Refractory epilepsy: treatment options

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Presentation plan

- Define osteoporosis
- Why might people with epilepsy be at risk
  - "indirect" factors
  - vitamin D
  - anti-epileptic drugs
- What can be done
  - risk assessment
- Many thanks to Dr Sofia Eriksson (consultant neurologist, NHNN)

Osteoporosis – Definition

Occurrence of non-traumatic fractures in the setting of low Bone Mineral Density (BMD)

Osteoporosis – Risk factors

- Age (particularly >65/75)
- Gender (Females > Males)
  - Untreated early menopause
- Ethnicity (Caucasian > Afro-American)
- Low levels of physical activity
- Smoking
- Alcohol excess
- Hormonal status (Post menopausal women and testosterone deficient men)
- Low BMI (<18.5 kg/m2)
- Vitamin D deficiency?
- Anti-epileptic drugs?

NICE guidelines?

- Highlights general risk of osteoporosis and fragility fractures
- No direct mention of epilepsy
- No direct mention of vitamin D
- Only one mention of anti-epileptic drugs (in the context of them interfering with vitamin D metabolism)
**NICE guidelines?**

- “… maintain a high level of vigilance for treatment emergent adverse effects, for example bone health issues…”
- “…examples of blood tests include … full blood count, electrolytes, liver enzymes, vitamin D levels, and other tests of bone metabolism”

**Bone disease – epilepsy**

- Incidence of fractures double in patients with epilepsy compared to controls
- **WHY?**
  - Frequent falls
  - Lower physical activity
  - Reduced exposure to sunlight/reduced vitamin D
  - Nutrition
  - Anti-epileptic drugs
  - Co-morbidity

**Antiepileptic drugs**

- Increase in bone turnover markers after starting AED
- Hypovitaminosis D in about 50% started on CBZ or VPA
- Dose response relationship between risk of fractures and CBZ, PHB, OXCBZ, VPA - supporting biological drug effect
- Cumulative association with duration of AED use each year of 9% increase of fracture risk
- Not enough data for newer AED

**Vitamin D**

- Severe deficiency -> defective bone mineralisation
- Subtle insufficiency -> increased bone turnover -> age-related bone loss and osteoporosis
- Dietary sources of Vitamin D limited
- Synthesised in skin - dependent on sunlight
- Vitamin D insufficiency is very common

**Vitamin D in people with epilepsy: NHNN, 2010**

- **Vitamin D levels (246 patients)**
  - Checked = 105 (30.35%)
  - Not checked = 241 (69.65%)

- No significant difference between EI and non EI

**What shall we do about it?**

- Offer advice on regular exercise, smoking, alcohol and dietary intake of calcium
- Check (or prompt GP to check) “bone profile” every 2-5 years
- DEXA scan for patients >40y if additional risk factors
- Use FRAX tool to guide further investigations/referral http://www.shef.ac.uk/FRAX
- Recommend vitamin D supplementation if vitamin D levels found to be low
- Give standard supplement of Vitamin D (400IU/day) when starting AED??
FRAX calculations

Calculation Tool

Please answer the questions below to calculate the 10 year probability of fracture with BMD.

Questionnaire:
1. Age (between 50 and 79 years at date of birth)
2. Sex
3. Weight (kg)
4. Height (cm)
5. Previous fracture
6. New fracture risk
7. Current smoking
8. Ex-smoking
9. Alcohol intake
10. Calcium intake
11. Oestrogen use
12. Oestrogen use (g/s/d)
13. Secondary osteoporosis

FRAX interpretation

- **Low risk** - reassure, give lifestyle advice, and reassess in 5 years or less depending on the clinical context.
- **Intermediate risk** - measure BMD and recalculate the fracture risk to determine whether an individual’s risk lies above or below the intervention threshold.
- **High risk** - can be considered for treatment without the need for BMD, although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women.

FRAX calculations: if your BMI is 23, gain 2 stone!
Conclusions

- Epilepsy is associated with increased risk of a range of non-epilepsy related morbidity and mortality.
- People with epilepsy as a group demonstrate higher prevalence of known risk factors for osteopenia - many of which are reversible - and fractures, the consequences of which can be devastating.
- The precise significance of (i) low levels of vitamin D and (ii) use of anti-epileptic drugs is not known - but they are likely to be significant factors.
- The excess risk that enzyme inducing anti-epileptic drugs pose compared with non-enzyme inducing drugs is not known, but research into the mechanisms and epidemiology are ongoing.
- Those involved in treating people with epilepsy are in a strong position to identify those who may be a greater risk for poor bone health.