

Anti-epileptic drugs and osteoporosis

What is osteoporosis?

Osteoporosis occurs when the struts that form the mesh-like structure inside bones become thin. This causes the bone to become fragile and break easily, even after a minor bump or fall. You might hear these breaks described as 'fragility fractures'. The terms 'fracture' and 'broken bone' mean the same thing.

Fractures can occur in many parts of the body, but they are most common in the wrists, hips and spine. It's these broken bones that can cause pain, rather than osteoporosis itself. Spinal fractures can also cause height loss and a curved spine.

What are anti-epileptic drugs?

Anti-epileptic drugs are used mainly to stop the seizures, sometimes called 'fits' caused by epilepsy. Epilepsy is a very common neurological condition requiring life-long treatment for many people of all ages.

How do anti-epileptic drugs cause osteoporosis and increase the risk of broken bones (fractures)?

The exact mechanism by which anti-epileptic drugs affect bone strength is not entirely understood. Whilst a variety of mechanisms have been proposed, it is thought that some anti-epileptic drugs alter the way vitamin D is broken down and used by the body. Vitamin D helps the body absorb calcium which is a vital nutrient for bones. Most people obtain the majority of their vitamin D from exposure to sunlight. Severe vitamin D deficiency can also cause osteomalacia (softening of the bones) in adults, which is also called rickets in children. Anti-epileptic drugs are more likely to affect the strength of your bones if you are taking high doses of these drugs; if you have taken lots of different types of anti-epileptic drugs and if you have been taking them for many years.

Furthermore, the direct effects of anti-epileptic drugs may also increase the risk of fall-related fractures by causing drowsiness and slowing down of the body's protective reflexes as well as affecting balance and coordination (this is more likely as you get older).

What else associated with epilepsy increases fracture risk?

If you have epilepsy you are more likely to have fractures but it is likely to be due to a combination of factors including the direct effects of the anti-epileptic drugs, but also the seizures themselves causing bones to break. Fractures (including spinal compression fractures) can be sustained during a seizure or from a fall resulting from a seizure. Other contributory factors if you have epilepsy (especially if you have other health conditions) include lack of exposure to sunlight which can cause lower vitamin D levels, and reduced activity levels or physical restrictions which can impair bone health and consequently increase fracture risk.

Do all anti-epileptic drugs cause osteoporosis and increase fracture risk?

Various studies have indicated a loss of bone density and increased risk of fractures in people using long-term anti-epileptic drugs. Most of the research in this area has been in people taking the older anti-epileptic drugs such as phenytoin (Epanutin), phenobarbital, carbamazepine (Tegretol), primidone (Mysoline) and sodium valproate (Epilim). These anti-epileptic drugs (with the exception of sodium valproate) are thought to stimulate a liver enzyme which destroys vitamin D, reducing the amount of vitamin D in the body. These are known as enzyme inducing anti-epileptic drugs. It is still unclear how sodium valproate decreases bone density.

A drug safety update from the MHRA (the UK government agency that ensures medicines are acceptably safe) has reviewed the evidence (April 2009) and found that long-term treatment with carbamazepine, phenytoin and primidone, and also long-term treatment with sodium valproate, can reduce bone density which may lead to osteoporosis and fractures in certain 'risk' groups.

Particularly at risk are people immobilised for long periods, those not getting enough calcium in their food and drink and when there is insufficient exposure to sunlight to maintain adequate vitamin D levels.

Currently there is only limited and conflicting research data from the studies of other or newer non-enzyme inducing anti-epileptic drugs, such as gabapentin, lamotrigine, topiramate and levetiracetam (Keppra) regarding their effects on bone. The findings from two recent research studies suggest that most anti-epileptic drugs are associated with an increased fracture risk. One of these studies analysed the data from several individual pieces of research and the other focussed on people aged 50 years and older taking anti-epileptic drugs. However more research is needed to evaluate the long-term effects of these medications on bone health.

If I am taking anti-epileptic drugs, do I need a bone density scan?

Bone density scans provide information about the strength of your bones and are generally indicated when the result is needed to help determine whether a drug treatment for osteoporosis would be beneficial. Although there are no definitive recommendations for people with epilepsy, if you have been taking anti-epileptic drugs long term and especially if you have other risk factors (see below) it may be useful to discuss your possible risk of osteoporosis and fracture with your doctor. The doctor will assess your need for a bone density scan based on your overall risk and refer you for a scan if necessary.

The importance of assessing fracture risk is included in a national guideline on the 'Management of Osteoporosis and the prevention of fragility fractures' from SIGN (Scottish Intercollegiate Guidelines Network, 2021). It recommends that healthcare professionals should consider a fracture risk assessment for anyone with epilepsy over the age of 50 who is taking an anti-epileptic drug (particularly the enzyme-inducing type) – especially if they have other risk factors for osteoporosis.

Your bones will be less strong as you move into older age, whatever your bone density result, so you are more likely to need scanning and an assessment of your fracture risk after the age of 50.

As I am taking anti-epileptic drugs, do I need an osteoporosis drug treatment to strengthen my bones?

The main aim of an osteoporosis drug treatment is to reduce the risk of fractures. Treatments will usually be recommended if it is considered that your risk of fracture is high. Your risk is assessed based on a combination of factors such as your age, personal and family history of fractures, lifestyle factors such as alcohol use and smoking as well as information about bone density - if a scan has been performed. Again, fracture risk is always higher in later life so you are more likely to be offered a drug treatment after the age of 50 years. You may be prescribed a vitamin D supplement with or without an osteoporosis drug treatment to ensure you are getting sufficient vitamin D. A calcium supplement may also be recommended if you are not getting enough calcium in your diet.

Should my vitamin D level be checked?

The NICE (National Institute for Health and Care Excellence) guideline (2012) on the management of epilepsy in adults and children recommends checking vitamin D levels and undertaking any other investigations that may be appropriate to assess bone health every 2-5 years for all adults who take enzyme inducing anti-epileptic drugs. However all current UK guidance suggests considering vitamin D supplementation in people who are felt to be at 'higher risk' (see above) including those taking sodium valproate or any of the enzyme inducing anti-epileptic drugs on a long term basis. The usual dose of vitamin D is 10-20 micrograms (mcg) or 400-800 international units (IU), although some doctors may prescribe higher doses.

What else can I do to prevent osteoporosis and fractures?

Factors which can help to maintain healthy bones are a well-balanced diet with adequate calcium rich foods; regular weight-bearing exercise but taking care to exercise within your capabilities particularly if you have any balance problems or physical disability; avoiding smoking and keeping alcohol consumption within the recommended limits.

I don't have epilepsy, but I take gabapentin for back pain caused by spinal compression fractures. Could this make my osteoporosis worse and increase my risk of further fractures?

Anti-epileptics medications such as gabapentin (Neurontin) can also be used to help with pain. If shape changes to the spine are severe as a result of vertebral fractures, spinal nerves can get pinched or trapped resulting in neuropathic (nerve) pain. These drugs work by damping down the nerve signals going to your brain, so pain messages aren't transmitted so effectively.

There is no conclusive research evidence to suggest that either gabapentin or another commonly prescribed medication, pregabalin, have any significant effects on bone when used to treat neuropathic pain. The above medicines will always be started in low doses and increased gradually until an effective minimal dose is achieved to help manage your pain.

Additionally, when anti-epileptic medications are prescribed for pain, they tend to be used for shorter periods compared to the long-term use of these drugs in people with epilepsy, which in itself constitutes a risk factor for bone health.

It's always important to weigh up risks and benefits when taking any medication, but if gabapentin is making a difference and reducing your pain, then this benefit (based on current evidence) far outweighs any potential risk to your bone health.

Getting more information and support

We hope this fact sheet will help you feel more informed and more confident when discussing your bone health with your medical team.

For more information about osteoporosis and bone health, including fact sheets on all available drug treatments, visit our website at theros.org.uk/info or order more of our printed publications.

If you need more information or support, talk to your healthcare professional.

You can also call our specialist Helpline nurses with any questions or concerns about bone health or living with osteoporosis, for free, on **0808 800 035**, or email them at nurses@theros.org.uk

You may also find the following organisations helpful:

Epilepsy Action

New Anstey House
Gate Way Drive
Yeadon, LEEDS
LS19 7XY

epilepsy.org.uk
0808 800 5050
helpline@epilepsy.org.uk

Epilepsy Society

Chesham Lane
Chalfont St Peter
Buckinghamshire SL9 0RJ

epilepsysociety.org.uk
01494 601400
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This information is based on the latest evidence and clinical practice. It should not replace advice from your own healthcare professionals.



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