Bone disease in thalassaemia

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Osteoporosis is a disease that is commonly associated with women who have gone through the menopause. Although this is the largest group of patients that we see in the osteoporosis/metabolic bone clinics there are other rarer conditions that are associated with osteoporosis. Osteoporosis literally means "porous bones" and is a thinning of the bone structure that makes the individual more prone to fractures (broken bones). Fractures can occur with less trauma and these are called fragility fractures. Osteopenia is a term used when the bones are less dense than a young adult's bones, but haven't quite reached the level of osteoporosis. It is estimated that up to 50-80% of people with thalassaemia have osteopenia or osteoporosis.

The consequences of this reduction in bone density for patients are bony pain and fragility fractures. Fractures are estimated to occur in 70-80% of people with thalassaemia, although 1 in 5 patients will have no bony symptoms. The pathology that underlies this bone disease is complex; with many possible factors influencing the bone including delayed sexual maturity, dysfunction of the parathyroid and thyroid glands, growth hormone deficiencies and direct toxicity of iron on bone cells. Bone is a dynamic tissue that is very metabolically active and is constantly undergoing break down and build up. We know from measuring proteins in the blood of patients with thalassaemia that there is a higher rate of bone loss (resorption) than bone formation and therefore the overall balance is that the bone density will be reduced and the bones more liable to fracture.

Treating low bone density

Lifestyle measures

There are things in our lifestyle that can influence our bones and anyone with bone disease should be trying to do what they can to optimise their bone health. Smoking is linked to lower bone density and fractures. Giving up smoking therefore, as well as having many other benefits in terms of reducing the risk of cancer, heart disease and strokes, can improve the health of your bones. Physical activity is also important to our bones. The stimulation of weight-bearing exercise improves bone density and bone strength. Exercise such as a walking, jogging or exercise classes with some impact e.g. aerobics stimulate the bone to maintain its density. Very high impact exercise is best avoided by patients with osteoporosis due to the risk of fracture, but walking is suitable for all.

Sex hormones

People with thalassaemia can have low levels of the sex hormones, which are also essential hormones for our bone health. If there are low levels of the sex hormones then treatment with testosterone replacement therapy or using the oral contraceptive pill or HRT in women may be appropriate. However these treatments aren't suitable in all patients and need to be discussed with your haematologist.

Bisphosphonate drugs

The bisphosphonates are a group of drugs that reduce bone resorption (breakdown). They have been extensively used in treating post-menopausal women with osteoporosis and are also used in treating some forms of cancer that affect the bones. It is difficult to do large studies of treatment in rare diseases, but studies lasting 1 or 2 years have shown these drugs to reduce the resorption of bone, improve the density of the bones and reduce back pain. Some of these drugs are oral and taken weekly e.g. alendronate. Others are intravenous (given via the veins) and are given less often: monthly, 3 or 6 monthly e.g. pamidronate or zoledronate.

Complications of long-term bisphosphonate use

Bisphosphonates have been used in osteoporosis for around 20 years. More recently there have been reports of potential side-effects of long-term use. The first of these is a condition called osteonecrosis of the jaw (ONJ). This is a condition that affects the inside of the mouth. A hole appears in the gum and the underlying bone is exposed. It doesn't heal for weeks and can take months to improve. ONJ does occur in patients who haven't taken any bisphosphonate, but the rate appears to be higher if you have received treatment with a bisphosphonate. The mechanism behind this isn't well understood. The risk of ONJ in post-menopausal osteoporosis is estimated at around 1:10,000. The rate in thalassaemia patients treated with bisphosphonates is not known.

The second reported rare side-effect is unusual fractures of the thigh bone (atypical femoral fractures – AFF). When a patient with osteoporosis breaks their hip it is usually across the neck of the femur (thigh bone), however we now have reported cases of fractures lower down the femur that occur on minimal trauma. There have been cases of these fractures in patients with thalassaemia treated with bisphosphonates. These fractures can be difficult to heal and cause significant. Again these are rare fractures, but cause significant problems for affected patients.

Both the American and UK guidelines for treating osteoporosis in thalassaemia patients advise using bisphosphonates in some patients, particularly those who have fractured. However long-term use may not be suitable. The bisphosphonates are long-acting drugs that stay in the bones working for years after they are given. This has led to the concept of

a “drug holiday” i.e. a break in treatment, usually for a couple of years, to try to reduce the incidence of these rare side-effects. Evidence in post-menopausal women suggests that a 2 year break in treatment does not lead to thinner bones or more fractures. Doctors therefore may suggest a break in bisphosphonate treatment in patients with thalassaemia, but this is determined on a case by case basis.

Conclusion

Osteoporosis is a common problem in patients with thalassaemia with consequences of bony pain and broken bones. There are treatments, such as bisphosphonates that have evidence for being used in osteoporosis in thalassaemia. There are rare side-effects of these drugs and we may be able to reduce these by having breaks in treatment – “drug holidays”. This is an area that would benefit from further research and ongoing collaboration between different specialities.