

Epilepsy and Anaesthesia

Dr Max Hodges

Royal Devon and Exeter Foundation NHS Trust

Self-assessment

Answer these questions before reading the tutorial. All the answers may be found within the text.

- 1) Regarding induction and maintenance of anaesthesia in well controlled epileptics:
 - a. Thiopentone has minor anticonvulsant activity T/F
 - b. Propofol is not an appropriate induction agent T/F
 - c. Ketamine can cause cerebral excitatory effects T/F
 - d. Halothane can cause epileptiform activity T/F
 - e. Muscle relaxants stop seizures T/F
- 2) Regarding the pharmacokinetics of muscle relaxants:
 - a. Vecuronium, rocuronium and mivacurium are metabolised in the liver T/F
 - b. Carbamazepine will cause prolonged duration of effect of aminosteroidal muscle relaxants T/F
- 3) Regarding anti-emetics:
 - a. Name the five main classes of anti-emetics?
 - b. Which of the above should be avoided in epileptics?
- 4) You are called to theatre urgently to see a patient who has started to convulse. The procedure was being performed under local anaesthetic, and the surgeon has infiltrated the site with 40ml of 0.5% bupivacaine. The patient weighs 60kg. Describe your management of this patient.

Introduction

Epilepsy is the most common serious neurological disease, with a prevalence commonly quoted as 5-10 cases per 1000 persons¹. Incidence varies due to a number of factors. In developed countries, it has been found to be around 50 cases per 100,000 persons per year. In developing countries, the incidence is higher (of the order of 100-190/100,000/year) for reasons which are not entirely clear. Thus from an anaesthetic perspective, it is important to understand the issues of safe management of epileptics in the perioperative period.

Definition of Epilepsy

Epilepsy may be defined as a paroxysmal, abnormal cerebral electrical discharge associated with a clinical change; taking a variety of forms, but usually including some impairment of consciousness. *Grand mal epilepsy* is defined by the typical tonic-clonic muscular movements accompanying the episode or “fit”.

Preoperative assessment

- A careful history is important. Attention should be paid to manifestations and severity of the patient's disease.
- Does the patient hold a current driving licence?
- All current medications and dosages should be noted (many anti-epileptic drugs cause enzyme induction, leading to reduced activity and duration of action of agents used during the course of anaesthesia).

Conduct of anaesthesia

- Prolonged preoperative starvation should be avoided to minimise metabolic disturbance. Antiepileptic medications should be continued up to and including the day of surgery.
- Choice of anaesthetic agent and other drugs used during anaesthesia should be adjusted, depending on their pharmacokinetic and pharmacological actions, in addition to their interaction with any concurrent medication the patient may be taking (see below).
- Hypocarbia reduces cerebral blood flow, and can potentially worsen any pre-existing abnormal EEG activity. Care should be exercised to avoid hyperventilation.

Recovery

- Patients should be observed during the recovery period, and any epileptiform activity described and recorded. It is important that shivering or confusion is not misdiagnosed, with subsequent implications for the patient.
- Patients with poorly controlled epilepsy should be nursed in an way that minimises their chance of harming themselves postoperatively.

Drug considerations

Induction and maintenance agents

Thiopentone

Thiopentone (thiopental sodium) is well documented to be powerfully anticonvulsant in the therapeutic range. For the treatment of cases of refractory status epilepticus, it is recommended as the drug of choice.

Methohexitone

Methohexitone is related to thiopentone and has a similar pharmacological profile. It differs in that it can cause an excitatory phase before loss of consciousness, with muscle twitching, increased tone and hiccups. It may precipitate convulsions in those with a history of epilepsy. Historically, it has been used for induction of anaesthesia where excitatory phenomena are not of concern (e.g. for ECT). However, it is no longer marketed in the UK.

Propofol

Propofol (2,6 diisopropylphenol) has been associated with excitatory effects on the CNS in up to 10% of patients. It is likely that this is not true cortical seizure activity, but rather the manifestation of subcortical excitatory-inhibitory centre imbalance. Indeed, many studies have shown that propofol decreases cortical activity during both anaesthesia and status epilepticus. Local guidelines suggest that, given the confusion surrounding the role of propofol in postoperative seizure activity, in patients who are well controlled and fit-free (especially those holding a drivers license), propofol should be avoided unless there is a clinical imperative.

Ketamine

Ketamine produces a state of dissociative anaesthesia. It may cause vivid and unpleasant dreams, hallucinations and delirium. Given its cerebral excitatory effects it should normally be avoided in epileptics, unless there are strong clinical indications for its use.

Etomidate

Etomidate has a high incidence of extraneous muscle movements (which can be minimised by co-induction with an opioid or a short acting benzodiazepine). It is important that these movements are not misdiagnosed as epileptiform activity.

Inhalational anaesthetics

The majority of inhaled anaesthetics cause burst suppression on the EEG, and are thus safe for use in epileptics. The one exception is enflurane which causes epileptiform activity and therefore should be avoided.

Muscle Relaxants

Non-depolarizing muscle relaxants fall into two chemical groupings

- Aminosteroidal compounds – vecuronium, pancuronium, rocuronium
- Benzylisoquinolinium compounds – (cis-)atracurium, mivacurium

The latter group are hydrolysed in the plasma, but the former group undergo a degree of hepatic metabolism, before the unmetabolized fraction is excreted in the urine or bile. This is relevant when a patient is concurrently taking anticonvulsants. All of the commonly used anticonvulsants (especially phenytoin, barbiturates and carbamazepine) cause enzyme induction in the liver. This can lead to markedly reduced duration of activity of the aminosteroidal muscle relaxants, particularly those which are primarily excreted via the liver (vecuronium and pancuronium).

Antiemetics

There are five main classes of antiemetics in current use:

- Dopamine antagonists
- Anticholinergics
- Antihistamines
- 5-HT₃ antagonists
- Steroids

Of these, the dopamine antagonists are well documented to cause extrapyramidal effects and dystonic reactions. These reactions may be confused with epileptic activity, and therefore the drugs should be avoided. Examples of these include the *phenothiazines* such as prochlorperazine, *butyrophenones*[†] (droperidol), and *benzamides* (metoclopramide).

Postoperative drug considerations

Should prolonged postoperative GI dysfunction ensue and oral or nasogastric therapy is not possible, then consideration should be given to parenteral or rectal anticonvulsant therapy. A number of anticonvulsants are available in suitable formulations, including carbamazepine, phenytoin and sodium valproate. Of these carbamazepine can be given rectally (125mg rectally is equipotent to 100mg orally) to a maximum of 1g/day in four divided doses. Both phenytoin and sodium valproate have the same intravenous dose as oral dose, and are given twice daily.

Status Epilepticus²

Definition

- Continuous seizure activity lasting >30 min
- Or
- Intermittent seizure activity lasting >30 min during which consciousness is not regained

Emergency Management

- ABC-
 - Airway
 - Breathing - 100% O₂
 - Circulation - IV access
 - Don't Ever Forget Glucose! - check and correct hypoglycaemia
- First line therapy
 - IV Benzodiazepines - Lorazepam (0.1mg/kg) or Diazepam (0.1mg/kg)
- Second line therapy if seizures not terminated within 10min
 - IV Phenytoin (15-17mg/kg) by slow infusion (rate <50mg/min)
- Intubation and ventilation to maintain normal PaO₂ and PaCO₂
 - Rapid Sequence Induction should be performed (although propofol is an acceptable substitute for thiopentone in this instance)
- Fluid resuscitation to maintain adequate systemic blood pressure and cerebral perfusion pressure
- If seizures are not controlled after 30 minutes with second line therapy, consider propofol or low dose thiopentone infusion anaesthesia preferably under EEG control. Alternatives include phenobarbitone and paraldehyde.
- Remember - muscle relaxants stop the seizure movements, but not the abnormal cerebral activity, therefore in the paralysed patient, anticonvulsants are also essential.

Local anaesthetic toxicity²

Maximum dose for infiltration (mg/kg)

Lidocaine	4
With adrenaline	7
Bupivacaine	2
With adrenaline	3
Prilocaine	6
With adrenaline/octapressin	8

Presentation of toxicity

- Light headedness, dizziness, drowsiness. Tingling around lips and extremities. Metallic taste, tinnitus, blurred vision.
- Confusion, incoherent speech, tremors or twitching, leading to convulsions, LOC and coma
- Bradycardia, hypotension, cardiovascular collapse and respiratory arrest.

Management

- Stop injection!
- ABC and 100% O₂
- CPR if pulseless
- Treat convulsions with midazolam (3-10mg), diazepam (5-15mg) or thiopentone (0.5-2mg/kg)
- Intubate and ventilate if required to prevent respiratory arrest

Answers

1. FTTF 2. FF

Conclusion

The role of the anaesthetist is to minimise the risk of perioperative seizures, whilst providing adequate analgesia and anaesthesia to allow optimum surgical operating conditions. A good working knowledge of the pharmacological properties of commonly used drugs in both anaesthesia and epilepsy is essential.

† Domperidone is also a dopamine antagonist and a butyrophenone. However, as it does not cross the blood-brain barrier it is much less likely to cause extrapyramidal effects. In its intravenous form, it was shown to cause serious arrhythmias in large doses, and has been withdrawn. It is available in tablet or suppository form, and is safe in these preparations for administration to epileptics.

References

- 1 Sander JW. The incidence and prevalence of epilepsy. Library of articles. www.e-epilepsy.org.uk September 2003.
- 2 Allman KG, McIndoe AK, Wilson IH. Emergencies in Anaesthesia. OUP. 2005.