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CASE REPORT: PHARMACOLOGICAL MANAGEMENT IN THE PATIENT WITH PARKINSON'S DISEASE

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Abstract: Goal. Study and signal the importance of perioperative management, focusing on adequacy to patients with Parkinson's Disease. **Method.** Analysis of data from medical records, with the patient's consent, provided by HCTCO - Hospital das Clínicas de Teresópolis Constantino Ottaviano. In addition to reviewing articles on the subject. **Result.** Parkinson's disease (PD) is a progressive degenerative disease, with a genetic background, which destroys dopaminergic cells in the substantia nigra in the central nervous system. In this case, the patient J.R.M. evolved with stiffness during the immediate postoperative period. The first therapeutic option, via nasogastric tube, is Levodopa, whose benefit is even greater when in association with Carbidopa, reducing the peripheral conversion of levodopa and, consequently, its undesirable side effects. Considering that there was no initial need to install a nasogastric tube in the preoperative period, with the risk of inducing the gag reflex and subsequent bronchoaspiration, at this time, the option of expectant management and support is an important alternative. **Conclusion**. Patients with PD have difficult perioperative management, from the point of view of anesthesiology. Suspension of antiparkinsonian drugs is contradictory, and it is recommended, whenever possible, to maintain these drugs, even via the nasogastric route, in patients with PD, as well as the use of pharmacological alternatives for adequate anesthesia in this population. It is necessary to carry out further studies on drug interactions in general anesthesia in patients on regular treatment with antiparkinsonians in order to present fewer risks and greater benefits for the target population.
Keywords: Parkinson's disease, dopamine, perioperative management

INTRODUCTION

Movement disorders pose one of the most difficult diagnoses in neurology, as their origins can be both organic and psychogenic. Parkinson's disease (PD), named in honor of James Parkinson, who described its clinical characteristics in 1817, has an incidence in the population over 65 years of 1 to 2% worldwide and an estimated prevalence in Brazil of 3.3%, becoming a growing problem in the country. (3,12,14) The senescence of the central nervous system is one of the most compromising physiological consequences, being responsible for several functions such as sensations of movement, psychological and internal biological, which, when altered, interfere directly on the functioning of the central nervous system. Basically, changes in the basal ganglia, each with its clinical presentation. PD is a disorder of the central nervous system, which is chronically and progressively expressed, characterized by the presence of multiple monoaminergic disorders, including deficits in the dopaminergic, cholinergic, serotonergic and noradrenergic systems (2,13) This pathology results from the loss of dopaminergic neurons of the substantia nigra that present intracytoplasmic inclusions known as Lewy bodies, that when the effect of dopamine is diminished, PD tends to manifest itself, since the lack of it results in the global increase of acetylcholine leading to an imbalance between these neurotransmitters and activating the process of muscle contraction, which occurs when there is a 25% reduction in the activity of dopaminergic neurons. (8) The dopaminergic system along with melanin neurons undergoes depigmentation. That is, the lighter the substantia nigra, the greater the loss of dopamine.(2)

However, the changes are not restricted to the substantia nigra and may be present in other brainstem nuclei (eg, dorsal motor

nucleus of the vagus), cerebral cortex, and even peripheral neurons, such as those in the myenteric plexus. With the degenerative process being located in other places besides the nigrostriatal system, there can be a number of non-motor symptoms and signs, such as alterations of smell, sleep disturbances, postural hypotension, constipation, emotional changes, depression, anxiety, psychotic symptoms, cognitive impairment and dementia, among others. (6.7)

It has two forms: primary, with unilateral onset, tremors in 40% of cases, bradykinesia, rigidity and balance disorders; and secondary, medicinal or originating from other diseases. Antiparkinsonian medications can cause increased involuntary movements through their influence on the basal ganglia. (30).

People with PD, as well as people with other brain disorders, are more prone to side effects from anesthesia and negative effects from the stress of the surgery itself. Therefore, every patient must be examined for specific conditions that may interfere with anesthesia and surgery. Each condition must be evaluated and treated as needed. (4) It is important to remember that not everyone is affected in the same way, and that does not mean that individuals with this pathology cannot have the surgeries and procedures they need. However, it is important to be aware of the possible risks, during perioperative management and anesthetic administration, that may arise so that the physician is prepared. (9,11,17) Drugs used to manage dopamine in patients with PD are considered the gold standard treatment, with a short half-life. When patients with PD are placed on NPO (nothing by mouth) status for surgery, they may miss several doses of this therapy, possibly resulting in exacerbation of Parkinson's disease symptoms. (23) Among these risks, parkinsonism was the complication of the case report. Parkinsonism is a general term that refers to a group of neurological disorders that cause movement problems similar to those seen in the disease, such as: Tremors, slow movement, and stiffness. (10) This reported episode of parkinsonism could be strongly related to the withdrawal of the drug used therapeutically in PD, leading to a neuroleptic malignant syndrome, associated with fever, mental confusion, and increased muscle enzymes. This syndrome is more common in people with severe symptoms of PD or in patients on high doses of levodopa. (11) With an etiology still to be understood, it is believed to occur due to the reduction of dopaminergic activity due to the blockade of D2 receptors or lack of dopamine in the central nervous system, causing relative cholinergic hyperactivity. (15) It is an idiosyncratic reaction that may also be related to genetic factors. (26)

The pathophysiology of PD and L-DOPA-induced dyskinesia is associated with aberrant neuronal activity and abnormally high levels of oscillatory activity and synchronization in various basal ganglia nuclei and cortex. We have previously shown that neuron firing activity in the substantia nigra reticulata is relevant in dyskinesia and may be driven by subthalamic nucleus hyperactivity. (1.28)

The lack of adequate management of patients with Parkinson's disease (PD) in the perioperative context may lead to possible risks that may arise when patients with PD undergo an operation. Therefore, extreme care must be taken to ensure proper administration of medications, transition to non-oral agents if indicated, and early mobilization to achieve a rapid recovery after surgery. (19,21,24). For better symptom management, careful consideration must be given to scheduling surgery as soon as possible, administering medications as closely as possible to the patient's dosing schedule, and providing nursing education on optimal medication handling for these patients.

GOAL

This case report proposes to evaluate and signal the importance of perioperative management, focusing on adequacy to patients with Parkinson's Disease. To review the perioperative management, taking into account the planning of drugs to stabilize Parkinson's Disease in relation to general anesthesia and the possible exacerbations that this type of patient may present in the face of a surgical episode. There are several complications that can occur during surgery in this individual, and they are often unpredictable. Therefore, greater care is required for these conditions and a quality study is required to avoid or reduce episodes such as the one that will be addressed in this study.

METHOD

For the preparation of this article, a case report was carried out at the Surgical Center of the Hospital das Clínicas de Teresópolis Constantino Ottaviano (HCTCO) and a brief literary review with discussion, having been searched for articles in the following databases: SciElo, PubMed and LiLACS. With descriptors: "(Parkinson's disease) AND perioperative care"; "(Parkinson's disease) AND surgery"; "(Parkinson's disease) AND dopamine"; "(Parkinson's disease) AND perioperative AND drugs". Articles that addressed studies in humans, published within up to 11 years, in Portuguese, English, Spanish, German and French were included, excluding articles that addressed specific operative techniques. The report was submitted to the Research Ethics Committee, awaiting approval. With the identification number, CAAE: 34112020.7.0000.5247.

CASE DESCRIPTION

J. R. M., 70 years old, female, with Parkinson's disease, using Prolopa (withdrawn three days before surgery), and Hypertensive using Hydrochlorothiazide and Losartan, P-2. Proposed Laparascopic Cholecystectomy Surgery. After being taken to the operating room, monitoring was performed, venoclysis in the left upper limb with 18G Jelco, prophylactic antibiotic (Cefazolin 2g) and drugs for preemptive analgesia (Dipyrone 2g and Tylatil 20mg) and prevention of nausea and vomiting (Dexamethasone 10mg) were administered. and Ondasenthrone 4mg).

She was induced for multimodal general anesthesia with Clonidine 75mcg, Magnesium Sulfate 2g, Ketamine 10mg, Fentanyl 200mcg, Propofol 150mg, Rocuronium 50mg, Lidocaine 2% 5ml in the periglottic region; performed IOT with TOT 7.0 with Cuff. The surgery was uneventful. Even withholding the use of anti-dopaminergic drugs that could precipitate an extra-pyramidal reaction, the patient developed parkinsonism in the immediate postoperative period, with generalized rigidity, lasting an average of one and a half hours. The conduct chosen at the time was expectant and supportive, due to the fear of administering some medication through the nasoenteral tube (ENS) and leading to the episode of vomiting and bronchoaspiration.

DISCUSSION

Parkinson's Disease (PD) is a degenerative and progressive disease, with a genetic background, that destroys the dopaminergic cells of the substantia nigra in the central nervous system (13,30), which causes an interruption in the regulation of agonist and antagonist circuits of the ganglia. of the base, being more eminent the decrease of the antagonistic influence (30), leading to the classic symptoms of tremor at rest, bradykinesia, rigidity, postural instability, typical gait, micrograph and reduced facial expression. (23) In addition to these so-called

motor symptoms, PD also has non-motor symptoms, namely: autonomic dysfunction, sleep disorders, depression, psychosis, and cognitive changes. (19)

Epidemiological data indicate that PD is the second most prevalent neurodegenerative disease in the world, after Alzheimer's disease. (26,30) The majority of the population affected by PD is over 65 years of age, and it is important to consider the implications of this clinical entity on the perioperative management of patients, given that in this specific population, situations in which surgical management is important are common, such as prostatic pathologies, gynecological and orthopedic surgeries (7). In terms of anesthesiology, roughly speaking, there is a tendency to choose general anesthesia in these patients, based on the principle that they have a neurological disease. (16) However, an important fact must be considered: general anesthesia can mask intraoperative neurological symptoms and cause a postoperative rebound exacerbation, which may suggest a greater benefit in choosing intraspinal anesthesia whenever possible. (17)

In order to avoid possible complications in the perioperative period of patients with PD, it is essential to have a good planning, considering options such as not interrupting the use of oral medications for these patients when opting, for example, to schedule the surgery at an intermediate time where the fact of not being in complete fasting is not so much implication (22) or, in cases of surgery that are not in the abdominal site, administration of Levodopa via nasogastric tube with a minimal amount of water can be performed (26).

The symptoms of PD can be reversed by the use of drugs that restore striatal dopaminergic neurotransmission, such as levodopa and some agents such as L-aromatic amino acid decarboxylase inhibitors, (DOPA) decarboxylase inhibitors, catechol-O-methyl transferase (COMT) inhibitors.) and type B monoamine oxidase (MAO-B) inhibitors, as well as synthetic dopamine agonists and, finally, drugs such as amantadine and anticholinergics once regularly used in the treatment of PD and now used less frequently. (30) The drugs used in the management of patients with PD are mostly administered orally, and their sudden withdrawal before surgery can cause severe worsening of symptoms. (20)

Among the different therapeutic options, Levodopa occupies the first place of choice for patients with PD, with a short half-life (about 90 minutes); if interrupted suddenly for a period longer than 6 to 12 h, it can cause a considerable clinical worsening of PD symptoms, in addition to causing the so-called hyperpyrexia-parkinsonism syndrome, which encompasses rigidity, hyperpyrexia, dysautonomia and increased creatine kinase, thus being indistinguishable from neuroleptic malignant syndrome. (26)

The medications used by patients with PD have numerous drug interactions with drugs and anesthetic techniques; those who use Levodopa, for example, tend to have more episodes of nausea and vomiting and, consequently, tend to have greater dehydration, and adequate fluid therapy during the perioperative period is important. (7) In these patients, adequate management of antiemetics is essential, and dopaminergic antagonists derived from phenothiazine, thioxanthene, and butyrophenone are absolutely contraindicated because they exacerbate PD symptoms; for the patient in question, Ondansetron, considered safe for use in patients with PD, was administered. (19)

Regarding general anesthesia in patients with PD, a drug that is normally in the arsenal is Propofol, both for induction and maintenance of general anesthesia; care must

be taken, however, with its motor side effects both in patients who present and in those who do not present movement disorders, since there are cases of dyskinesia reported in this population after the use of Propofol. (19.20)

Among the other drugs commonly used in anesthesia, it must be noted that Ketamine is contraindicated due to the risk of triggering an exacerbated sympathetic response. (26) Opioids such as Fentanyl, Alfentanil, and Morphine have been reported to have adverse motor effects, particularly muscle stiffness resulting from modulation of dopaminergic receptors in the basal ganglia, notably an inhibition of presynaptic dopamine release. (30) Regarding inhalational anesthetics, it is important to highlight that Halothane is not recommended, especially in patients being treated with levodopa, because it increases the sensitivity of the myocardium to catecholamines, which can trigger arrhythmogenic events, as are Isoflurane and Sevoflurane, which, although less arrhythmogenic, can induce hypotension, which can have serious effects in patients with parkinsonism. (26)

Finally, there is no evidence that the use of non-depolarizing neuromuscular blockers worsens PD symptoms, and rocuronium is a good option for these patients; on the other hand, succinylcholine, a depolarizing neuromuscular blocker, has been reported to cause severe hyperkalemia in PD patients, although it has already been used in some cases without further problems. (30)

Problems related to PD and that must be considered in the perioperative period are divided into those of a motor nature, such as, for example, akinesia, resulting from the exacerbation of bradykinesia and rigidity, which can lead to respiratory, bronchoaspiration, thrombotic problems, infections and pressure injuries, and those of a non-motor nature, typically the dysautonomic manifestations, including orthostatic hypotension, drooling, dysphagia, acute urinary retention and neuropsychological manifestations, such as anxiety, depression and cognitive loss. (26) In patients who are to undergo surgery and who report exacerbation of symptoms when they miss a dose of their usual medication, it is recommended to install a nasogastric tube for intraoperative administration of regular antiparkinsonian medication. (5.19)

Although there was no exacerbation of PD symptoms during the pre- and intraoperative periods, despite being off the usual medication for about 72 hours, J.R.M. evolved with stiffness during the immediate postoperative period; Given this scenario, the first therapeutic option, via nasogastric tube, is Levodopa, a dopaminergic precursor capable of restoring basal ganglia neurotransmission, and whose benefit is even greater when in association with Carbidopa, whose action is to inhibit dopa -decarboxylase, reducing the peripheral conversion of levodopa and, consequently, its undesirable side effects. (28) Considering that the patient did not initially need a nasogastric tube in the preoperative period and the risk of inducing the gag reflex and subsequent bronchoaspiration at this time, the option of expectant management and support is an important alternative.

CONCLUSION

Parkinson's disease is a clinical entity whose pathophysiology is explained by the destruction of dopaminergic pathways in the Central Nervous System, notably in the substantia nigra, causing mainly motor disorders in the affected population. The treatment of PD is mainly done with dopaminergic precursors, such as Levodopa, taken orally.

Patients with PD have difficult perioperative management, from the point of view of

anesthesiology, taking into account not only the drug interaction between the drugs commonly used in PD and regular anesthesia drugs, especially general anesthesia, but also the complications arising from the necessary preoperative suspension due to recommended fasting.

The patient presented in the case above, despite the preoperative and intraoperative clinical stability, evolved with stiffness in the immediate postoperative period, which may have been caused either by the prolonged suspension of the antiparkinsonian drug or by a side effect of the medications used in the patient's anesthesia. Among the possible options for reversing rigidity are nasogastric administration of Levodopa or expectant management, the latter being the most appropriate considering the increased risk of vomiting and bronchoaspiration induced by the placement of a nasogastric tube in the immediate postoperative period.

In view of the patient's evolution, it is understood that the suspension of antiparkinsonian drugs is contradictory, and it is recommended, whenever possible, to maintain these drugs even if via the nasogastric route in patients with PD, as well as the use of pharmacological alternatives for the adequate anesthesia of this population. Finally, it is understood that the installation of a nasogastric tube in the face of post-anesthetic rigidity in a patient with PD presents an important risk for the patient, since it can trigger the vomiting reflex and consequent bronchoaspiration, therefore, the recommended conduct expectant and supportive in these cases.

It is necessary to carry out further studies on drug interactions of drugs used in general anesthesia in patients on regular treatment with antiparkinsonians in order to list the best options, that is, those that present fewer risks and greater benefits in this target population.

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