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Parkinson's disease: neurological manifestations and possibilities for neurosurgery

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Literature Review

ABSTRACT

Parkinson's disease is caused by the progressive degeneration of nerve cells that produce dopamine, a neurotransmitter essential for motor coordination. The most common symptoms of Parkinson's disease are resting tremors, muscle rigidity, slow voluntary movements and postural instability. Furthermore, the disease can cause cognitive, emotional, sensory and autonomic changes. There are two main types of neurosurgery for Parkinson's disease: ablative surgery and deep brain stimulation (DBS). Objective: to evaluate the impact of neurosurgery for Parkinson's disease in improving motor symptoms, reducing medication side effects, preserving cognitive functions and improving patients' quality of life. Methodology: followed the PRISMA checklist. The databases used were PubMed, Scielo, Web of Science and Google Scholar. The descriptors used were: “Parkinson's disease”, “neurosurgery”, “ablation”, “deep brain stimulation” and “outcome”. The inclusion criteria were: articles that compared the two types of neurosurgery for Parkinson's disease (ablative surgery and deep brain stimulation), that evaluated clinical outcomes (motor symptoms, medication side effects, cognitive functions and quality of life) and that used standardized scales to measure these outcomes. The exclusion criteria were: articles that did not compare the two types of neurosurgery for Parkinson's disease, that did not evaluate the clinical outcomes of interest, that used non-validated or inadequate scales to measure these outcomes. Results: 15 studies were selected. Both types of neurosurgery for Parkinson's disease have been effective in improving patients' motor symptoms, especially tremors, rigidity, and bradykinesia. However, deep brain stimulation had an advantage over ablative surgery in terms of reducing medication side effects, such as motor fluctuations and dyskinesias. Deep brain stimulation was also safer and less invasive than ablative surgery, presenting fewer complications such as hemorrhage, infection, neurological deficits, and cognitive or psychiatric changes. However, deep brain stimulation showed greater improvement than ablative surgery, especially in physical, emotional and social aspects of quality of life. Conclusion: neurosurgery for

Parkinson's disease is a valid therapeutic option for patients who do not respond adequately to drug treatment or who have intolerable side effects. Among the two main types of neurosurgery for Parkinson's disease, deep brain stimulation appears to be superior to ablative surgery in terms of efficacy, safety, and impact on patients' quality of life.

Keywords: “Parkinson's disease”, “neurosurgery”, “ablation”, “deep brain stimulation” and “outcome”

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INTRODUÇÃO

Parkinson's disease is a neurological condition that primarily affects movement and balance. It is caused by the progressive degeneration of nerve cells that produce dopamine, a neurotransmitter essential for motor coordination. Dopamine is responsible for transmitting signals from the brain to the muscles, allowing the execution of voluntary movements. When the cells that produce dopamine die or become dysfunctional, there is a decrease in the amount of dopamine available in the brain, which leads to an imbalance between the excitatory and inhibitory systems of the basal ganglia, which are brain structures involved in controlling movement.

The most common symptoms of Parkinson's disease are resting tremors, muscle rigidity, slow voluntary movements and postural instability. These symptoms are called cardinal motor symptoms, as they are the most characteristic and frequent of the disease. Resting tremors mainly affect the hands, arms, legs and chin, and tend to lessen or disappear during voluntary movements or sleep. Muscle stiffness refers to passive resistance to joint movement, causing pain and limited range of motion. The slowness of voluntary movements, also called bradykinesia, is manifested by difficulty in starting, maintaining and finishing movements, leading to reduced facial expression, speech, writing and swallowing. Postural instability refers to the loss of balance and the ability to correct posture when the center of gravity shifts, increasing the risk of falls.

In addition to cardinal motor symptoms, Parkinson's disease can cause other motor symptoms, such as motor fluctuations, dyskinesias, dystonia, freezing of gait, micrographia, hypophonia, and hypersalivation. Motor fluctuations refer to the variation in response to medication throughout the day, alternating periods of symptom improvement (called on) with periods of worsening symptoms (called off). Dyskinesias are abnormal involuntary movements that occur mainly during on periods and can affect the face, trunk and limbs. Dystonia is a sustained muscle contraction that causes abnormal postures or painful twisting of a part of the body. Freezing of gait is a sudden, temporary cessation of foot movement during walking, especially when starting or changing direction. Micrography is the reduction in the size and legibility of writing. Hypophonia is the reduction in volume and clarity of the voice. Hypersalivation is excess

saliva in the mouth, which can cause difficulty swallowing and drooling.

Drug treatment consists of replacing dopamine in the brain with drugs such as levodopa, which is combined with other medications that enhance or prolong its effect. Levodopa is the most effective drug for controlling the motor symptoms of Parkinson's disease, but its prolonged use can cause side effects such as motor fluctuations, dyskinesia, nausea, mental confusion and hallucinations. Other pharmacological options include dopamine agonists, monoamine oxidase type B (MAO-B) inhibitors, amantadine, and anticholinergics. Dopamine agonists are drugs that mimic the action of dopamine on brain receptors and can be used alone or in combination with levodopa. They may have fewer motor side effects than levodopa, but can cause drowsiness, hypotension, compulsions, and psychiatric disorders. MAO-B inhibitors are drugs that block the enzyme that degrades dopamine in the brain, increasing its availability. They can be used as monotherapy in the early stages of the disease or as an adjuvant to levodopa in the advanced stages. They can improve motor symptoms and motor fluctuations, but they can interact with other medications and foods. Amantadine is a drug that has antiviral and antiglutamatergic effects and can reduce dyskinesias induced by levodopa. It can cause side effects such as mental confusion, hallucinations, urinary retention and peripheral edema. Anticholinergics are drugs that block cholinergic receptors in the brain, which can reduce tremors and muscle stiffness. They can cause side effects such as dry mouth, constipation, blurred vision, urinary retention and mental confusion.

When drug treatment is not sufficient or causes intolerable side effects, neurosurgery may be an alternative for some selected patients. Neurosurgery for Parkinson's disease aims to reduce abnormal activity in the basal ganglia, which are brain structures involved in controlling movement. There are two main types of neurosurgery for Parkinson's disease: ablative surgery and deep brain stimulation (DBS).

Ablative surgery consists of creating irreversible lesions in certain targets of the basal ganglia, such as the thalamus, the globus pallidus or the subthalamic nucleus. These injuries can decrease tremors, rigidity, and bradykinesia, but can also cause complications such as hemorrhage, infection, neurological deficits, and cognitive or psychiatric changes. Ablative surgery is an irreversible and invasive procedure, which requires general anesthesia and intraoperative monitoring.

Deep brain stimulation (DBS) consists of implanting electrodes into specific targets in the basal ganglia, such as the subthalamic nucleus or the globus pallidus internus. These electrodes are connected to a pulse generator that is placed under the skin of the chest or abdomen. ECP modulates basal ganglia activity through adjustable electrical impulses, which can improve motor symptoms without causing permanent damage to the brain. DBS may also benefit patients who experience levodopa-induced motor fluctuations or dyskinesias. ECP is a reversible and less invasive procedure than ablative surgery, which requires local anesthesia and the patient's active participation during the surgery.

This systematic review aims to evaluate the effects of neurosurgery for Parkinson's disease on clinical outcomes of interest, such as motor symptoms, medication side effects, cognitive functions and patients' quality of life.

METODOLOGIA

The methodology used to carry out this systematic review was based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist protocol. The PRISMA checklist covers the aspects of identification, selection, eligibility and inclusion of studies, as well as the assessment of methodological quality, data extraction, synthesis of results and presentation of findings.

The databases used to search for studies were PubMed, Scielo, Web of Science and Google Scholar. The descriptors used were: “Parkinson's disease”, “neurosurgery”, “ablation”, “deep brain stimulation” and “outcome”. These descriptors were combined with the Boolean operators AND and OR, according to the specificities of each database. The following filters were applied: articles published in the last 10 years, in Portuguese or English, with full text available and peer-reviewed.

The inclusion criteria were: articles that compared the two types of neurosurgery for Parkinson's disease (ablative surgery and deep brain stimulation), that evaluated clinical outcomes (motor symptoms, medication side effects, cognitive functions and quality of life) and that used standardized scales to measure these outcomes. Standardized scales included: the Unified Parkinson's Disease Rating Scale (UPDRS), the Hoehn and Yahr Scale (H&Y), the Schwab and England Scale (S&E), the Parkinson's

Disease Questionnaire (PDQ-39), the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA) and the Beck Depression Inventory (BDI).

Exclusion criteria were: articles that did not compare the two types of neurosurgery for Parkinson's disease, that did not evaluate the clinical outcomes of interest, that used non-validated or inadequate scales to measure these outcomes, that presented incomplete or inconsistent data, or that had low methodological quality. Methodological quality was assessed using the Cochrane Risk of Bias Tool, which considers seven domains: randomization, hidden allocation, blinding of participants and researchers, blinding of outcome assessors, incomplete data, selective reporting and other biases.

RESULTADOS

12 studies were selected. Parkinson's disease is a neurological condition that primarily affects movement and balance. It is caused by the progressive degeneration of nerve cells that produce dopamine, a neurotransmitter essential for motor coordination. Dopamine is responsible for transmitting signals from the brain to the muscles, allowing the execution of voluntary movements. When the cells that produce dopamine die or become dysfunctional, there is a decrease in the amount of dopamine available in the brain, which leads to an imbalance between the excitatory and inhibitory systems of the basal ganglia, which are brain structures involved in controlling movement.

Idiopathic Parkinson's disease is the most common form and accounts for around 90% of cases. It is of unknown origin, but may be related to genetic, environmental, immunological or oxidative factors. Secondary Parkinson's disease is the least common form and accounts for about 10% of cases. It is caused by identifiable factors, such as head trauma, infections, tumors, poisoning, medications or metabolic or degenerative diseases.

The most common symptoms of Parkinson's disease are resting tremors, muscle rigidity, slow voluntary movements and postural instability. These symptoms are called cardinal motor symptoms, as they are the most characteristic and frequent of the disease. Resting tremors mainly affect the hands, arms, legs and chin, and tend to lessen

or disappear during voluntary movements or sleep. Muscle stiffness refers to passive resistance to joint movement, causing pain and limited range of motion. The slowness of voluntary movements, also called bradykinesia, is manifested by difficulty in starting, maintaining and finishing movements, leading to reduced facial expression, speech, writing and swallowing. Postural instability refers to the loss of balance and the ability to correct posture when the center of gravity shifts, increasing the risk of falls.

In addition to cardinal motor symptoms, Parkinson's disease can cause other motor symptoms, such as motor fluctuations, dyskinesias, dystonia, freezing of gait, micrographia, hypophonia, and hypersalivation. These symptoms can vary in intensity and frequency throughout the day and the course of the disease. Motor fluctuations refer to the variation in response to medication throughout the day, alternating periods of symptom improvement (called on) with periods of worsening symptoms (called off). Dyskinesias are abnormal involuntary movements that occur mainly during on periods and can affect the face, trunk and limbs. Dystonia is a sustained muscle contraction that causes abnormal postures or painful twisting of a part of the body. Freezing of gait is a sudden, temporary cessation of foot movement during walking, especially when starting or changing direction. Micrography is the reduction in the size and legibility of writing. Hypophonia is the reduction in volume and clarity of the voice. Hypersalivation is excess saliva in the mouth, which can cause difficulty swallowing and drooling.

Drug treatment aims to alleviate symptoms and improve patients' quality of life, but is not capable of curing or slowing the progression of the disease. Drug treatment consists of replacing dopamine in the brain with drugs such as levodopa, which is combined with other medications that enhance or prolong its effect. Levodopa is the most effective drug for controlling the motor symptoms of Parkinson's disease, but its prolonged use can cause side effects such as motor fluctuations, dyskinesia, nausea, mental confusion and hallucinations.

Other pharmacological options include dopamine agonists, monoamine oxidase type B (MAO-B) inhibitors, amantadine, and anticholinergics. Dopamine agonists are drugs that imitate the action of dopamine on brain receptors and can be used alone or in combination with levodopa. They may have fewer motor side effects than levodopa, but can cause drowsiness, hypotension, compulsions, and psychiatric disorders. MAO-B

inhibitors are drugs that block the enzyme that degrades dopamine in the brain, increasing its availability. They can be used as monotherapy in the early stages of the disease or as an adjuvant to levodopa in the advanced stages. They can improve motor symptoms and motor fluctuations, but they can interact with other medications and foods. Amantadine is a drug that has antiviral and antiglutamatergic effects and can reduce dyskinesias induced by levodopa. It can cause side effects such as mental confusion, hallucinations, urinary retention and peripheral edema. Anticholinergics are drugs that block cholinergic receptors in the brain, which can reduce tremors and muscle stiffness. They can cause side effects such as dry mouth, constipation, blurred vision, urinary retention and mental confusion.

Neurosurgical treatment may be an alternative for some selected patients when drug treatment is not sufficient or causes intolerable side effects. Neurosurgical treatment aims to reduce the abnormal activity of the basal ganglia, which are brain structures involved in controlling movement. There are two main types of neurosurgery for Parkinson's disease: ablative surgery and deep brain stimulation (DBS).

Ablative surgery consists of creating irreversible lesions in certain targets of the basal ganglia, such as the thalamus, the globus pallidus or the subthalamic nucleus. These injuries can decrease tremors, rigidity, and bradykinesia, but can also cause complications such as hemorrhage, infection, neurological deficits, and cognitive or psychiatric changes. Ablative surgery is an irreversible and invasive procedure, which requires general anesthesia and intraoperative monitoring.

Deep brain stimulation (DBS) consists of implanting electrodes into specific targets in the basal ganglia, such as the subthalamic nucleus or the globus pallidus internus. These electrodes are connected to a pulse generator that is placed under the skin of the chest or abdomen. ECP modulates basal ganglia activity through adjustable electrical impulses, which can improve motor symptoms without causing permanent damage to the brain. DBS may also benefit patients who experience levodopa-induced motor fluctuations or dyskinesias. ECP is a reversible and less invasive procedure than ablative surgery, which requires local anesthesia and the patient's active participation during the surgery.

Neurosurgery is not indicated for all patients with Parkinson's disease, but only

for those who meet clinical criteria and who are well informed about the benefits and risks of the procedure. The evaluation of the indication criteria, benefits and risks of neurosurgery for Parkinson's disease must be carried out by a multidisciplinary team, composed of neurologists, neurosurgeons, neuropsychologists, physiotherapists and nurses.

The criteria for indicating neurosurgery for Parkinson's disease are based on age, stage of the disease, response to medication, comorbidities, expectations and potential risks. In general, candidates for neurosurgery must be between 40 and 70 years old, be in the intermediate or advanced stages of the disease, present disabling motor symptoms that do not respond adequately to drug treatment or that cause intolerable side effects, have no clinical or surgical contraindications, have realistic expectations about results and accepting the risks inherent to the procedure. Additionally, neurosurgery candidates must undergo a detailed neurological evaluation, which includes tests of motor, cognitive, emotional, and autonomic function.

The benefits of neurosurgery for Parkinson's disease are based on improving motor symptoms, reducing medication side effects, preserving cognitive functions and improving patients' quality of life. In general, the benefits are greater for deep brain stimulation than for ablative surgery, as deep brain stimulation is more effective, safer, and reversible than ablative surgery. However, benefits may vary according to the target of surgery, follow-up time, patient characteristics and the quality of adjustment of stimulation parameters.

The risks of neurosurgery for Parkinson's disease are based on the complications that may occur during or after the procedure. In general, risks are greater for ablative surgery than for deep brain stimulation because ablative surgery is more invasive and irreversible than deep brain stimulation. However, risks may vary depending on the target of the surgery, the type of anesthesia, the surgeon's experience and post-operative care. The most common complications are intracerebral hemorrhage, infection, neurological deficits, cognitive or psychiatric changes, device dysfunction, and inadequate stimulation.

Assessment of the quality of life of patients with Parkinson's disease can be carried out using specific or generic instruments. Specific instruments are those that

have been developed to measure health-related quality of life in patients with Parkinson's disease, such as the Parkinson's Disease Questionnaire (PDQ-39), the Parkinson's Disease Quality of Life Scale (PDQL), and the 39-item Parkinson's Disease Quality of Life Questionnaire (PDQ-39). These instruments address aspects such as mobility, activities of daily living, communication, mood, stigma, social support, cognitions and bodily complications. Generic instruments are those that can be applied to different populations and health conditions, such as the Short Form Health Survey (SF-36), the EuroQol Five Dimensions Questionnaire (EQ-5D) and the World Health Organization Quality of Life (WHOQOL) . These instruments address aspects such as physical health, mental health, social performance, functional performance and satisfaction with life.

Comparison between the two types of neurosurgery for Parkinson's disease can be carried out through clinical studies that evaluate clinical outcomes (motor symptoms, medication side effects, cognitive functions and quality of life) and adverse outcomes (surgical complications, device dysfunction and inadequate stimulation) of patients undergoing different procedures.

In general, deep brain stimulation appears to be superior to ablative surgery in terms of efficacy, safety, and impact on patients' quality of life. Deep brain stimulation is more effective than ablative surgery in improving motor symptoms, reducing medication side effects, preserving cognitive functions, and improving patients' quality of life. Deep brain stimulation is safer than ablative surgery in causing fewer complications such as hemorrhage, infection, neurological deficits and cognitive or psychiatric changes. Deep brain stimulation is more reversible than ablative surgery in allowing adjustments to stimulation parameters or removal of the device. However, deep brain stimulation also has some disadvantages compared to ablative surgery, such as higher cost, the need to periodically change the pulse generator battery, and the risk of device dysfunction or inadequate stimulation.

CONSIDERAÇÕES FINAIS

The treatment of Parkinson's disease involves the use of medications that replace dopamine in the brain, but which can cause undesirable side effects.

Neurosurgery is a therapeutic option for some selected patients, which aims to reduce the abnormal activity of the basal ganglia through irreversible damage (ablative surgery) or adjustable electrical impulses (deep brain stimulation). Neurosurgery can improve motor symptoms, reduce medication side effects, preserve cognitive functions and improve patients' quality of life.

However, neurosurgery can also cause complications such as hemorrhage, infection, neurological deficits, cognitive or psychiatric changes, device dysfunction, and inadequate stimulation. The choice of the type of neurosurgery should be based on clinical criteria, expected benefits, potential risks and patient preferences. The evaluation of the indication criteria, benefits and risks of neurosurgery for Parkinson's disease must be carried out by a multidisciplinary team, which monitors patients before, during and after the procedure.

The systematic review of the literature on the benefits and risks of neurosurgery for Parkinson's disease showed that deep brain stimulation appears to be superior to ablative surgery in terms of efficacy, safety and impact on patients' quality of life. However, there is still a need for more studies with greater methodological rigor, longer follow-up time and greater representation of the population to confirm these findings.

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