Lesson S05: PreAnesthetic Assessment of the Patient for Deep Brain Stimulation

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Needs assessment

With an expanding society of persons living to advanced age, movement disorders such as Parkinson’s disease remain consistently prevalent. Deep brain stimulation is a recognized approach to management of uncontrollable movement. This technique has advanced significantly over the past 4 decades and the role of the anesthesiologist is vital to achieving a positive outcome. To provide optimal care, the anesthesiologist should possess a clear understanding of the procedure, the specific needs of patient, and the requirements of the surgical team.

Objectives

At the end of the lesson, the participant will be able to:

1. List indications for deep brain stimulation.
2. Describe the salient features of Parkinson’s disease.
4. Identify the target for deep brain stimulation for Parkinson’s disease.
5. List complications of the procedure.
6. Outline an anesthetic plan for each stage.
7. Describe the signs, symptoms and treatment of air embolism.
8. List the effects of dexmedetomidine.
10. List the anesthetic concerns for a patient with Parkinson’s disease.
Case Presentation

A 76 year old male with Parkinson’s disease was scheduled for insertion of electrodes for deep brain stimulation. The patient was alert and oriented. A marked tremor interfered with his quality of life. Current medications included levodopa (Sinemet®), bromocriptine (Parlodel®), selegiline (Eldepryl®), pramipexole (Mirapex®) and amantadine (Symmetrel®). This regimen afforded only fair movement control. He was clinically depressed and sertraline hydrochloride (Zoloft®) had been prescribed. He had a history of hypertension which was treated with hydrochlorothiazide and diltiazem; diabetes, controlled with diet and glyburide; and gastroesophageal reflux disease.

Introduction

Deep brain stimulation (DBS) techniques have evolved over the past 4 decades. Thalamic DBS was developed initially as therapy for Parkinson’s disease and was shown to be an effective treatment for movement disorders, including dystonias.1 Brain targets such as the subthalamic nucleus and the internal globus pallidus were investigated. DBS has been shown to improve intractable epilepsy, cephalgias, restless legs syndrome, multiple sclerosis, pantothenate kinase-associated neurodegeneration, Tourette syndrome, major depressive disorders, obsessive compulsive derangements and other movement disorders, including essential tremor, and post traumatic tremor.2–8 Several studies in Europe and Canada have reported the use of DBS to treat refractory pain, especially for failed back surgery, although DBS has been slow to gain approval in the United States for this purpose. With such a wide range of disorders treatable with DBS, anesthesiologists are often called to assist with patients with multiple pathologies.

Parkinson’s Disease

Parkinson’s disease is a neurodegenerative condition resulting from neuronal loss in the dopaminergic substantia nigra pars compacta (SNCs). Projections from the SNCs to the striatum normally control fine movements. The initial response to a reduction in dopaminergic input is upregulation of the dopamine receptors in the striatum. With increasing loss of somata in the SNCs, clinical symptoms appear. Dysfunction initially occurs unilaterally in the form of micrographia, hand tremor, decreased arm swing, and foot dragging. Eventually, bilateral symptoms appear as bradykinesia, resting tremor and postural instability. A therapeutic response to levodopa (L-dopa) can be documented. Almost 90% of Parkinsonian patients will have significant vocal fold bowing and adduction, and pharyngeal residues of solids can be found on evaluation of swallowing.

Parkinson’s disease is a clinical diagnosis, confirmed at postmortem analysis by demonstration of Lewy bodies and the loss of dopaminergic neurons in the SNCs. The degeneration of SNC dopaminergic neurons, which project to the striatum as the nigrostriatal pathway, leads to a reduction in striatal dopamine content and eventually to the clinical phenotype.

Deep Brain Stimulation

One early hypothesis suggested that DBS inhibited neuronal activity by mimicking the outcome of ablative surgeries. Recent studies have challenged that view. Although somatic activity near the DBS electrode may exhibit substantial inhibition or complex modulation patterns, the output from the stimulated nucleus follows the DBS pulse train by direct axonal excitation. The intrinsic activity is replaced by high frequency activity that is time locked to the stimulus and exhibits a more regular
pattern. Changes in firing pattern may prevent transmission of pathologic firing and oscillatory activity, reducing adverse symptoms by compensatory processing of sensorimotor information.\(^9\)

DBS often requires the use of several distinct procedure locations, e.g., the radiology suite, the operating room, or the neurophysiology laboratory. Placement of the electrodes is usually a long process performed with minimal sedation and considerable monitoring. Following successful placement, the patient must return about 2 weeks later for insertion of the generator in the upper chest. This part of the procedure is performed under general anesthesia in the operating room as it requires a large incision and tunneling.

In the patient’s room or holding area, the DBS procedure begins by attaching a frame to the patient’s head after administration of local anesthesia or regional block. The patient is then taken to the radiology suite where preoperative images are obtained. Thereafter, the patient is moved to the neurophysiology laboratory or operating room. A burr hole is made under local anesthesia and sedation, if necessary. The optimal positions for the electrodes are identified, usually with little or no sedation. Following placement of the stimulators and testing, the patient receives an MRI or CT scan to confirm placement of the electrodes and to rule out potential hematoma. In most centers, the patient is observed overnight and discharged the next day.

Recently, techniques have been developed for frameless navigation targeting for DBS. These approaches simplify the preoperative planning of electrode trajectories and eliminate frame placement and scanning on the day of surgery, thus shortening the process. Also, the time away from Parkinson’s medications is reduced and access to the airway is easier. However, current frameless DBS equipment is cumbersome and limits the area over which deep brain mapping can be performed.\(^{10}\)

**Preanesthetic Assessment**

Routine evaluation includes complete blood count, electrolyte screening panel including blood sugar level (which should be controlled at or below 120mg/dl), urinalysis to exclude urinary tract infection, and assessment of renal and liver function. Most of these patients have multiple co-morbidities and baseline screening is useful. Review of blood count commonly reveals iron deficient anemia. A chest X-ray should be carefully reviewed for any evidence of aspiration, a common occurrence in Parkinsonian patients. Cardiac co-morbidities may also require an electrocardiogram. The patient’s current antihypertensive medications should be continued and beta blocker therapy given the day of the procedure if indicated. Blood pressure should be controlled at or below 150 systolic to minimize the risk of hemorrhage. A blood specimen for type and screening of blood prior to surgery should be obtained. While blood transfusion is rarely necessary, should it be required, it will be an emergent situation. One of the serious complications of DBS is intracerebral hemorrhage, which has been estimated to occur in about 3-5% of patients.\(^{11}\) Aspirin and coumadin should be discontinued several days before DBS. Antiseizure medications such as carbamazepine or valproate may cause thrombocytopenia even though leukopenia is more common. Therefore, the type of antiseizure drugs used and any history of bleeding should be carefully evaluated preoperatively, and platelet and white blood cell counts measured.

Most Parkinson’s Disease therapies aim to increase dopamine availability. However, these drugs often have short half lives and effectiveness is limited with time. Associated side effects include dry mouth, orthostatic hypotension, nausea, vomiting, visual disturbances and urinary retention. Drug interactions also occur, especially if monoamine oxidative inhibitors are used. To produce maximum
effect during brain stimulation, medications are withheld on the day of surgery. Patients will often develop increasing discomfort as the procedure continues. For those patients receiving DBS for the treatment of epilepsy, the side effects and drug interactions of anti-epileptic agents must be considered. Side effects include hepatic enzyme induction, competitive metabolic inhibition and plasma protein level and binding. Drug interactions directly effect the duration of effect of other agents. Ingestion of herbal preparations such as gingko, ginger, garlic and ginseng among others may interfere with clotting. If the DBS procedure is intended for pain reduction, narcotic patches and their doses should be identified.

Patient cooperation is important as patients are kept awake during much of the procedure to facilitate identification of areas of the brain and accurate electrophysiologic recording. Prior to the procedure, the patient should be assessed for their baseline ability to answer questions typically used to monitor impact on speech centers and to perform simple evaluative tasks such as “squeeze my hand or move your toes.” Language and competency should be ascertained as well as whether the patient is able to read with or without the use of glasses so that a proper baseline is established when assessing impact on vision. For patients with seizure disorders, the anesthesiologist should determine if the type of aura experienced prior to a seizure so that appropriate medications may be promptly given to avert a seizure.

Premedication depends on the procedure and the specific needs of the patient. Small doses of benzodiazepines may benefit anxious patients or patients with arthritis who have limited tolerance for lying flat or still. Benzodiazepines are also suitable for patients for which seizure activity is not expected to be provoked such as ablation of identified epileptic foci. Intravenous diazepam given prior to contrast injection may reduce the incidence of contrast-associated seizures with the exception of the amytal test which is preceded by cerebral angiography. Amobarbital 30mg is injected into an artery supplying eloquent cerebral areas to determine neurologic function prior to devascularization and sedative drugs are not recommended. For Parkinsonian patients, premedication may consist of antiemetics and antacids as difficulty in swallowing and aspiration is common. Anticonvulsants are usually given preoperatively but in reduced doses at the discretion of the neurosurgeon. Some evidence suggests that hemodynamic stability may be increased during pin head holder insertion if clonidine is given orally 90 minutes before placement.12

Neurosurgeons and neurophysiologists often have protocols in place for sedation and hemodynamic control. The anesthesiologist should be familiar with these protocols and discuss their content with the other members of the team preoperatively.

Airway evaluation is of particular importance in the preanesthetic assessment for patients undergoing DBS. With waning of the effects of maintenance drugs, patients may become rigid and mouth opening may be very difficult. Primary laryngospasm is a known complication of Parkinson’s Disease and acute withdrawal of treatment can cause airway obstruction.13 Patients who have been receiving dilantin may have gum hypertrophy and impaired dentition such as loosening of teeth that may hamper placement of an airway. When DBS is performed, the head is typically held in a frame, secured to the table, with a bar that crosses in front of the mouth. Sedation may be increased if the procedure is lengthy or intraoperative complications develop. Should aspiration, vomiting or respiratory depression occur, a means to support ventilation must be immediately available. Careful preoperative assessment of the airway is imperative and the difficult airway cart should be available with a variety of blades and tube sizes as well as a means to perform fiberoptic intubation. Availability of a GlideScope® is desirable. Supraglottic airways are particularly valuable as they can be placed with little or no head
movement and with minimal opening of the mouth. A tracheostomy kit should also be available. The anesthesiologist should be knowledgeable of the mechanics of the frame and learn how to release the face piece in the event of an emergency.

**Anesthetic management**

The neuronal circuitry between the striatum and the globus pallidus and the subthalamic nucleus (STN) where GABAergic pathways are involved is complex. Limited use of anesthetic agents with GABAergic activity (like benzodiazepines or propofol) is preferred but not always possible.

Anesthetic concerns for patients with Parkinson’s Disease include the following:

- increased sensitivity to anesthetic agents
- increased risk of laryngospasm and diaphragmatic spasm
- increased risk of aspiration
- hallucinations (visual and tactile)
- decreased vital capacity which may lead to pulmonary complications
- post-operative delirium
- muscle tremors that produce ECG changes mimicking ventricular fibrillation
- extrapyramidal symptoms

Side effects of L-dopa consist of depletion of myocardial norepinephrine stores, peripheral vasoconstriction, hypovolemia, and orthostatic hypotension. Hypertensive patients may experience wide swings in blood pressure. Glycopyrrolate offers protection against neostigmine induced bronchoconstriction in normal subjects. However, in Parkinsonian patients, bronchospasm and obstruction are more likely induced by parasympathetic hyperactivity and susceptibility to the muscarinic effects of neostigmine. Therefore, glycopyrrolate in usual doses may be inadequate. Use of neostigmine is best avoided.

Anesthetic management is divided into 3 stages:

**Stage 1**

The placement of a frame to secure the patient’s head occurs in either the patient’s room or in a holding area. A scalp block can be used or local infiltration at the site of the pins. A small amount of sedation is often beneficial. As noted above, all involved personnel should be familiar with the mechanics of the frame and how the face piece may be removed in an emergency.

**Stage 2**

In the CT or MRI suite, problems associated with the delivery of anesthesia in a remote location may arise. Often, little or no sedation is required but monitoring must continue. The head frame makes it more difficult for the patient to find a comfortable position. DBS may infrequently be used in children. Propofol and dexmedetomidine have been proven useful in both CT and MRI studies.14,15
Stage 3

In the operating room, a burr hole is made and implantation of the electrodes is performed by a team typically consisting of a neurosurgeon, an electrophysiologist, and a neurologist. Pulse, amplitude, and electrical port measurements are adjusted to optimally inhibit STN output to the thalamus or other area of the brain to be stimulated. Patients typically experience anxiety but little or no pain. Standard monitors are applied and invasive monitoring is rarely necessary. The neurosurgeon monitors electrical activity. As the patient is awake, the best monitor for the anesthesiologist is the patient’s response to either verbal or movement commands. Use of an awareness monitor may add information in determining wakefulness if more sedation becomes necessary. Such a monitor may also assist in detecting sudden deterioration if neurological activity decreases without the administration of medication.

Hemodynamic stability can best be achieved with small doses of narcotics. Labetalol, 5-10mg may be used in a patient with a history of hypertension. Hydralazine is another choice. When other agents have failed nicardipine infusion is effective and easily titrated. Scalp infiltration with bupivacaine will reduce perturbations of blood pressure on incision.

Prior to making the burr hole, local anesthesia is injected by the surgeon around the operative site and a small dose of midazolam (1-1.5mg) and/or fentanyl (25-50ug) are given. Midazolam may have prolonged effects in elderly patients and, as such, the surgeon and neurophysiologist may wish to withhold administration of this agent. If necessary, sedation with consciousness may be achieved with a bolus injection of propofol (20-30mg) followed by a propofol infusion of 10-20ug/kg/min (up to 50-60ug.kg/min in one study). As the surgeon places the electrodes, communication between the operator and the patient is essential. Any patient movement may seriously compromise precise placement. To facilitate cooperation, patient aptitude must be maintained. In some centers, no sedation is used; or a combination of midazolam, fentanyl in small divided doses and a propofol infusion (which acts at the GABA receptors) has been used to allow adequate sedation for many hours. Remifentanil 0.1ug/kg/min may cause rigidity, and a bradycardic effect especially in patients who have received beta blocking medications.

Dexmedetomidine is a highly specific α2-receptor agonist that offers “cooperative sedation”, anxiolysis and analgesia without respiratory depression. An awake and cooperative patient must be capable of undergoing neurocognitive testing and dexmedetomidine is particularly valuable when eloquent areas of the brain are stimulated. Patients can be awakened easily by verbal stimulation. Cerebral effects are consistent with a desirable neurophysiologic profile including neuroprotective characteristics. Sympatholytic and antinociceptive properties give hemodynamic stability during periods of critical neurosurgical stimulation, as demonstrated in a study of 11 patients undergoing microelectrode recording (MER) of the STN. The quality of MER was also evaluated in this study as a function of BIS® (>80), and prompt clinical arousal. An acceptable dose of dexmedetomidine was determined to be 0.1-0.4μg/kg/hr. The drug is not approved for use in Europe because of a potential dose dependent hypotension and bradycardia. Dexmedetomidine has anticonvulsant effects in rats. But in a series of patients for whom the drug was used as a sedative during awake craniotomy, the anticonvulsant effect was specifically questioned and the results were inconsistent. When patients need not be awake for parts of the procedure, propofol in a moderate dose infusion (80-100 ug/kg/min) may be added to the dexmedetomidine technique. Spasticity may also be an indication for deeper sedation. Successful use of this agent has also been described in adolescents and in 11 patients who underwent insertion of probes for deep brain stimulation.
Should the patient suddenly experience severe pain, small doses of remifentanil 0.01-0.05 mcg/kg/min over 3-5 minutes combined with propofol 15ug/kg/min is effective. Fentanyl is less useful because it has a cumulative effect and a longer onset of action than that of remifentanil. But in some circumstances, doses of 25mcg the drug may be beneficial. Alfentanil offers no advantage.

If sedation becomes excessive or should the surgeon request reversal, naloxone or flumazenil may be given to reverse narcotic and benzodiazepine effects. Flumazenil involves the receptor site on the GABAA receptor chloride channel complex and has been implicated in neuroexcitatory phenomena, especially seizures.\(^{24}\) The duration of action of flumazenil is shorter than that of midazolam or diazepam and the sedative effects of these drugs may resurface postoperatively. This especially pertains to older patients in whom the half-life of the benzodiazepines is extended. Naloxone should be given in increments of 0.1mg as sudden reversal of analgesia may cause the patient to move and result in scalp tearing. Patients with a supraglottic airway can be awakened and tolerate the airway, especially if lidocaine 50mg has been given intravenously. Intelligible sounds can be appreciated.

Non-glucose solutions should be used for fluid replacement. The amount should be limited as urinary catheters are usually not used. The decision to place a urinary catheter depends on the patient’s ability to cooperate, the intended duration of the procedure and the presence of urinary frequency or prostatic hypertrophy. If necessary, a urinary catheter may be inserted during a brief period of sedation before the head frame is fixed to the OR table.

Some patients may not be eligible for DBS under local anesthesia for medical or psychological reasons. Studies have reported the use of general anesthesia with higher doses of remifentanil and propofol with bispectral analysis monitoring.\(^{25,26}\) The STN and the typical bursting pattern are identifiable but a widening of the baseline noise is not.\(^{25}\) Clinical improvement was acceptable in these studies.\(^{26}\)

**Complications**

In a recent analysis of 258 DBS cases the complication rate was found to be 11.6%, including airway, respiratory, neurologic and psychological problems.\(^{10}\) Age > 64 years was determined to be an independent risk factor. Intracranial hemorrhage and seizures occurred in 3.6%. Two patients requested termination of the procedure and both had evidence of a small intracranial hemorrhage. Postoperative hemiplegia occurred due to spasm or clot formation. Aspiration was reported in 1.6% of patients; and coughing or sneezing in 1.2% of patients.\(^{10}\)

Coughing can be the result of a dry mouth, “smoker’s cough” or an embolic event. When the patient is positioned in a semi-sitting position, the negative pressure gradient between the surgical field and the right atrium allows entrainment of air into the venous circulation from epidural veins, opened either at the incision or at any of the pin head sites.\(^{27}\) Occurrence is more likely in patients who are awake and spontaneously breathing (as compared to ventilated and paralyzed patients) because of the transfer of negative intrathoracic pressure to the central venous system with the initiation of each breath. Coughing is the first symptom of entrained air, followed by chest pain, dyspnea and tachypnea. Side stream capnography should be standard as it rapidly detects decreased end tidal CO2 (ETCO2) even when oxygen is supplied by nasal cannula. Continuous Doppler monitoring interferes with neural recording and cannot be used effectively. Decreased SPO2 (4-5 points) and tachycardia represent early changes. Should this occur, the surgeon must be informed immediately; the field flooded with saline and wax applied to the bone edges. The head should be lowered and the legs elevated. Lidocaine 50mg
may help to decrease coughing. Arterial blood gas analyses confirm the diagnosis with high PaCO2 and low PaO2. If hemodynamic stability returns promptly, it may not be necessary to abandon the procedure.

Postoperative pain is generally not severe as the brain itself has no pain endings. Morphine may be administered in small increments (2-4mg) intravenously or acetaminophen (Tylenol®) with or without codeine may be ordered. In some instances, patients have been discharged on the same day following awake craniotomy where there have been no complications, sedation was minimal and operating time short.28 Following DBS for Parkinson’s Disease or dystonia, an overnight stay is recommended for neurologic monitoring and resumption of drug therapy.

**Management of the Case**

The patient was brought to the OR holding area where an intravenous cannula was placed. He was cooperative and able to tolerate placement of the stereotactic head frame with local anesthetic infiltration at the pin sites. He reported claustrophobia during previous MRI exams and was sedated with a propofol infusion, 50 ug/kg/min during the 40 minute study. During this time, blood pressure, oxygen saturation and end-tidal carbon dioxide were monitored. On returned to the operating room he was awake and calm and requested urinary catheterization.

After standard monitoring was placed, the patient received fentanyl, 25 ug and propofol, 70 mg and a urinary catheter was placed. During that time a “scalp block” was placed with 0.5% bupivacaine at the supraorbital nerves and the greater occipital nerves. The patient regained consciousness and was able to cooperate for the testing and the remainder of the procedure.

**Conclusion**

Propofol, fentanyl, midazolam and dexmedetomidine have emerged as the most useful agents during minimally invasive neurosurgical procedures that require cooperation by the patient. These agents are least likely to result in physiologic disturbances. Anesthetic care is required in several locations in the hospital during electrode placement for DBS and necessitates considerable flexibility.

Administration of an H3 antagonist, often combined with dexamethasone, can minimize the risk of nausea and vomiting. Lips can be moistened and ice chips given in small quantities to improve comfort and decrease the need to cough.

Special attention should be paid to airway management and positioning. A comfortable position without pressure on vulnerable tissues is required. Facilitation of communication between the operating team and the patient is essential to a successful outcome.
References


POST-TEST

1. **Deep brain stimulation:**
   a. Usually requires general anesthesia
   b. Has been used successfully for many movement disorders
   c. Is effective only for Parkinson disease
   d. Only has about 50% success rate

2. **The combination of drugs shown to most suitable for DBS is:**
   a. Remifentanil, isoflurane and dexmedetomidine
   b. Fentanyl, midazolam and dexmedetomidine
   c. Best to use none at all
   d. Propofol, morphine and glycopyrrolate

3. **Side effects of levodopa are least likely to include:**
   a. Dry mouth
   b. Orthostatic hypotension
   c. Gum hypertrophy
   d. Urinary retention

4. **Parkinson Disease:**
   a. Is diagnosed conclusively postmortem
   b. Causes loss of dopaminergic neurons in the SNc
   c. Initially appears to be a unilateral disease
   d. All of the above

5. **Complications of DBS:**
   a. Most frequently include intracranial hemorrhage
   b. Have been reported in about 11% of patients
   c. Always require immediate CT scan
   d. Are extremely rare
6. **Venous air embolism:**
   a. Can be rapidly detected by side stream capnography
   b. Is more likely to occur in spontaneously breathing patients
   c. Does not necessarily require that the procedure be aborted
   d. All of the above

7. **Insertion of the generator for the electrodes:**
   a. Requires general anesthesia
   b. Is usually done on the same day as the electrodes are inserted
   c. Cannot be completed for at least 1 year
   d. Commonly is in the groin

8. **Fluid replacement during DBS:**
   a. Should be generous to avoid hypotension
   b. Is usually withheld completely
   c. Requires some dextrose as the patient has not eaten for many hours
   d. Should be restricted to maintenance replacement, especially if no catheter is in place

9. **The preoperative preparation of a Parkinsonian patient for DBS is least likely to include:**
   a. Administration of an H3 antagonist
   b. Withholding of antihypertensive medications
   c. Stopping bromocriptine
   d. Assessment of complete blood count

10. **Side effects of L–Dopa include:**
    a. Depletion of myocardial norepinephrine stores
    b. Peripheral vasodilation
    c. Hypervolemia
    d. Hypertension