Dexmedetomidine for epileptic surgery in children

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1) Goals:

1. Outline the anesthetic considerations of epileptic surgery in children
2. Review the effects of different anesthetics on EEG
3. Learn the pharmacokinetics and dynamics of dexmedetomidine
4. Define the pro and cons about using dexmedetomidine
5. Construct an anesthetic plan for epileptic surgery

2) Case:

You are scheduled to be the anesthesiologist for an 8 year old girl undergoing a craniotomy for epileptic brain surgery tomorrow. While browsing through the patient’s chart, you see she has a history of a seizure disorder refractory to medical treatment. She has global developmental delay, left-sided hemiparesis and is non-verbal. Otherwise, her past medical history is significant only for a history of tuberculosis meningitis as a child. Her medications are listed as levetiracetam, chlorazepate, rufinamide, and topiramate. Past surgical history includes a G-tube placement at age 3, but you do not have access to the anesthetic record.

Questions:

What is epilepsy? What is the incidence in children? What are the underlying causes? What are the treatment options? What are the anesthetic implications of patients with epilepsy?
The morning of the scheduled procedure, you meet the patient and her family. Her medical history is as described in her chart. Her parents report that her last seizure was two days ago, and they vary in frequency for several a day to once or twice a week. Despite her developmental delay and hemi-paresis, her parents are concerned she will not tolerate a mask induction well, but also don’t want to subject her to an awake IV start.

After discussing the risks of anesthesia, and your anesthetic plan, you have a brief discussion with the surgeon, who tells you they will be performing intra-operative EEG monitoring and therefore would like to use ‘whatever anesthesia won’t interfere with that’.

Questions:
How would you induce anesthesia? Would you premedicate this child? What anesthetic options do you have? What are the possible interactions of anesthetics and the ‘seizure brain’? What anesthetics have anticonvulsant and proconvulsant properties?

You decide to use a dexmedetomidine infusion as part of your anesthetic for this case.

Questions:
What about dexmedetomidine makes it a good choice for this case? What dose of dexmedetomidine would you use? How does dexmedetomidine work? When would you not use dexmedetomidine? What are common side effects of dexmedetomidine and how would you address them?

After induction, intubation, placement of two large bore IVs and an arterial line you start your EEG-friendly anesthesia. All things are moving smoothly intra-operatively and the surgeon is telling you that she/he wants to do the intra-operative EEG in about 20 minutes.

Questions:
What would you do now? How do you adjust your anesthetics? Are you concerned about intra-operative awareness?
The case proceeds smoothly, the neurosurgeons are pleased with the resection, and inform you that there is no further need for EEG monitoring.

Questions:
How do you continue your anesthetic? When would you stop dexmedetomidine? When propofol (if used) and why?

3) Discussion:
Epilepsy is a disorder of the nervous system characterized by paroxysmal, recurrent seizures. 2 million people in the United States are diagnosed with epilepsy and 0.5 – 1% (300,000) are children under the age of 14. Underlying disorders may be infectious, malignant, traumatic, metabolic, pharmacologic or idiopathic. The diagnosis is based on history, description of seizures, physical examination and EEG findings. Treatment options are based on the compilation of findings and include antiepileptic drugs, specific diets and surgical procedures like implantation of vagal nerve stimulator or resection of structural lesions. Patients with epilepsy might need sedation/anesthesia for procedures other healthy patients would not require due to frequent seizure activity and/or their intellectual and developmental disabilities. Some antiepileptic drugs, such as lamotrigine and topiramate, have adverse effects such as behavioral problems or aggressive behavior. Valproic acid is associated with platelet abnormalities; aplastic anemia is a rare complication of phenytoin, carbamazepine and felbamate. The traditional anticonvulsant drugs (carbamazepine, phenytoin, and Phenobarbital) enhance cytochrome p450 system’s metabolism and may necessitate adjustments of dosing anesthetics, muscle relaxants and opioids. The ketogenic diet is an adjuvant therapy for intractable epilepsy. Ketosis fosters metabolic acidosis which can be exacerbated by carbohydrate containing products, such as sweetened oral premedication and dextrose containing infusions. Dextrose can lead to a fall in plasma ketones and increase the risk of seizures.

Anesthetics can have proconvulsant and anticonvulsant properties. Typically, lower anesthetic doses have been associated with proconvulsant tendencies (except opioids)

<p>| Anesthetic | Proconvulsant | Anticonvulsant |</p>
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(reproduced from Kofke WA) + isolated case, ++ 1-5 cases, +++ reproducible, controlled study or many cases

Dexmedetomidine is an α-2 adrenoceptor agonist with sympatholytic and antinociceptive properties. It seems not to hinder interpretation of the EEG, unlike the majority of anesthetics used in daily practice.

Loading dose 0.5 – 1 mcg/kg over 10 minutes, maintenance is 0.5 – 1 (2) mcg/kg/hr.

Protein binding is 94%

Metabolism is in the liver by direct glucuronidation and cytochrome p450-mediated metabolism to inactive metabolites. Excretion is through the kidney (95%) and feces (4%). The elimination half-life is 2 hrs.

Effectiveness and safety in patients under 18 years is not established (yet).

Precautions to consider:

- In patients with diabetes mellitus hypotension and/or bradycardia seem more pronounced.
- Avoid in patients with heart block and ventricular dysfunction
- Dose reduction is required in hepatic and renal insufficiency
- Hypovolemia can lead to exaggerated bradycardia and hypotension

Common adverse reactions:

- Hypertension (12 – 13%)
- Hypotension (25 – 54%)
- Brady arrhythmia (5 – 14%)
- Atrial fibrillation (4%) and cardiac dysrhythmia/sinus arrest
- Tachycardia (2 – 5%)
- Nausea (3 – 9%)
- Respiratory depression (37%)

Bradycardia is a very common side effect and can be treated in most cases with anticholinergic agents like glycopyrrolate or atropine.

Propofol-infusion will need to get stopped 20 minutes before the intra-operative EEG measurements to not to cause alterations of the EEG. During that period it is important to run dexmedetomidine (1-2 mcg/kg/hr) and an opioid (e.g. remifentanil 1 mcg/kg/min or fentanyl 3 mcg/kg/hr) at highest level for minimizing the risk of intra-operative awareness.

Recovery time for dexmedetomidine is at least an hour, so it is probably advised to lower or stop the drug after the EEG measurements are done. To minimize the risk of lactate acidosis while running propofol infusions in pediatric patients’ one might also consider stopping propofol and finishing the case with an inhalational anesthetic (e.g. desflurane or isoflurane).

4) References:


Micromedex 2.0