Seizures

KEY POINTS

- Seizures occur in up to 10% of patients receiving palliative care
- Most seizures are brief, self-limited and rarely harmful, but they can be extremely frightening to family members
- Pethidine/meperidine will cause seizures if used on an ongoing basis due to an accumulation of neurotoxic metabolites. Pethidine/meperidine should therefore NOT be used in palliative care patients

- Seizures are relatively common at the end of life in children, as children are more likely to have life-limiting neurological conditions

- Opioid-induced myoclonus is often misinterpreted as seizure activity by caregivers and clinicians, myoclonus tends to respond to conservative treatment, including correction of dehydration and reduction and/or rotation of opioid

ASSESSMENT

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Treatment is usually symptomatic and a full seizure work up is, in most cases, not necessary in the context of a serious illness, which is known to cause seizures

Causes of seizures include:

- Brain tumour or metastasis
- Head trauma
- Strokes – ischemic or haemorrhagic
- Drug toxicity (e.g. pethidine/meperidine)
- Metabolic or electrolyte abnormalities

- Hypoglycaemia
- Hyponatraemia
- Hypercalcaemia

- Infections of the central nervous system
- Cancers most likely to metastasize to the brain are lung, breast, and malignant melanoma

Common causes in children:

- Epilepsy
- Degenerative neurological conditions
  - Metabolic and genetic disorders
- Hypoxic ischemic encephalopathy
- In children with a longer prognosis, a review by a neurologist to optimize antiepileptic treatment may be appropriate
- For children who have a history of epilepsy, if the child can no longer swallow medications in the terminal phase of their illness, they should be given antiepileptics by an alternative route, such as Subcutaneous midazolam

MANAGEMENT

- Clear airway and ***provide supplemental oxygen (if available and the patient is not actively dying***)
- Benzodiazepines are the first-line treatment. If the seizure does not resolve within 5 minutes, consider:
  - **Lorazepam 4 mg IV over 2 minutes, OR**
  - **Midazolam 10 mg Buccal/Subcutaneous/IM or IV over 2 minutes**
  - **Diazepam 10 mg PR or IV**
- Can repeat ONCE after 5-10 minutes, if the seizure persists
- If benzodiazepine ineffective, give phenytoin 20 mg/kg IV STAT or phenobarbital 10-15 mg/kg (up to 1000 mg) STAT
  - IV (dilute with normal saline to administer 100 mg/min)

- IM (undiluted), with larger doses (>1.5mL volume of fluid) split between multiple injection sites)

PROPHYLACTIC MANAGEMENT OF SEIZURES

- Seizure prophylaxis with anticonvulsants has only been proven useful in patients with brain metastasis due to malignant melanoma and patients with brain metastasis from other cancers who have already had a seizure
- **Levetiracetam 250 mg PO BID; titrate to achieve seizure control, maximum of 3000 mg/day. Note: can also be administered subcutaneously, 1 mg PO = 1 mg Subcutaneous**
- **Carbamazepine 50-100 mg PO BID; if necessary, increase by 50-100 mg increments every 1-2 weeks. Usual maintenance dose = 800-1200 mg/day (divided BID)**
  - **Note: important to titrate slowly, to avoid Stevens-Johnson Syndrome risk, use modified-release tablets for doses larger than 100 mg**
- **Valproate 150-200 mg PO BID (use modified-release formulation); titrate by 150-200 mg BID every 3 days to 2500 mg/day**
  - **Note: most patients require no more than 1500 mg/day total dose**
- Other common antiepileptics include levetiracetam, lamotrigine, and topiramate
- Corticosteroids are helpful in the prevention and management of seizures which are secondary to brain metastasis, by decreasing the oedema surrounding a tumour mass
- Radiotherapy can be helpful in preventing seizures in patients with metastatic brain disease (if available and appropriate for the patient's general condition)
- Opioids very rarely cause seizures, except pethidine/meperidine, switching to another opioid is recommended if using pethidine/meperidine

- As in adults, benzodiazepines remain first-line treatment in status epilepticus. Consider lorazepam or midazolam first. Evidence suggests diazepam is less effective
  - If IV access is not immediately available, consider non-IV routes of administration, e.g. buccal, intranasal, rectal
  - If still seizing ≥5 minutes after a single dose, may repeat once
  - If seizures persist after ≥2 first-line treatments, consider available second-line treatments, e.g.phenytoin, phenobarbital, levetiracetam, or valproic acid

Acute Treatment

- **Lorazepam**
  - **0.1 mg/kg/dose IV, IO, Buccal, Subcutaneous, or PR (Maximum: 4 mg/dose)**
  - **Note: Sublingual tablet(s) are given buccally between the gum and cheek. Massage the outside of the cheek gently to help dissolve the tablet**
- **Midazolam**
  - **0.1 mg/kg/dose IV, IO, or Subcutaneous (Maximum: 5 mg/dose) OR**
  - **0.5 mg/kg/dose Buccal (Maximum: 10 mg/dose) OR**
  - **0.2 mg/kg intranasally (Maximum: 5 mg/nostril)**
  - **Note: Midazolam injectable solution can be given buccally between the gum and the cheek. Use a syringe to draw up the appropriate dose from the vial/ampoule**
- **Diazepam**
  - **0.3 mg/kg/dose IV, IO, or Subcutaneous (Maximum: 5 mg/dose in <5 years old; 10 mg/dose in ≥5 years old) OR**
  - **0.5 mg/kg/dose PR (Maximum: 20 mg/dose) OR**

- **Phenobarbital**
  - **20 mg/kg/dose IV or IO (Maximum: 1000 mg/dose)**
  - **Mixed in NS or D5W, infused over 20 minutes**
  - **If seizures persist after 10 minutes, may give additional 5-10 mg/kg/dose**

- **Phenytoin**
  - **20 mg/kg/dose IV or IO (Maximum: 1500 mg/dose)**
  - **Mixed in NS only. Insoluble precipitates form if mixed in D5W**
  - **Infused over 20 minutes**
  - **If seizures persist after 10 minutes, may give additional 5-10 mg/kg/dose**

Prophylactic/Maintenance Treatment

- **Phenobarbital**
  - **Initial: <12 years old: 2.5 mg/kg/dose PO BID or 5 mg/kg/dose PO daily**
  - **>12 years old: 1.5 mg/kg/dose PO q12h or 3 mg/kg/dose PO daily**
  - **Usual range: 3-8 mg/kg/day according to serum drug monitoring and clinical response**

- **Levetiracetam**
  - **Initial: 5-10 mg/kg/dose PO BID**
  - **Usual range: 15-30 mg/kg/dose PO BID**
  - **Maximum: 50 mg/kg/dose BID or 1500 mg/dose PO BID (whichever is less)**

- **Valproate**
  - **INITIAL: 2.5-5 mg/kg/dose PO BID**
  - **Increase by 2.5-5 mg/kg/dose PO BID at weekly intervals**
  - **MAINTENANCE: 20-30 mg/kg/dose PO BID or 1500 mg/dose BID (whichever is less)**
- **Parents should be trained in the use of SL lorazepam or rectal diazepam or IN midazolam as an abortive medication if a child is likely to have a seizure at home**

PITFALLS/CONCERNS

- There are many drug-drug interactions that occur with anticonvulsant medications
- It is important to monitor the dose and duration of treatment with corticosteroids frequently, especially when used for more than 4 weeks, to prevent long-term side effects such as steroid myopathy, hyperglycaemia, and gastrointestinal bleeding among others

PALLIATIVE TIPS

- Avoid prophylactic anticonvulsant therapy for patients with brain tumours (primary or metastases) if the patient has never had any seizures, due to lack of benefit and risk of medication burden
- If seizures last longer than 5 minutes, or if they occur at frequent intervals and the patient does not recover fully between intervals, the patient is in status epilepticus (see Acute Management of Seizures)

- Rectal administration of medications to treat status epilepticus can be done using a syringe with a small feeding tube cut at 5 cm to deliver medication up to 4 to 5 cms beyond the anal margin for an older child and less for an infant

REFERENCES

- American Epilepsy Society. American Epilepsy Society Guidelines 2016. *Epilepsy Curr.* 2016;16(6):399-400.
- British Columbia Children's Hospital. BC Children's and Women's Hospital (C&W) Online Formulay. 2023 [cited 2023 Aug 8]. BC Children's and Women's Hospital (C&W) Online Formulary. Available from: http://www.pedmed.org/DrugApp/index.html
- Heafield M. Managing status epileptics. *BMJ.* 2002;320:953-4.
- Lau E. *Drug Handbook and Formulary.* 2020th ed. Wolters Kluwer Clinical Drug Information; 603 p.
- McKenzie KC, Hahn CD, Friedman JN. Emergency management of the pediatric patient with convulsive status epilepticus. *Paediatr Child Health.* 2021;26(1):50-57.
- Watson M, Lucas C, Hoy A, Back I. *Oxford Handbook of Palliative Care.* Oxford: Oxford University Press; 2005.
- Weil S, Noachtar S. Epileptic seizures and myoclonus. In: Voltz R, Bernat JL, Borasio GD, Maddocks I, Oliver D, Portenoy R, editors. *Palliative Care in Neurology*. New York: Oxford University Press; 2004. p. 178-186.
- Ziai WC, Hagen N. Headache and other neurological complications. In: Berger AM, Portenoy RK, Weissman DE, editors. *Principles and Practice of Palliative Care and Supportive Oncology.* Philadelphia: Lippincott Williams & Wilkins; 2002. p. 515-531.