ANAESTHESIOLOGIST’S ROLE IN THE MANAGEMENT OF AN EPILEPTIC PATIENT

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SUMMARY

Epilepsy surgery is slowly becoming popular in India. Management of epileptic patients in the intensive care unit and in the perioperative period demands thorough knowledge and understanding of the varied aspects of anaesthesia. This article highlights the management of status epilepticus and the perioperative management of an epileptic patient.

Keywords : Status epilepticus, Epilepsy surgery, Anaesthetic management.

Introduction

Epilepsy is as old as mankind. It was first described about 3000 years ago in Akkadian (oldest written language) in Mesopotamia (Iraq). The seizure was attributed to the God of moon. At the turn of 17th century, William Gilbert had introduced the magnetic and electric phenomenon responsible for epilepsy and discarded the mystical and supernatural theory to a scientific approach.1

The word epilepsy is derived from Greek verb ‘epilamvanein’ (“to be seized” or “to be attacked”). Epilepsy is a group of electrical disturbances of brain function where the usual periods of normal EEG activity and behaviour are disrupted by episodes of gross electrical disturbances.2 A seizure or convulsion is a finite event; it has a beginning and an end. Epilepsy on the other hand is a chronic disorder characterized by recurrent seizures.3

Epilepsy is one of the common neurological disorders, second only to stroke.3 In developed countries the age adjusted incidence is 24-53 per 1,00,000 person years, with higher incidence in males and in lower socioeconomic class. The age adjusted prevalence is 4-8 per 1000 population.4 Though there are no incidence studies in India, the overall prevalence rate of epilepsy is 5.59 per 1000 population, with no statistical difference between men and women or urban and rural population.5

Role of an anaesthesiologist

An anaesthesiologist may encounter an epileptic patient in three clinical settings:

1. In an intensive care unit for the management of status epilepticus.
2. Perioperative management for epilepsy surgery.
3. Perioperative management for non epilepsy surgery.

Though the basic principles of management essentially remains the same in all the three clinical situations, this review shall focus on the management of status epilepticus and epilepsy surgery.

Status epilepticus

The operational definition is two or more seizures without full recovery of consciousness between seizures or recurrent epileptic seizures for more than 30 minutes.6

The overall mortality rate among adults with status epilepticus is approximately 20%.7 Status epilepticus should be stopped quickly, ideally within 30 minutes from the start of episode. Status epilepticus causes profound physiological changes that may result in severe systemic complications and may also damage or even kill cerebral neurons.8

Management of status epilepticus

The management protocol of status epilepticus has been outlined in table - 1.7,9,10 Fosphenytoin, a new drug has gained popularity in the management of seizures. It is a water soluble prodrug of phenytoin which is converted to phenytoin (t1/2 15 minutes) by non-specific phosphatases. Doses of fosphenytoin are expressed as phenytoin equivalents (PE), which are amounts of phenytoin released from the prodrug. Since it is not formulated with propylene glycol, it can be administered at phenytoin equivalent rates of upto 150 mg per minute. Though the onset of effect, hypotension and adverse cardiac effects are similar with both phenytoin and fosphenytoin loading, infusion site reactions (phlebitis and soft tissue damage) are less common with fosphenytoin.9

For refractory status epilepticus, use midazolam as a slow intravenous bolus injection in a dose of 0.2 mgkg-1.
followed by 0.75 – 10 g kg⁻¹ hr⁻¹ or propofol in a dose of 1-2 mg kg⁻¹ hr⁻¹ followed by 2-10 mg kg⁻¹ hr⁻¹. Thiopentone sodium administered in a dose of 10-15 mg kg⁻¹ slowly over a period of one hour followed by a dose of 0.5–1 mg kg⁻¹ hr⁻¹ is highly effective, but cardiovascular toxicity is occasionally life threatening and post-infusion weakness may delay weaning from ventilatory support.

### Table - 1 : Management protocol for status epilepticus.

<table>
<thead>
<tr>
<th>MINUTES</th>
<th>MANAGEMENT</th>
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| 0       | 1. Assess and control airway.  
2. Monitor vital signs (including temperature) establish ECG and spO₂ recording.  
3. Draw venous blood for biochemical analysis (including RBS).  
4. Draw arterial blood for ABG analysis.  
5. Work up to define cause.  
5. Manage other medical problems. |
| 5       | 1. Start IV infusion (normal saline).  
2. If hypoglycemic or if blood glucose measurement is not available, give glucose-
   Adults : 100mg thiamine IV followed by 50ml of 50% glucose.  
   Children: 2 ml kg⁻¹ of 25% glucose. |
| 10      | 1. Benzodiazepines -  
   Lorazepam : 0.1 mg kg⁻¹ (max rate 2 mg kg⁻¹ upto 4 mg total dose).  
   Diazepam : 0.2 mg kg⁻¹ (max rate 5 mg kg⁻¹ upto 20 mg total dose).  
   Seizure persists -  
   Phenytin: 20 mg kg⁻¹ (max: adults@50ml/min; children@1 mg kg⁻¹ min⁻¹).  
   Fosphenytoin: 20 mg kg⁻¹ PE (@ 150 mg min⁻¹).  
   Monitor ECG / BP during infusion. |
| 40      | Seizure persists -  
   Additional phenytoin (5-10 mg kg⁻¹) or fosphenytoin (5-10 mg kg⁻¹ PE).  
   Expect respiratory depression / apnea, assist ventilation |
| 60      | Seizure persists -  
   Phenobarbital 20 mg kg⁻¹ (max @ 60 mg min⁻¹).  
   Taper infusion at 12 hours to observe further seizure activity. If seizures recur, reinstate infusion in intervals of at least 12 hours. |

**Anaesthesia for epilepsy surgery**

**Surgical procedures**

Although medications are the mainstay of management in an epileptic patient, it may occasionally be ineffective or their side effects unacceptable. In such situations, surgical management is looked upon as an alternative, especially when epileptic focus can be localised. In advanced countries around 30% of the epileptic patients may require surgery, while in India the potential surgical patients amount to 10,000 to 20,000 per year.

Patients with refractory epilepsy often undergo surgery to resect an epileptogenic focus or to interrupt a seizure pathway. These procedures include:

- Temporal lobectomy
- Amygdalohippocampectomy
- Extratemporal cortical excision
- Hemispherectomy
- Corpus callosotomy

**Other surgical procedures**

Vagal stimulation and electrical stimulation of the centromedian thalamic nucleus are also used to treat intractable epilepsy. However the results are not very encouraging.

**Anaesthetic considerations**

When surgery is contemplated the role of an anaesthesiologist is paramount. In our center, the neurologist, neurosurgeon, neuroradiologist and neuroanaesthesiologist comprise the epilepsy surgery core group, which identifies and discusses the problems of each patient regularly. The role of neuroanaesthesiologist during anaesthetic management of patients for epilepsy surgery are multidimensional.

1. Appropriate anaesthetic technique for epileptic patients.
2. To provide sedation and monitored anaesthetic care during awake craniotomy.
3. To induce intraoperative seizures for intraoperative electrocorticography.
5. To provide brain protection so as to achieve good neurological recovery.
6. Provide rapid recovery for postoperative neurological assessment.
7. Management of refractory status epilepticus.

**Preoperative investigations**

The services of anaesthesiologist are often required to perform different investigative procedures in an epileptic patient.

1. Radiological procedures : MRI and positron emission tomography (PET) scans are carried out in patients with seizures to identify the surgical lesion. Intravenous sedation is recommended during these procedures.
2. Intracranial electroencephalograph (EEG) electrode insertion : Intracranial EEG electrodes are used to
maximize sensitivity and specificity in electrographic localization of a seizure focus. Stereotactic electrode insertion can be done under local anaesthesia, while epidural electrodes or grids are placed under general anaesthesia.

iii) Thiopentone test: This test is performed to provide data regarding the EEG localization of seizure focus. This technique is used to produce a gradual increase in blood levels of thiopentone, thereby producing electroencephalographic beta activity. Such beta activity will occur in normally functioning neural tissue, whereas the seizure foci will show an abnormal response.

iv) Wada test: It is carried out to ascertain the dominant cerebral hemisphere. A small dose of amobarbital (amytal sodium) is injected into the carotid artery to lateralize the cerebral speech dominance. Alternatively methohexital (3 to 5 mg) can be injected after 1 mg test dose.

Preanaesthetic evaluation

Surgery for epilepsy is usually major and time consuming due to intraoperative electrocorticography. Therefore, it is imperative on the part of the anaesthesiologist to undertake meticulous and detailed preoperative evaluation of these patients. The preoperative concerns are:

1. General fitness of the patient: Epilepsy surgery is elective and the patient needs to be in good health.
2. Concomitant medical problems: These patients may have associated medical illnesses which need to be evaluated as the patients are optimized prior to surgery.
3. The genetic syndromes: associated with seizure disorders may have anaesthetic implications.

i) Autosomal dominant disorders
(a) Huntington’s chorea: Patients may have abnormal response to thiopentone.
(b) Tuberous sclerosis: There may be associated cardiac arrhythmias, cardiac tumors, renal and pulmonary dysfunction.
(c) Neurofibromatosis (Von Recklinhausen’s disease): Patients may have compromised airway, fibrosing alveolitis, atlanto-axial instability and prolonged neuromuscular blockade.

ii) Autosomal recessive disorder: Airway compromise is frequently observed in patients with hemihypertrophy.

iii) X-linked disorder: Patients of Lesch Nyhan disorder may have associated urate nephropathy and aspiration pneumonitis.

4. Drug interaction: Anaesthesiologist must have knowledge pertaining to interaction of anaesthetic drugs with anticonvulsants.
5. Gingival hypertrophy: Fibrous hyperplasia and bleeding tendency of the gums associated with chronic phenytoin therapy may pose as a troublesome airway.
6. Anaemia: Pallor if present, should also be thought in terms of megaloblastic anaemia.
7. Preoperative counselling: There are a lot of psychosocial concerns associated with an epileptic patient. The personality development is often poor with low self esteem. The anaesthesiologist needs to provide a good preoperative psychological support and should discuss the perioperative aspects of the surgery.

Premedication

i) Benzodiazepine is an ideal premedicant because of its anticonvulsant properties. However, in patients undergoing thiopentone test, awake craniotomy or electrocorticography, the premedication is restricted to an antacid and an antiemetic.

ii) Since the patient’s head and neck are inaccessible during surgery, it is appropriate to premedicate the patients with atropine or glycopyrrolate.

iii) Morning dose of anticonvulsants are continued.

Monitoring

Continuous monitoring of ECG (HR), NIBP, SpO₂, EtCO₂, temperature and urine output are essential. In children the blood volume is smaller than adults, while the size of surgical incision is relatively large. The blood loss may be more significant than the adults. Hence central venous pressure monitoring is useful in paediatric patients.

Anaesthetic management

Although modern anaesthesia has multiple benefits and is fairly safe, it is important to realize that anaesthetic complications may either result in major catastrophe like permanent brain damage or death or leave minor neurological sequelae like headache, backache or peripheral nerve injury. The same holds true for epilepsy surgery also. The optimal anaesthetic agents for epilepsy surgery are yet to be ascertained. Although there are few good outcome trials, the animal studies and surrogate outcome studies are often obtuse or contradictory. Nevertheless, the goals of anaesthetic management are:

1. To maintain haemodynamic stability.
2. Avoidance of any increase in ICP.
3. Minimal impact on electrocorticographic monitoring
4. Provide brain protection.
5. To avoid any secondary systemic insults.
6. Rapid and smooth emergence.

To achieve all these above goals, the anaesthesiologist must have detailed and thorough knowledge of various anaesthetic agents particularly their pro and anti convulsant properties.

**Proconvulsant and anticonvulsant effects of anaesthetics**

There are various anaesthetics which can exhibit both proconvulsant and anti convulsant properties with different doses and under different physiologic conditions. Consequently, the anaesthetic management in epileptic patients must be planned accordingly.

**Intravenous anaesthetics**: Thiopentone and benzodiazepines have anticonvulsant properties. However benzodiazepines can induce brief periods of EEG and clinical seizure activity in patients with Lennox-Gastaut syndrome, a form of secondary generalized epilepsy. Methohexitone on the other hand produces seizure activity during its administration by intravenous, intramuscular as well as rectal route (Table - 2). Ketamine, however activates epileptogenic foci in epileptic patients. Clinical reports of seizure following parenteral administration of ketamine have been documented in both epileptic and non-epileptic patients. Etomidate possesses both pro and anticonvulsant properties. Higher dose suppresses and low dose etomidate induces involuntary motor activity. Therefore, the dose and the rate of etomidate administration determines which of the contrasting effects on the seizure threshold will occur in a particular setting. Intravenous droperidol when given along with fentanyl as a component of neurolept anaesthesia was not observed to produce epileptiform activity on EEG. The role of propofol in epileptiform surgery is somewhat controversial. Although the clinical reports suggest that it has anticonvulsant properties, abnormal EEG activity have been documented following administration of propofol in epileptic patients.

**Inhalational anaesthetics**: Nitrous oxide (N₂O) has extremely low epileptogenic potential, and is considered to be safe in epileptic patients. However, it has no anticonvulsant properties. Halothane and isoflurane do not provoke seizure activity in anaesthetized patients. However, reports of convulsions have been documented following use with N₂O. Enflurane, however produces both EEG changes and abnormal motor activities (Table - 3). Seizure manifestations are evident at minimal alveolar concentrations of 1 to 2, which are accentuated by hyperventilation, auditory, visual and tactile stimulations. There are EEG evidence of seizure activity with sevoflurane. Convulsions have been reported following use of sevoflurane in a neonate, young children and parturients. Suppression of refractory status epilepticus and EEG has been reported both with isoflurane and desflurane.

| Table - 2 : Effects of intravenous anaesthetics on seizure activity in epileptics. |
|---------------------------------|-----------|-----------|
| Agents                          | Clinical  | EEG       |
| Thiopental                      | -         | -         |
| Methohexital                    | +         | +         |
| Etomidate                       | +         | +         |
| Benzodiazepines                 | +         | +         |
| Ketamine                        | +         | +         |
| Propofol                        | -         | +         |

(+) presence of seizure ; (-) absence of seizure

| Table - 3 : Effects of inhalational agents on seizure activity in epileptics. |
|---------------------------------|-----------|-----------|
| Agents                          | Clinical  | EEG       |
| N₂O                             | -         | -         |
| Halothane                       | -         | -         |
| Enflurane                       | +         | +         |
| Isoflurane                      | -         | -         |
| Sevoflurane                     | +         | +         |
| Desflurane                      | -         | -         |

(+) presence of seizure ; (-) absence of seizure

**Opioid anaesthetics**: Though there are clinical reports of seizures with the use of morphine, but no epileptiform activity has been reported during and following the use of morphine. Meperidine’s neurotoxicity is well known in inducing seizures and is attributable to its metabolite normeperidine.

**Fentanyl and its analogues**: Clinical reports of convulsions with the use of fentanyl and its congeners have been published. But, the EEG findings were not corroborated. Recently, it has been documented that fentanyl, alfentanil and remifentanil activates epileptiform activity in patients with temporal lobe epilepsy.
Muscle relaxants: None of the muscle relaxants including atracurium used in clinical anaesthesia have been reported to cause either EEG or clinical seizure activity. However, the long term infusion of atracurium in ICU setting needs to be investigated.

Anticholinesterases: Clinical seizure or EEG activity have yet to be reported following the use of cholinesterase inhibitors during clinical anaesthesia.

Local anaesthetics: They possess both proconvulsant and anticonvulsant properties due to their membrane stabilizing effects. At subtoxic doses, local anaesthetics can act as anticonvulsants, sedatives and analgesics, while at higher concentration, resistant excitatory pathways can cause frank convulsions.

Drug interactions
A matter of concern in anaesthetic practice during epilepsy surgery is the interaction between the antiepileptic drugs and anaesthetic agents. It has been demonstrated that patients treated chronically with various anticonvulsants are resistant to non-depolarizing muscle relaxants and to usual clinical dose of opioids. A comparatively higher doses of fentanyl were required in epileptic patients receiving anti-epileptic drugs. Among the non-depolarizing muscle relaxants, only atracurium has been shown to have same effect whether or not the patients were on chronic phenytoin therapy. Vecuronium when used during concurrent phenytoin therapy has both a decreased effect and a shorter duration of action. The mechanism of this resistance to opioids and neuromuscular agents is possibly due to hepatic enzyme induction by antiepileptics which tends to increase clearance and decrease the half life of opioids and non-depolarizers.

Management of ICP
Intracranial hypertension is rarely a problem in epilepsy surgery. However, maintenance of ICP at a lower level aids in surgery. Thiopentone and propofol produces the most consistent reduction in cerebral blood volume and ICP. Isoflurane and sevoflurane have similar effects when used in sub MAC concentrations and in the background of opioids and hyperventilation. Increased ICP can result from poor positioning and venous obstruction, light plane of anaesthesia, inadequate analgesia and hypercarbia.

Intraoperative electrocorticography (ECoG)
A normal functioning brain is ideal for ECoG. But, the major constraint during anaesthesia is the depressant effects of anaesthetics on the normal EEG. The only valid reason for awake craniotomy is to facilitate ECoG. Neurolept anaesthesia (fentanyl and droperidol) technique is the choice for intraoperative ECoG monitoring and seizure foci removal during awake craniotomy.

If general anaesthesia is preferred, the maintenance of anaesthesia should consist of N₂O and a narcotic with or without lower concentration of isoflurane. For foci identification enflurane may be very useful. Although sevoflurane has greater neuro-excitatory properties than isoflurane, the widespread irritative response to sevoflurane administration is not helpful in localizing the epileptogenic area. Amongst the newer synthetic opioids, alfentanil and fentanyl are used intraoperatively to localize seizure focus. But, alfentanil appears to be a better choice for intraoperative ECoG monitoring. Remifentanil can also be used during awake epilepsy surgery as its sedation does not adversely affect intraoperative interictal spike activity. When unmasking of epileptogenic foci is planned during N₂O - narcotic anaesthesia, a common reasonable approach is to use methohexital intraoperatively in 10-25 mg increments, along with hyperventilation.

Fluid management
The target for fluid management during epilepsy surgery is to maintain normovolemia. Normal saline is regarded as fluid of choice because of slightly high osmolality. Rarely, epilepsy surgery can be associated with large blood loss. Though the adult patients may tolerate a low haematocrit, but in children avoiding blood transfusion may become hazardous particularly in anaemic or hypovolemic child.

Emergence
Early awakening is a priority in epileptic patients as most of the surgeries are non-emergent procedures and the patients have a good preoperative conscious level and neurological status. Moreover, early awakening allows a rapid and complete neurological examination. Suitable pharmacological agents (i.e., lignocaine, esmolol or labetolol) should be administered so as to blunt the hypertensive response to extubation and emergence. Paediatric epileptic patients may remain drowsy after corpus callosotomy and hemispherectomy. To overcome this problem anaesthetic management needs to be tailored accordingly.

Postoperative care
Post craniotomy patients need to have adequate pain relief. Codeine can be a suitable choice in children as it has less respiratory depression and sedation. Nausea and vomiting may be a problem in the postoperative period. Effective control of postoperative sickness can be achieved with metoclopramide or ondansetron.
Blood levels of an antiepileptic drug can significantly be affected by anaesthetics and the changes in body physiology resulting from surgery. The blood levels of carbamazepine and phenytoin increase substantially after anaesthesia and surgery. Increasing levels of antiepileptic drugs may cause clinical toxicity, which may mimic an intracranial complications. Conversely, if the antiepileptic drug levels decrease unexpectedly, seizure can be precipitated. Thus the blood levels of anti-epileptic drugs should be obtained preoperatively and closely monitored in the postoperative period.

Awake craniotomy

The terminology means, craniotomy carried out under local anaesthesia and conscious sedation. Awake craniotomy is performed in those epileptic patients where the epileptic foci lies close to eloquent areas of the brain (i.e. motor areas, speech or to temporal structures critical to short term memory). Majority of these patients have temporal lobe epilepsy.

Neuroleptanaesthesia was developed to maintain normal cerebral cognitive function while eliminating the perception of nociceptive stimuli. Combination of fentanyl and droperidol was traditionally being used with advantages like excellent cardiovascular stability and rapid postoperative recovery. However, unconsciousness, postoperative extrapyramidal excitation, restlessness and confusion were among the major side effects associated with its use.

Recently however, with the advent of newer anaesthetic agents, neurolept anaesthesia has evolved into “conscious sedation”. Propofol is being used successfully and predictably to maintain sedation and hypnosis. The introduction of newer opioids, alfentanil and remifentanil have contributed to improve intraoperative analgesia while offering better control of postoperative recovery and discharge time. The success in winning patient’s cooperation maximizes with an excellent field block. This can be achieved by infiltrating local anaesthetics into the scalp in a circular fashion, along with supratrochlear, supraorbital, auriculotemporal, lesser and greater occipital nerve blocks. The anaesthesiologist must provide adequate preoperative pain and attention to detail. The choice of anaesthetic agent is of lesser importance. Remifentanil with isoflurane is perhaps the best choice for surgery. For awake craniotomy, propofol with fentanyl is the preferred technique. During electrocorticography low concentration of isoflurane or propofol with fentanyl is ideal. Management of refractory status epilepticus needs to be tailored according to the neurological and haemodynamic status of the patient.

Conclusion

Achieving the various goals of anaesthesia for epileptic patients is a challenge. Safe anaesthesia requires a high degree of preparation, vigilance and attention to detail. The choice of anaesthetic agent is of lesser importance. Remifentanil with isoflurane is perhaps the best choice for surgery. For awake craniotomy, propofol with fentanyl is the preferred technique. During electrocorticography low concentration of isoflurane or propofol with fentanyl is ideal. Management of refractory status epilepticus needs to be tailored according to the neurological and haemodynamic status of the patient.

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