AANA JOURNAL COURSE

Update for nurse anesthetists

*6 CE Credits

Parkinson disease

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In this Journal *course, the manifestations, etiologic and pathophysiologic factors, and incidence of Parkinson disease are reviewed along with current medical management. Medications and other factors that have an impact on the course of* Parkinson disease are discussed. Suggested preanesthetic, intraoperative, and postoperative interventions are provided.

Key words: Anesthetic management, neuroanatomy, Parkinson disease.

Objectives

At the completion of this course, the reader should be able to:

1. Describe the clinical manifestations and clinical course of Parkinson disease.
2. List the known etiologic factors related to Parkinson disease.
3. Discuss variables that modify the course of Parkinson disease.
4. Review the pharmacological agents that are used to treat this disease.
5. Describe anesthesia considerations for patients with Parkinson disease.

Introduction

Parkinson disease (PD) is a degenerative neurologic disorder that affects the extrapyramidal system, leading to a lack of coordinated motor control. The excitatory effects of acetylcholine are left unchecked by a decrease in dopamine levels, resulting in symptoms such as tremor, muscular rigidity, hypokinesia, and postural instability.[1] One in 1,000 middle-aged adults and 50 in 1,000 older adults are affected by PD.[2] Because PD has no known cure, therapy is directed at ameliorating symptoms.[3] This course reviews the pathophysiologic and etiologic factors associated with PD and provides a review of the anesthetic assessment, intraoperative management, and postoperative care of patients with PD. Contemporary issues related to the medical and surgical management of PD also are explored.

Pathophysiologic factors

Parkinson disease is a dopamine deficiency disorder that involves the selective destruction of dopamine-producing tissues in the midbrain called the substantia nigra. Dopamine has an integral role as a neurotransmitter helping to regulate motor coordination. This coordination involves complex neuronal interplay among fibers in the basal ganglia as part of the extrapyramidal system. Inputs to the basal ganglia are directed from the cerebral cortex to modulate motor control. The basal ganglia are 5 primary structures in the telencephalon that include the caudate and putamen (striatum), substantia nigra, globus pallidus, and the subthalamic nucleus.

Two basic output pathways are defined through the basal ganglia. In the direct output pathway, striatal D_1 receptors respond to dopamine by causing an excitatory output to the medial globus pallidus. Conversely, striatal D_2 receptors respond to dopamine by causing inhibition of the indirect output pathway involving the subthalamic nucleus and lateral globus pallidus. The net result of inadequate dopamine production is inhibition of the direct output pathway and increased activity of the indirect output pathway.[4] Inhibitory output is mediated to the thalamus and cerebral cortex, resulting in classic PD symptoms (Table).[5]

Etiologic factors

Nigral cell death is the defining pathology that distinguishes PD. Cell death in the substantia nigra results in the presence of Lewy bodies with a loss of pigment

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Table. Classic Parkinson disease symptoms

Bradykinesia	Slowness in movement, which includes difficulty initiating movement and incompleteness of movement
Tremor	Tremor appears in the limbs during rest.
	Tremor most often involves the hand. A tremor involving the thumb and index finger is very typical and is called a pill-rolling tremor.
Rigidity	Rigidity sometimes is mistaken for arthritis and is defined as increased resistance to stretch.
Postural instability	Defined as imbalance and the inability to correct posture according to environmental needs.
	The shuffling gait associated with Parkinson disease results from postural instability and bradykinesia.

(Adapted from Liebermann.[5])

in this central nervous system (CNS) structure.[5] In 1913, Otto Lewy discovered a round, pink staining body—the Lewy body—in the cytoplasm of PD nerve cells. On autopsy, the presence of Lewy bodies in the substantia nigra and the noradrenalin cells of the locus ceruleus are considered essential for diagnosing PD. Until the advent of positron emission tomography, however, the clinical diagnosis of PD was based strictly on symptomatology. The etiologic factors for selective destruction of dopamine-producing fibers in the substantia nigra continue to be investigated.

Genetic links have been found (chromosome 4) in some patients with PD, but most cases are not familial. A popular hypothesis related to PD is that environmental toxins selectively kill dopamine neurons over time. This hypothesis is supported by the fact that PD is primarily a disease of advanced age. The higher incidence of PD demonstrated in persons working with pesticides and certain metals or chemicals seems to support the environmental toxin hypothesis.[6]

Oxidative stress has an important role in the neurodegenerative processes associated with PD. The substantia nigra has an intrinsically low ability to neutralize oxygen free radicals. Deficiencies in superoxide dismutase have been documented in some patients with PD. Unfortunately, it is not known whether deficient oxygen radical processing is a result or a cause of nigral destruction.[2] Iron processing is associated with oxidative processes, and several studies demonstrate increased iron levels in the substantia nigra of patients with PD. It remains unclear whether elevated iron levels antedate injury to dopamine-producing neurons in the CNS.[7]

Lifestyle factors also may contribute to the incidence of PD. Dietary intake of excess animal fats, certain herbal teas, and a toxin in chick peas may be associated with an increased incidence of PD.[6] Certain "recreational drugs" are thought to contribute to the development of PD. Methamphetamine, for example, is known to cause the degeneration of dopamine-producing neurons. Another popular "club drug" called Ecstasy (MDMA; 3,4-methyl-enedioxymethamphetamine) is structurally similar to methamphetamine. Ecstasy is known to cause a disruption in the transport of both dopamine and serotonin.[8] While these findings support the oxidative stress hypothesis, the interaction among genetic factors and environmental stress is confounding, making elucidation of causes of PD difficult.
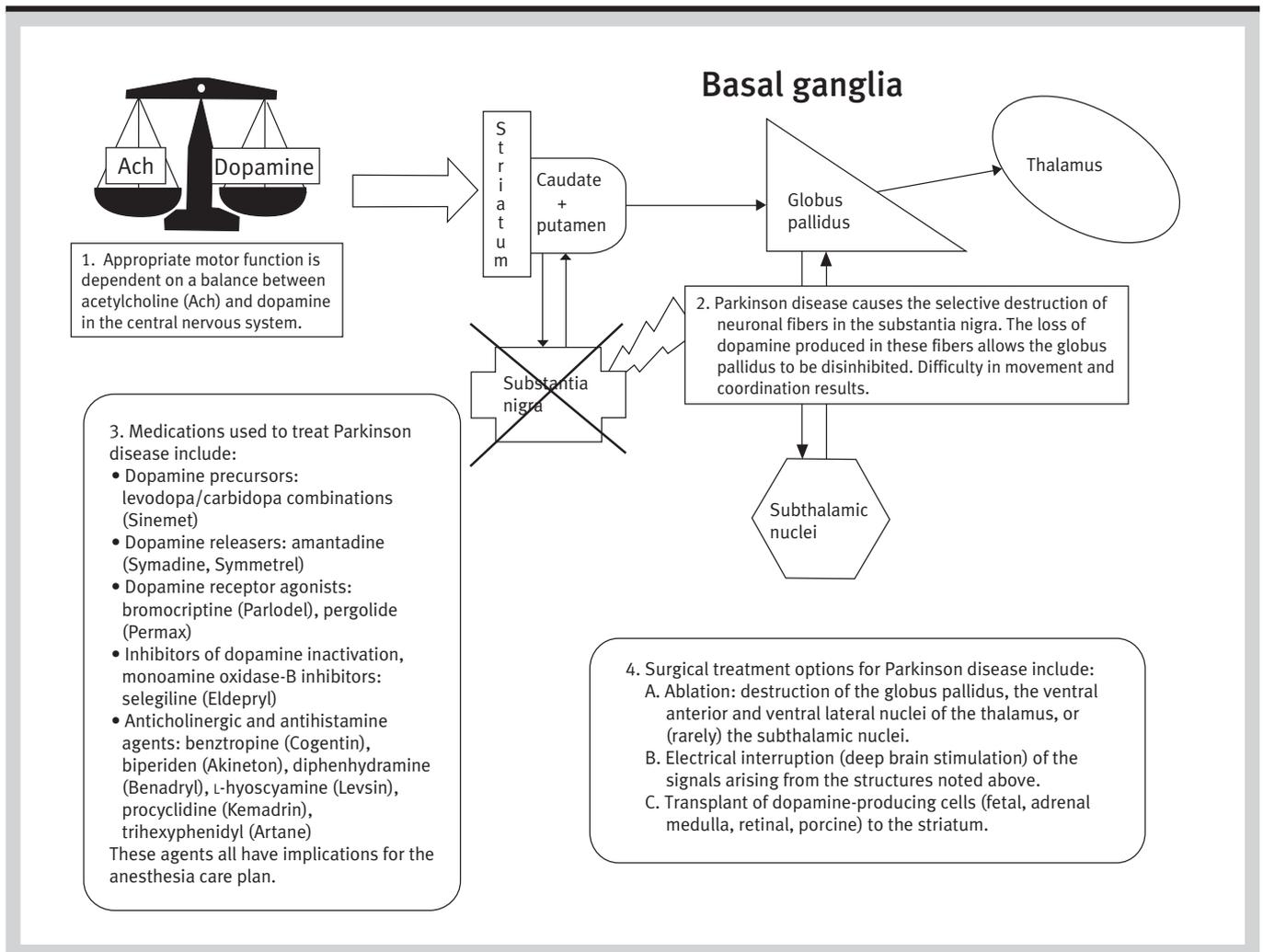
It is interesting, and somewhat counterintuitive, to note that cigarette smoking is associated with a diminished incidence of PD. This relationship is well documented, but its explanation remains unclear. Proposed explanations for the "protective" effects of cigarette smoking include stimulation of dopamine release and up-regulation of nicotinic receptors, carbon monoxide inhibition of hydrogen peroxide, competitive inhibition of neurotoxins, and the inhibition of monoamine oxidase.[9] Caffeine consumption also is associated with a decreased incidence of PD.[10] Since caffeine is a known CNS stimulant, it may have an important role in neurotransmission and extrapyramidal modulation.[11]

Literature review

To provide evidence-based perioperative care, the anesthetist must be aware of new ways to treat PD. While the medications used to treat PD are not new, many investigators now advocate using medications other than levodopa during the initial stages of PD. Recent data suggest that dopamine agonists have neuroprotective effects, which delay CNS fiber destruction. Dopamine receptor agonists such as bromocriptine meslyate and pergolide mesylate are effective during the initial treatment of PD. Monoamine oxidase inhibitors such as selegiline hydrochloride are used to selectively increase the level of dopamine in the basal ganglia. Anticholinergic agents such as benztropine mesylate decrease the transmission of acetylcholine and theoretically restore the balance between excitatory and inhibitory neurotransmission. Amantadine hydrochloride, a nonspecific antiviral agent, also may be useful during the initial stages of PD. Entacapone and other catechol *O*-methyltransferase (also called COMT) inhibitors have been shown to be effective adjuncts to levodopa therapy.[12,13]

The inexorable progression of PD despite available pharmacological therapy has led to a resurgence of interest in surgical therapies. Surgical therapy for PD can be classified broadly into 3 areas: ablative therapies, deep

Figure. Pathophysiology and treatment of Parkinson disease

Basal ganglia

1. Appropriate motor function is dependent on a balance between acetylcholine (Ach) and dopamine in the central nervous system.

2. Parkinson disease causes the selective destruction of neuronal fibers in the substantia nigra. The loss of dopamine produced in these fibers allows the globus pallidus to be disinhibited. Difficulty in movement and coordination results.

3. Medications used to treat Parkinson disease include:
- Dopamine precursors: levodopa/carbidopa combinations (Sinemet)
- Dopamine releasers: amantadine (Symadine, Symmetrel)
- Dopamine receptor agonists: bromocriptine (Parlodel), pergolide (Permax)
- Inhibitors of dopamine inactivation, monoamine oxidase-B inhibitors: selegiline (Eldepryl)
- Anticholinergic and antihistamine agents: benztropine (Cogentin), biperiden (Akineton), diphenhydramine (Benadryl), L-hyoscyamine (Levsin), procyclidine (Kemadrin), trihexyphenidyl (Artane)

These agents all have implications for the anesthesia care plan.

4. Surgical treatment options for Parkinson disease include:
- A. Ablation: destruction of the globus pallidus, the ventral anterior and ventral lateral nuclei of the thalamus, or (rarely) the subthalamic nuclei.
- B. Electrical interruption (deep brain stimulation) of the signals arising from the structures noted above.
- C. Transplant of dopamine-producing cells (fetal, adrenal medulla, retinal, porcine) to the striatum.

brain stimulation (DBS), and transplantation procedures.[14] Thalamotomy is an ablative procedure that targets the removal of the ventral intermediate nucleus of the thalamus to reduce tremor. The procedure is not new, but recent advances in neurologic imaging before surgery have made the procedure safer.[15] These advances may require anesthesia involvement during structural brain imaging procedures done via computed tomography, magnetic resonance imaging, or positron emission tomography. Removal of neurologic circuits associated with other thalamic structures such as the globus pallidus is another ablative procedure that has been found to offer improvement for some people with PD.[16] Subthalamic nucleotomy is an intriguing ablative procedure that remains experimental because of the deep neurologic structures involved with this surgical intervention.[14]

DBS offers a way of controlling PD symptoms without permanently removing CNS structures. DBS involves the application of high-frequency stimulation to targeted brain structures via an implanted "pacing" wire connected to a programmable pulse generator.[17]

DBS offers the advantage of selectively blocking the amount of neurologic outflow and is titratable without permanently removing tissue. Compared with ablative procedures, DBS offers similar neurologic outcomes for suppression of severe tremor in PD.[18]

Experimental transplantation procedures involving embryonic neurons have increased the number of functional dopaminergic fibers for patients with severe PD. Freed and colleagues[19] reported clinical benefits to younger, but not older, patients who received embryonic transplant. Ethical considerations, the lack of available embryonic tissue, and complications related to immunosuppression make transplantation of porcine cells and of human retinal cells viable investigational options for the treatment of advanced PD.[20] The Figure summarizes the pathophysiology and contemporary medical or surgical treatment options available for patients with PD.

The anesthetist should recognize that ablative, DBS, and transplantation procedures are reserved for patients with PD with severe functional disability. Neurosurgery for PD is lengthy, making perioperative management,

including positioning and close monitoring, even more important. Understanding contemporary medical or surgical treatment options helps the anesthetist anticipate needs for the preoperative assessment, intraoperative management, and postopertive care of patients with PD.

Preoperative assessment

The medication history provides clues about PD severity and can affect the intraoperative anesthesia plan. The coadministration of levodopa, a metabolic precursor to dopamine, and carbidopa, a peripheral decarboxylase inhibitor that prevents the breakdown of levodopa outside the CNS, is the most effective medical treatment for PD.[4] Levodopa administration has implications for the intraoperative anesthesia plan since it can cause nausea, vomiting, orthostatic hypotension, and cardiac irritability. Regardless of the pharmacologic regimen used, the anesthetist should note that abrupt withdrawal of any medication to treat PD may exacerbate PD symptoms. Patients should be instructed to take PD-specific medications the day of surgery unless otherwise indicated.[3]

A focused assessment specific to neurologic function, respiratory function, and cardiac function is appropriate for patients with PD. During the assessment, unilateral tremor while signing the surgical consent or during venipuncture are subtle clues that should trigger additional investigation. Skeletal muscle rigidity manifested in the proximal muscles of the neck is an early sign of PD, alerting the anesthetist to the potential for difficult airway management. Paresthesia is not part of the normal PD process, but any movement or sensation abnormalities should be documented. Other significant findings during the preoperative assessment may include pupillary abnormalities, diaphragmatic spasms, and oculogyric crises. PD does not cause decreased cognitive function, but patients may exhibit dementia or signs of depression in advanced stages of the disease process.[21]

PD is classified into 5 stages with functional ability related to the degree of neurologic degeneration. Stage I (onset) involves difficulty with unilateral movement. The disease eventually progresses to stage V (severe disease), which is characterized by immobilization of the patient. In the absence of diagnosed PD, a surgical patient with unexplained muscle stiffness or minor tremor should be referred for postoperative neurologic examination.

PD is not a primary cause of respiratory or cardiac dysfunction. The dyskinesia associated with advanced PD, however, often causes chest rigidity and is associated with chronic obstructive pulmonary disease. Careful respiratory assessment, including documentation of preanesthetic oxygen saturation, is essential. Compro-

mised respiratory function should be evaluated by arterial blood gas analysis or chest radiograph. The majority of medications used to treat PD cause increased cardiac irritability and blunting of autonomic regulatory responses. Close assessment of cardiac status and volume status is of particular importance.[3]

Intraoperative management

The intraoperative anesthetic management of patients with PD includes preparing for the induction of anesthesia, avoidance of specific anesthetic agents that exacerbate PD symptoms, and preparing for emergence from anesthesia. Before induction, aspiration prophylaxis may be considered due to alterations in muscular tone and coordination that may predispose the patient to pulmonary aspiration. A nonparticulate antacid such as sodium citrate and an H_2 blocking agent such as famotidine can be administered 30 to 60 minutes before induction. The gastroprokinetic metoclopramide should be avoided because it induces antidopaminergic activity and may exacerbate extrapyamidal symptoms.[22]

An anxiolytic such as midazolam is appropriate after the anesthesia interview since emotional stress has been found to trigger PD symptoms. Ensure that a benzodiazepine is not contraindicated from a surgical perspective, eg, awake thalamotomy, pallidotomy, or DBS. Diphenhydramine also is a valuable sedative for patients with tremor.[23] Positioning on the operating room table takes on added importance for patients who have changes in physical mobility. Assuring proper positioning and padding before anesthesia induction and throughout surgery helps diminish injury risk for patients with PD.[1]

Relatively few contraindications exist regarding the choice of induction agents and anesthesia techniques for patients with PD. Hypotension related to hypovolemia, catecholamine depletion, and autonomic instability often are side effects of medications used to treat PD. For patients with severe PD, blood pressure should be monitored invasively and the anesthetist should be prepared to administer a direct-acting vasopressor (phenylephrine or epinephrine) for profound hypotension. Awake or rapid-sequence intubation is indicated only in the most severe cases of PD in which the disease has resulted in respiratory compromise or esophageal spasms that increase aspiration risk.[24] There is no reported contraindication to the use of succinylcholine that is specific to patients with PD.

Ketamine is the only commonly used induction agent that should be avoided in patients with PD. Ketamine produces sympathomimetic responses that may exacerbate PD symptoms. The choice of muscle relaxants is not influenced by the presence of PD and should be

evaluated according to the type and duration of surgery, the need for immediate airway access, and coexisting disease. With the exception of halothane, PD does not limit the choice of inhalation anesthetics. Halothane sensitizes the myocardium to the effects of catecholamines and could promote instability when combined with pharmacologic agents used to treat PD.[24]

Perioperative pain management may include the use of systemic opioids. However, opioids decrease central dopaminergic transmission resulting in dystonia, or a "woody chest." Alfentanil has been implicated in producing acute dystonic reactions in patients with PD.[24] Judicious use of nonsteroidal anti-inflammatory drugs and local anesthetic infiltration also can be considered for perioperative analgesia.

Extubation can proceed normally as long as the anesthetist recognizes that patients with PD are at greater risk for developing postextubation respiratory compromise due to hypokinesis of the chest cavity. In its advanced stages, PD interferes with all muscles of respiration, including intercostal, diaphragmatic, accessory, and abdominal muscle groups, potentially leading to the need for prolonged ventilatory support. An anticholinesterase-anticholinergic combination may be used if indicated to reverse neuromuscular blockade. An additional dose of an anticholineric agent such as glycopyrrolate, 0.2 mg intravenously, is indicated if the anesthetist notes excessive secretions that often are part of the PD disease process. Anticholinergic effects also will diminish the excitatory effects of acetylcholine that contribute to dystonia.

Postoperative management

Postoperative management of patients with PD should include a plan for the resumption of preoperative medications to avoid exacerbation of PD symptoms. Careful assessment of neurologic function and movement should be documented postoperatively. Postoperative tremor can be treated with diphenhydramine, 25 mg intravenously, which also is useful as a drying agent. Problems with chest wall rigidity or respiratory compromise should be assessed carefully and can be treated with an anticholinergic such as glycopyrrolate or atropine to decrease acetylcholine output. Scopolamine should be avoided because it potentially causes changes in mental status and may confound the neurologic examination of patients with PD.[2]

Opioids are acceptable for pain management, but these drugs should be replaced with alternative agents such as oral or intravenous nonsteroidal anti-inflammatory drugs as soon as possible. If it is not otherwise contraindicated, ketorolac is a good choice for pain management in patients with PD because it does not interfere with respiratory function. Postoperative nausea and vomiting are more likely for patients with PD. Treatment plans must avoid phenothiazines, droperidol, and other butyrophenones because they are dopamine antagonists that potentially exacerbate PD symptoms. Ondansetron and dolasetron are good choices for the management of postoperative nausea and vomiting since they do not interfere with the transmission of dopamine.[24]

Key points

Anesthesia care of patients with PD depends on knowledge and skills of the anesthetist related to the following key areas:

• Classify the patient with respect to severity of PD symptoms: mild (unilateral tremor), moderate, or severe (very restricted movement).

• Determine the medications used to control PD symptoms and the duration of drug therapy.

• Document a neurological assessment. Investigate movement and strength, pupillary response, and diaphragmatic movements. A "stiff" neck during airway evaluation may be indicative of PD.

• Evaluate respiratory function. Anticipate chest rigidity in patients with advanced PD.

During the intraoperative phase, the following elements are important:

• Carefully position the patient and monitor pressure points.

• Anticipate and appropriately treat hypovolemia, hypotension, and arrhythmias.

• Avoid or consider avoiding the following agents: metroclopramide, droperidol, haldoperidol, promethazine, compazine, ketamine, alfentanil, meperidine, and halothane.

• Before extubation, assess spontaneous breathing pattern, presence of gag reflex, ability of patient to focus, and presence of 4 twitches or sustained tetanus.

During the postoperative phase, bear these considerations in mind for patients with PD:

• A plan to resume scheduled PD medications is a priority.

• Fully assess and document neurologic function.

• Consider diphenhydramine for tremor, but avoid meperidine for shivering since it may exacerbate PD symptoms.

• Evaluate respiratory function.

• Use intravenous ketorolac or other nonopioid analgesics, if possible. for postoperative pain.

• Ondansetron or dolasetron may be used for postoperative nausea and vomiting.

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