ESA Information Statement: Anti-epileptic Drugs and Bone Heath

1. There is accumulating evidence that patients with epilepsy taking long term anti-epileptic drugs have an increased rate of bone disease and an increased risk of fractures.
2. The causes of these associations are likely to be multifactorial, but may involve an effect of the anti-epileptic drug on both bone health and balance.
3. There is current currently no evidence to support the effectiveness of any particular strategy for prevention of these adverse outcomes.

Background

Many, but not all, studies have reported that anti-epileptic drugs (AED) are associated with metabolic bone disease and are a major iatrogenic risk factor for fractures (reviewed in [1]). Controlled studies estimate that chronic AED users have an approximately doubled incidence of fracture risk [2, 3]. There remains uncertainty about the type(s) of bone disease associated with AED treatment, and the pathogenesis of AED-associated fractures. The pathogenesis of AED-associated fractures is likely to be multifactorial, due to factors including (a) low bone strength (explained by reduced bone mineral density (BMD) and impaired bone quality secondary to osteoporosis and/or osteomalacia), (b) increased propensity to fall, and (c) fractures associated with seizures or loss of consciousness.

There is need for improved understanding of the pathogenesis of AED-associated bone disease, for better definition of the risk associated with specific AED regimens, and for the development of evidence-based preventive, monitoring and treatment approaches. There are currently no consensus guidelines available for the monitoring and treatment of bone disease in AED-treated patients. However, given the body of evidence associating epilepsy and AED use with a doubling of fracture risk [2], there is a need for interim guidelines for clinicians.

Patient education [6] to raise awareness of bone health issues, and to address lifestyle factors influencing BMD should be optimized where possible, including cessation of smoking, limitation of alcohol intake, adequate diet (including calcium intake), exercise and careful sun exposure [7].

Heller [8] recommended that all adults who are commencing or prescribed long-term AEDs should be evaluated with baseline fasting serum calcium and phosphate levels and bone densitometry. If abnormal serum biochemistry or BMD is noted, further evaluation such as 25-OHD and PTH levels, bone turnover markers and specialist referral would be recommended.

Heller's editorial [8] suggested that all patients taking barbiturates, phenytoin and possibly carbamazepine should be considered for calcium and vitamin D supplementation. Given the recent evidence that patients taking valproate are also at risk of bone loss, this could be added to the list.

Drezner's review [9] of treatment of bone disease in patients taking anti-epileptic medication recommends prophylactic vitamin D therapy at doses up to 2000 IU daily from the time of commencement of AED therapy, or in the case of established osteopenia/osteoporosis, a dose of 2000-4000 IU daily, together with optimized calcium intake. Higher dosages of vitamin D would be required in osteomalacia. The author is cautious in addressing the issue of bisphosphonate use in this population, particularly in younger patients, and emphasizes the need for further research into best practice for prevention and treatment of bone disease associated with AED use.

As less is known regarding the potential effect of newer AEDs on bone health, supplementation with calcium and vitamin D in patients with identified deficiencies would seem prudent in this population until further specific information is available.

Patients treated with AEDs should be monitored for increased risk of falls and interventions to prevent falls instituted where appropriate.

Involvement of the patient's general practitioner in these general health and preventative measures is advisable. In cases with evidence of or high risk of bone disease or fractures, referral to an endocrinologist should be considered.

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