms of PD.^{2,3} The half-life of levodopa is short (around 90 min), while that of agonists varies. Abrupt suspension of medication may cause parkinsonism-hyperpyrexia syndrome, which is indistinguishable from malignant neuroleptic syndrome, since it is associated with stiffness, hyperpyrexia, dysautonomia and increased creatine kinase.⁹⁻¹¹ Although it is a rare phenomenon, there have been documented cases that occurred several days after the suspension of DOPA. Another complication that may be caused by abrupt suspension of medication is akinetic crisis, which may cause respiratory problems and great anxiety in patients. On the other hand, the use of high doses of medication may trigger the onset of severe dyskinesias, which in some cases may compromise the patient's life.⁸ Therefore, management of drugs must be

done cautiously. This management has two perioperative scenarios:

– Preoperative drug management:

1. Levodopa administered orally. It is recommended until the morning of the surgery. A dose may be administered the same morning with a minimal amount of water. Although the half-life of levodopa is 90 min, its effect may last several hours, which will facilitate perioperative mobility. After surgery, the treatment should be resumed as soon as possible.
2. Dopaminergic agonists (pramipexole, ropinirole, and rotigotine). These may be used until surgery. Rotigotine may be continued throughout the perioperative period, since it is administered in patches.
3. Selegiline and rasagiline. These are MAO-B inhibitors and should be discontinued three weeks before surgery, if the patient's condition allows. Its combination with other serotonergic drugs (meperidine) may precipitate a serotonin syndrome.
4. Amantadine. This may be continued until surgery.
5. Entacapone, tolcapone (COMT inhibitors). These may be continued until surgery.
6. Anticholinergic agents. These are becoming increasingly obsolete due to their limited efficacy and numerous side effects, and should be discontinued before surgery. They may cause confusion and interfere with various drugs.

– Postoperative drug management:

1. Levodopa. The use of levodopa by nasogastric probe (NGP) is limited by the indication of complete fasting, common in the immediate postoperative period.^{12,13} However, it may be used after a few hours, administered by NGP with a minimal amount of water, as long as the intervention does not involve abdominal surgery. In cases of dysphagia, a solution of 1–1.5 g of levodopa in 1 litre of water can be prepared with 1 g of vitamin C, administering 100 ml of the solution by NGT every 2 h, until the patient tolerates it.
2. Rotigotine. This is a D1/D2/D3 dopamine receptor agonist. It is used as a transdermal patch of 2 mg, 4 mg, 6 mg and 8 mg. The usual dose is between 6 and 16 mg/day, which may be increased to 24 mg. Various studies and cases have shown its effectiveness and feasibility in perioperative administration, with no safety problems. It is an ideal drug for cases of dysphagia. Therefore, the rotigotine patch is a very good option for perioperative management of PD.
3. Apomorphine. This is a D1/D2 selective dopaminergic agonist of equivalent potency to levodopa. It is administered subcutaneously. It has a peak at 3 min and the effects appear at 6 min with a maximum at 30 min. Its half-life is similar to that of levodopa. Among its noteworthy side effects are nausea, vomiting and orthostatic hypotension, which must be prevented with domperidone (20 mg/8 h orally) or ondansetron (4–8 mg/12 h IV). Doses must be individualised and calculated by performing an apomorphine test, which must be scheduled before the surgery.

4. Intravenous amantadine. We are waiting for data from the “Perioperative treatment of Parkinson patients with parenteral amantadine” study, which took place between January 2008 and January 2010.

– Anaesthetics and other perioperative drugs^{4–6,8,14}:

1. Propofol is the anaesthetic of choice.
2. Thiopental reduces the release of dopamine at the striatal level, and although the consequence of this is unclear, it may worsen Parkinsonism. Ketamine is contraindicated as it may lead to a sympathetic over response.
3. Inhaled anaesthetics have complex effects on brain dopamine. Since most patients are treated with levodopa, anaesthetics such as halothane must be avoided as they can sensitise to catecholaminergic action of the heart. Others such as isoflurane and sevoflurane, although less arrhythmogenic, may induce hypotension, which may be severe in patients with dysautonomia, such as the case with parkinsonian patients.
4. Non/depolarising muscle relaxants are safe, rocuronium being the agent of choice for PD. Succinylcholine may be safe, although cases have been reported where it induced hyperkalemia in patients with PD.¹⁵
5. Phenothiazines, butyrophenones (including droperidol) and metoclopramide may worsen PD and, therefore, are contraindicated in the perioperative management of this disease.
6. Drugs with serotonergic effects should not be added. Meperidine coupled with selegiline has been observed to cause serotonin syndrome with hyperpyrexia, tremors, tachycardia and stiffness. MAOIs should be discontinued some three weeks before surgery.
7. The pain caused by the surgical procedure needs to be differentiated from the pain induced by PD, especially that due to stiffness. The best treatment for genuine parkinsonian pain is dopamine treatment with anti-parkinsonian drugs.
8. Opioids may induce stiffness and must be used with caution.¹⁶ Fentanyl may cause stiffness and low-dose morphine may reduce dyskinesias, however, at high doses it may worsen akinesia.¹⁷

A Practical Perioperative Approach to Patients With Parkinson's Disease

General Considerations

1. The same treatment the patient was undergoing will be maintained, and will only be suspended during the complete fasting time required prior to the surgical procedure.
2. In premedication, one tablet of Sinemet or Madopar may be administered one hour before surgery with a tablespoon of water.
3. Treatment may be resumed as soon as oral tolerance tests allow, under the same regimen the patient had

before. For non-abdominal surgery, this may start 2–3 h after surgery.

Surgery That Subsequently Requires Strict Complete Fasting: Abdominal Surgery

During the complete fasting period, rotigotine patches may be used. Doses should be individualised as they differ at various stages of the disease: mild, moderate and advanced. Changes in surgery-related medication are not necessary, except for MAOIs, which must be discontinued three weeks earlier, or when a long postoperative period is expected. In this case, an apomorphine test is recommended to determine the proper dose for this drug.

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

1. The conversion with levodopa is only tentative. For the purpose of perioperative treatment, 300 mg of levodopa would be equivalent to 8 mg of rotigotine.
2. If the patient was already taking rotigotine then the same dose can be maintained, raising it to 24 mg a day according to the clinical situation.
3. Subcutaneous apomorphine may be used every 3–4 h as needed. The apomorphine doses should be established before surgery, as mentioned previously. Apomorphine can be scheduled with an antiemetic agent administered parenterally, such as ondansetron 4–8 mg/12 h.
4. When urgent or unscheduled surgery is needed, management is similar. If the patient was taking MAOI then serotonin interactions need to be monitored. If apomorphine is needed, it should be started with tentative doses of 3 mg. General considerations should be maintained.

Surgery Requiring Complete Fasting for a Few Hours: Non-Abdominal Surgery

Medication may be administered by NGP with a minimal amount of water, two hours after surgery.

Surgery Requiring Subsequent Intensive Care

If the patient needs to be intubated and thus sedated and relaxed, no additional medication is required. When the patient begins to wake, the procedure is similar to that defined for complete fasting.

Surgery That Can Be Performed With Local or Regional Anaesthesia and That Requires Patient Immobility

The typical example is ophthalmological surgery. Problems may be caused by tremors or treatment-induced dyskinesias.

1. Dyskinesias may be controlled with appropriate programming depending on the type of dyskinesia. Since these surgeries are often very short, surgical time can be adjusted to the treatment response time. If the surgery is prolonged, general anaesthesia with propofol is a better choice.
2. The same is applicable for those patients with severe tremors, which may interfere with the execution of the surgery; general anaesthesia is preferable since the treatment of the tremors is often suboptimal.
3. General anaesthesia is preferable for most of these patients.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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