Osteoporosis and AED’s: A Quick Look

Patients with epilepsy are 2-6 times greater risk of fractures than the general population. Antiepileptic drugs (AEDs) also carry a risk of fracture. Enzyme inducing AEDs and Valproic Acid have been associated with osteoporosis.

<table>
<thead>
<tr>
<th>AED</th>
<th>Associated with BMD loss</th>
<th>MOA for causing osteoporosis</th>
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</thead>
<tbody>
<tr>
<td>Phenytoin (PHT)</td>
<td>Y</td>
<td>• Turnover of Vit D accelerated due to increased activity of CYP P450s</td>
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<tr>
<td>Phenobarbital (PHB)</td>
<td>Y</td>
<td>• Reduced intestinal absorption of Ca → low serum Ca → secondary hyperparathyroidism → decreased BMD → fractures</td>
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<tr>
<td>Carbamezapine (CBZ)</td>
<td>Y</td>
<td>• Direct increase in bone turnover</td>
</tr>
<tr>
<td>Valproic Acid (VPA)</td>
<td>Y</td>
<td>• Increase sex hormone binding globulin concentrations → diminish testosterone and estrogen.</td>
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RECOMMENDATIONS (for patients on enzyme inducing AEDs and Valproic Acid):

**Prevention:**

1. **Calcium and Vitamin D supplementation** on all patients with epilepsy
   - Calcium 1000-1200mg/day (this includes dietary intake)
     - Ca estimation: 300mg for living in USA + 300mg for each additional serving of Ca (cheese, milk, yogurt, etc).
   - Vitamin D 800-1000IU daily
2. Reduce other risk factors if possible (see list below)
3. Consider **DEXA scan:**
   - Prior to starting enzyme inducing AEDs in postmenopausal women
   - 5-12 years after starting AED therapy depending on risk
     - High risk → 5 years (No consensus on risk stratification. Must use a patient centered approach)
     - Low risk → up to 12 years before first DEXA
   - Repeat DEXA every 2-5 years for patients on PHT, PHB, CBZ, VPA and depending on previous at risk for osteoporosis or showing s/sx of bone loss
     - Risk factors include: female, family history of fracture, smoking, ETOH use, chronic malnutrition, weight <58kg, rheumatoid arthritis

**Treat:**

4. Treat osteoporotic patients with a bisphosphonate (alendronate, risendronate or zoledronic acid) if eligible (CrCl >30ml/min, able to stay upright > 30 min after ingestion)
   - Treatment thresholds per National Osteoporosis Foundation 2013 Guidelines.
     - Hip or vertebral fracture
     - T-score ≤ -2.5: at the femoral neck, total hip or lumbar spine
     - **Osteopenia:** T-score between -1.0 and -2.5 at the femoral neck or lumbar spine
     - AND
     - **FRAX ≥ 3%** for hip fracture ≥ 20% for major osteoporotic fracture
   - Treat for 5 years then make assessment for drug holiday or new therapy
5. Patients on corticosteroids for more than 3 months should be evaluated for osteoporosis and bisphosphonate therapy according to the American College of Rheumatology 2010 guidelines for steroid-induced osteoporosis.

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Resources:

Svalheim S et al. Acta Neurol Scand 2011;124:89-95
Souverein PC et al. Neurology 2006;66:1318-1324
**Risk Factors:**

**Genetic**
- White/Asian/Native American
- FH of osteoporosis/fractures (first degree relative)
- Small body frame (wt<58 kg)
- Female

**Lifestyle**
- Current smoking
- Excessive alcohol
- Sedentary
- Little sun exposure

**Diet**
- Low calcium
- High phosphorus (?)
- Eating disorders

**Drugs**

- Corticosteroids
- Long term heparin
- Excessive thyroid
- Anticonvulsants**
- Lithium
- Tamoxifen
- Aromatase inhibitors
- GnRH agonists (ex: Lupron)
**OB/Gyn History**
Late menarche (> 15)
Early menopause (< 45) or bilateral oophorectomy
Amenorrhea (> 1 year pre-menopause)

**Medical History**
Hyperparathyroidism
Cushing’s disease
Personal history of fracture as an adult**
MS
Dementia
Endometriosis
COPD

**Fall Risk**
Medications
Gait
Decreased vision
Decreased strength
Home environment