

## **Epilepsy - Comorbidities**

### ***Bone Health in Epilepsy.***

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**28<sup>th</sup> June 2013.**

Patients with epilepsy are reported to have at least double the risk of bone fractures when compared to the general population (1). While this association has been long reported, further research is required in order to better determine the reasons for the association, and to inform both patients and clinicians of the best practice approach to minimise fracture risk (2). For patients, treatment of their epilepsy remains the foremost consideration for prevention where possible of seizures, consequences of poorly-controlled epilepsy and injury sustained during seizures. However, patients and clinicians should be aware of potential treatment side-effects and other consequences of epilepsy (3). In the case of epilepsy, bone health should be monitored alongside other potential comorbidities such as anxiety and mood issues, weight, and specific side effects of anti-epileptic medication. It must be remembered that an association does not necessarily imply causation, and longitudinal well-designed and controlled studies are required to further examine the issue. Whether the increased fracture risk seen in patients taking anti-epileptic medication is a medication side-effect or another consequence of epilepsy remains to be proven. There can also be additional risk factors for bone disease and increased fracture risk in patients with epilepsy, which should be assessed, including family history of osteoporosis, for instance. Causes of fractures in epilepsy can include injury occurring during seizure either due to a fall or biomechanics, falls at other times due to balance impairment (4, 5), and in some patients, reduced bone density or bone quality.

Early research in this field was often performed in patients living in an institutionalised setting, and therefore could be confounded by other risk factors for bone health impairment such as comorbid medical conditions, low exercise levels, poor nutrition, low sunlight exposure (contributing to lower vitamin D levels) and sometimes higher rates of smoking (6). Many studies have been performed in both adults and children with epilepsy to determine bone health parameters, and many, but not all studies have shown significant reductions in bone density or effects upon other measures of bone health in association with epilepsy or particular anti-epileptic medication usage. The conflicting results and differing characteristics of the populations and studies have made it difficult to put in place internationally-recognised guidelines for the monitoring and treatment of bone health in epilepsy. However, based on some of the proposed mechanisms for bone disease, we can deduce some logical clinical approaches, such as periodic testing of bone density, vitamin D levels and supplementation, and optimising calcium intake (7). The bone density (DXA) scan involves a very small dose of radiation, so is not utilised in pregnant ladies and for different reasons (a temporary reduction in bone density) nor is it done in ladies who are breastfeeding their baby. Regulations, availability and reimbursement practices for DXA vary between regions and countries, but where available, a bone density test when long term epilepsy treatment is proposed gives useful baseline information, and can be compared to further testing a couple of years later. Vitamin D levels should also be optimised – this can be achieved through diet, supplements, or some sun exposure (however the amount of sun exposure needs to be carefully balanced against advice regarding skin cancer risks). Some medications used for epilepsy (such as phenytoin, carbamazepine, and oxcarbazepine) are classed as inducers of an enzyme system in the liver, which when taken can also increase metabolism of other drugs and also of vitamin D (8). Monitoring with blood tests for levels of vitamin D, and supplementing Vitamin D where required is recommended. A good diet including calcium intake should also be advised. Exercise is useful for general fitness as well as bone health, and is sometimes seen to be reduced in patients with epilepsy. Therefore, exercising within any limitations associated with underlying medical conditions should be encouraged (9, 10) and should be undertaken with medical guidance. If a patient

reports falls, a falls assessment and allied health review with a view to falls prevention could be initiated, although specific scientific evidence of falls and balance intervention programs in patients with epilepsy is limited. In patients who do have reduced bone density (which may be reported as osteoporosis or osteopenia on their bone density scan results), specific bone health advice should be sought from a specialist. Similarly, advice should be sought if there are hormonal changes seen in patients with epilepsy, some of which can also affect bone health(11). Data as to the effectiveness of types of bone anti-resorptive or anabolic therapy, considering the often younger age of patients, is limited and this area is a subject of ongoing review and study (7).

Clinicians and researchers continue to search for causes and effects in this area. Some recent developments include studies examining whether a variation in the gene for the vitamin D receptor may be associated with the increased fracture risk. Clinical and laboratory studies of bone health in children and adults are in progress at many centres internationally, and studies of responses to specific bone therapeutics should become available in future. The aim of the ongoing research is to better determine the causation of the problem, what the risk factors are, and what the best treatment and prevention strategies are. Ongoing interest in bone health in epilepsy in the clinic and in research should assist to better inform patients and doctors in making clinical decisions and improve outcomes for patients in the longer term.

*Please note that this commentary does not constitute clinical advice. Patients should consult their doctor for information relevant to their own personal medical circumstances. Clinical practice and research information may change over time, and patients are advised to consult their own doctors for medical treatment and advice.*

#### References:

1. Vestergaard P. Epilepsy, osteoporosis and fracture risk - a meta-analysis. *Acta Neurol Scand.* 2005 Nov;112(5):277-86.
2. Petty SJ, O'Brien TJ, Wark JD. Anti-epileptic medication and bone health. *Osteoporos Int.* 2007 Feb;18(2):129-42.
3. St Germaine-Smith C, Liu M, Quan H, Wiebe S, Jette N. Development of an epilepsy-specific risk adjustment comorbidity index. *Epilepsia.* 2011 Dec;52(12):2161-7.
4. Petty SJ, Hill KD, Haber NE, Paton LM, Lawrence KM, Berkovic SF, et al. Balance impairment in chronic antiepileptic drug users: a twin and sibling study. *Epilepsia.* 2010 Feb;51(2):280-8.
5. Shiek Ahmad B, Hill KD, O'Brien TJ, Gorelik A, Habib N, Wark JD. Falls and fractures in patients chronically treated with antiepileptic drugs. *Neurology.* 2012 Jul 10;79(2):145-51.
6. Nilsson OS, Lindholm TS, Elmstedt E, Lindback A, Lindholm TC. Fracture incidence and bone disease in epileptics receiving long-term anticonvulsant drug treatment. *Arch Orthop Trauma Surg.* 1986;105(3):146-9.
7. Meier C, Kraenzlin ME. Antiepileptics and bone health. *Ther Adv Musculoskelet Dis.* 2011 Oct;3(5):235-43.
8. Brodie MJ, Mintzer S, Pack AM, Gidal BE, Vecht CJ, Schmidt D. Enzyme induction with antiepileptic drugs: cause for concern? *Epilepsia.* 2013 Jan;54(1):11-27.
9. Elliott JO, Seals BF, Jacobson MP. Use of the Precaution Adoption Process Model to examine predictors of osteoprotective behavior in epilepsy. *Seizure.* 2007 Jul;16(5):424-37.
10. Ablah E, Haug A, Konda K, Tinius AM, Ram S, Sadler T, et al. Exercise and epilepsy: a survey of Midwest epilepsy patients. *Epilepsy Behav.* 2009 Jan;14(1):162-6.
11. Pack AM, Reddy DS, Duncan S, Herzog A. Neuroendocrinological aspects of epilepsy: important issues and trends in future research. *Epilepsy Behav.* 2011 Sep;22(1):94-102.