Withdrawal of Treatment and Ethical Considerations

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Seizure Management: Update on Parenteral Medicaton

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Objectives

• Review recent evidence for subcutaneous use of newer antiepileptic drugs (AEDs) to manage seizures at the end of life
• Consider role of newer AEDs vs midazolam to manage seizures at the end of life
Overview

• Importance of seizure management
• Standard practice
• Evidence for use of newer AEDs
  1. Levetiracetam
  2. Sodium valproate
• Role of newer AEDs at end of life
• Summary
Seizures at the end of life

- Significant anxiety and distress for patients and families
- Risk of relapse of epilepsy on stopping treatment is 40-50%
- High risk of hospital admission
- Dysphagia common in patients with brain tumours (up to 90%)\textsuperscript{1-2}

Seizure management at the end of life

- When unable to manage oral AED:
  - Consider half-life of regular AED
  - Check definite history of seizures
  - Consider alternative route

- Prophylactic use of antiepileptic medication not recommended
Standard Practice

• 1st line: Midazolam
• 2nd line: Phenobarbital
• Little supportive evidence\textsuperscript{3-5}
• No formal guidance
• No widely accepted conversion from AEDs
• Familiarity (inc compatibility), availability, overall benefit

Midazolam for seizure control

- Starting dose 10-30mg/24hrs via CSCI
- Usual dose 30-80mg/24hrs
- Dosage dependent on multiple factors
Disadvantages of Midazolam/Phenobarbital

- Sedation
- May limit pharmacological options to manage agitation
- Not patient’s usual AED – concerns re: efficacy → anxiety
Levetiracetam (Keppra)

• 1\textsuperscript{st} line AED for patients with brain tumours
  Carter J, Neerkin J, Stone P. Levetiracetam use in patients with brain tumours towards the end of life; a feasibility study preparatory to a pharmacokinetic study. (Poster EAPC 2015)

• Effective for various types of seizure and used in status

• Few drug interactions

• Generally well tolerated

• Side effects: CNS depressant effects, psychiatric effects
Levetiracetam

- Small but increasing evidence base to support subcutaneous use
- Case reports and small studies have demonstrated efficacy, tolerability and compatibility:
  - Beatty et al. The use of subcutaneous levetiracetam for the control of seizures in adults at the end of life. (Poster EAPC 2015) Prospective study, 10 patients, CSCI.
  - Steigleder T, Steil S, Ostgathe C. Treatment of palliative care patients with epilepsy by subcutaneous levetiracetam. 5 patients, bd infusions, plasma level checked in one patient after 4 days (therapeutic).
Levetiracetam SC: Published Evidence

BD SC regime:

CSCI:
  - 20 patients over 6.5 years
- Murray-Brown FL, Stewart A. BMJ Supportive & Palliative Care 2016;6:12–13
Levetiracetam SC

- PO:SC ratio 1:1
- SC bd: IV preparation diluted in 100ml 0.9% saline and infused over 30 min
- CSCI: IV preparation diluted in WFI/0.9% saline. Volumes may be too large for Graseby depending on dose.
- Note unable to dilute as per manufacturer’s recommendations (dilute dose in 100ml diluent) if using via CSCI
Sodium Valproate

• Limited evidence from case reports/series but increasing practice

  “In a case series of 6 patients with seizures and one with neuropathic pain, a median (range) dose of 1000mg (400–1800)/24h was given using the IV preparation diluted with 30mL of WFI. Duration of use ranged 3–39 days, with only one patient experiencing mild erythema at the infusion site.”

McKenna M (2013) personal communication to Andrew Wilcox (PCF)
Sodium Valproate SC

• PO:SC ratio 1:1
• Used successfully via CSCI
• Diluted with 0.9% saline/WFI
Other factors to consider

- Cost
  - Midazolam 5mg/mL 2mL = £0.63, 10mL = £2.50
  - Levetiracetam 100mg/mL 5mL = £12.73
  - Sodium valproate 100mg/mL 3mL = £7.00, 4mL = £11.58

- Availability

- Volume

- Compatibility
How should we manage seizures when patients are unable to swallow?

• Individualised approach taking into account: regular AED(s) and doses; seizure control, risk, frequency; patient and family’s concerns and priorities; prognosis

• Consider newer AEDs as alternative to midazolam, particularly if patient not imminently dying

• Document consent/rationale (off licence use)
Summary

• Common practice to use midazolam to manage seizures at the end of life
• Small but increasing evidence base for subcutaneous use of newer AEDs
• Subcutaneous administration of newer AEDs may be appropriate for some patients to manage seizures towards the end of life
Any questions?