Prevention and treatment of osteoporosis in women

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Abstract

Osteoporosis is a disease with a significant disease burden worldwide, affecting more than 75 million people in the US, Europe and Japan. With an ageing population the incidence of osteoporosis is growing. Osteoporotic fractures have significant individual morbidity but also strain Healthcare services. There is no screening service for osteoporotic fractures in the UK and physicians must actively identify patients who are at risk of osteoporotic fractures as well as managing appropriately patients who have sustained osteoporotic fractures. Diagnosis of osteoporosis is done with Dual energy X-ray Absorptiometry (DXA) scans to measure Bone Mineral Density (BMD). The World Health Organisation Fracture Risk Assessment (FRAX) score is used to identify patients who are at risk of fractures. Pharmacological treatment is recommended for those who obtain a risk score sufficient enough to warrant treatment. The treatment of osteoporosis includes calcium and vitamin D replacement, bisphosphonates, denosumab, teriparatide and hormone replacement therapy in women. Potential therapies that are currently undergoing clinical trials include Abaloparatide and Romosozumab.

Keywords bone mineral density; DXA scan; fragility fracture; FRAX score; osteoporosis; postmenopausal

Case presentation

An 83-year-old female patient was diagnosed with osteoporosis when she presented with fracture right neck of femur at the age of 70 years. At the time of diagnosis, she had vitamin D deficiency and daily dietary calcium intake of less than 500 mg. Subsequently she was commenced on calcium and vitamin D supplements and oral bisphosphonate treatment for osteoporosis. However, she could not tolerate the oral bisphosphonate as she complained of gastrointestinal irritation type symptoms. Therefore, she was subsequently commenced on intravenous (IV) bisphosphonate treatment. She had IV zoledronic acid 5 mg once a year for next 3 years. There was apparent increase in bone mineral density after 3 years of IV bisphosphonate treatment, based on dual-energy X-ray absorptiometry (DXA) at treatment review. Vertebral fracture assessment (VFA) showed no vertebral fractures. Patient was given a drug holiday (bisphosphonate was stopped, and patient continued on calcium and vitamin D supplements) due to an apparent increase in bone mineral density. After 2 years of drug holiday, the bone mineral density had reduced significantly. She was commenced on IV zoledronic acid 5 mg treatment once a year. After 2 years of starting IV zoledronic acid treatment, she complained of sudden onset of back pain. An X-ray spine showed minor anterior wedging of thoracic vertebrae (T7, 8 and 9) as well as biconcave fracture of T12 and lumbar vertebra L3. The patient was commenced on teriparatide therapy as the third-line management for her severe osteoporosis. The bone mineral density on DXA scanning found significant increase in lumbar spine and no significant change in left femoral neck bone mineral density, after 2 years of teriparatide treatment. VFA did not show any new vertebral fractures. The patient was commenced on denosumab treatment to consolidate the effect of teriparatide therapy for next 3 years.

Epidemiology and impact

Osteoporosis has a significant disease burden and cost and represents a major public health problem worldwide. The World Health Organisation (WHO) study group found that it affects more than 75 million people in US, Europe and Japan and causes more than 8.9 million fractures, globally. The lifetime probability of osteoporotic fractures (hip, wrist, and vertebral) is 30–40%. With an aging population, the prevalence of osteoporosis is expected to only increase.

The impact can be considered on an individual and collective basis. Collectively the economic burden is staggering. In high-income countries, osteoporotic fractures account for more bed days than myocardial infarctions, breast or prostate cancer. For individuals, hip fractures alone are a cause for a significant disease burden. 20% of hip fracture patients require long-term nursing home care and only 40% fully regain pre-fracture mobility. Vertebral fractures affect individual daily activity, producing postural changes and chronic back pain. Thoracic vertebral fractures indirectly cause morbidity by increasing incidence of restrictive lung disease. Psychosocially, osteoporotic fractures account for reduced quality of life, seen most clearly in those who are bedridden as a result.

The challenge arises as many are not subjected to the appropriate testing to diagnose osteoporosis, nor are their early clinical risk factors established at an early enough stage. Inherent to its presentation, osteoporosis is asymptomatic until fractures occur. Screening methods have been difficult to establish and are not currently employed in the UK. Further, many people are not treated once having had osteoporotic fractures. Only 23% of women aged 67 and over receive bone mineral density test or prescription within 6 months of fracture.

Hence the aim of osteoporosis management is to identify women who are at risk of osteoporosis, prevent fragility fractures and to initiate appropriate treatment.

Pathophysiology

Bone remodelling, essential for bone strength, is mediated by osteoclasts and osteoblasts. Osteoclasts resorb mineralised bone (resorption of old bone), which is then replenished by

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osteoblasts (formation of new bone matrix). Hence, bone remodelling is a tightly controlled continuous coupling process between osteoclasts and osteoblasts, which sustains unremitting bone repair and maintenance of bone strength.

Osteoporosis is caused by an imbalance of the two biological processes (uncoupling of osteoblasts and osteoclasts), with an increase in osteoclast activity, leading to overall bone loss.

There are molecular signals in the form of cytokines which orchestrate the bone remodelling process. Most well-known is the receptor activator of nuclear factor kappa B ligand (RANKL) and osteoprotegerin (OPG) signalling system. RANKL is released from osteoblasts and binds to the receptor activator of nuclear factor κ B (RANK) on the osteoclast, a receptor located on quiescent osteoclasts. This binding results in osteoclastogenesis, also known as the differentiation and activation of osteoclasts. OPG is a decoy receptor for RANKL, its release prevents progression of this pathway by competing with RANKL to bind with RANK, therefore preventing osteoclastogenesis. Osteoclast-driven resorption of bone is mediated by the RANKL-OPG imbalance, where increased RANKL leads to increased osteoclastogenesis and subsequent bone loss. RANKL release is regulated by several cytokines and hormones: among these parathyroid hormone (PTH) and oestrogen have a predominant role. PTH increases the osteoclastic activity, whereas oestrogen suppresses the osteoclast activity, by their effect on RANKL-OPG pathway (Figure 1). In post-menopausal women, an inevitable deficiency in oestrogen leads to increased osteoclastic activity and thereby bone loss.

Diagnosis, definition and risk assessment of osteoporosis

WHO defines osteoporosis as "a progressive systemic skeletal disease characterised by low bone mass and micro architectural deterioration of bone tissue with consequent increase in bone fragility and susceptibility to fracture". Osteoporosis is characterised by low bone mass, which is measured as bone mineral density (BMD).

The WHO classifies BMD using a "T-score" (standard deviation's [SD] away from young adult mean bone mass value). Osteoporosis is defined as BMD with T-score equal to or less than −2.5 and osteopenia with a T-score between −2.5 and −1 SD (away from young adult mean bone mass value). Severe osteoporosis is the presence of one or more bone fragility fractures in addition to a low T-score. The WHO, BMD T-score classification is only applied to postmenopausal women and men older than 50 years of age. In premenopausal women and men younger than 50 years, instead of the T-score, a "Z-score" (SD from the age-matched normal bone mass value) should be used. This figure adjusts for chronological age, a Z-score of less than −2 as low bone mass. BMD is an independent risk factor for osteoporotic fracture. Hence, for each 1 SD decrement in BMD, the risk of fracture increases by two-fold. Therefore, initial BMD calculation is vital for the confirmation of diagnosis, prediction of fracture risk and monitoring osteoporosis management.

The WHO recommends DXA scanning for measuring the BMD. For diagnostic purposes alone, DXA at the femoral neck is the preferred site for generating a T-score, because of its highest predictive value for fracture risk. Degenerative changes in the spine, which are common in elderly patients, can falsely elevate the BMD, for this reason the spine not the preferred site for diagnosis of osteoporosis in post-menopausal women. Nevertheless, BMD calculation at the spine is the preferred site for assessing response to treatment.

BMD has been shown to have a high specificity but low sensitivity for osteoporosis, so it is not used in population screening and should not be routinely measured. Moreover, because of its low sensitivity, osteoporotic fractures are found to occur in women with a T-score of more than −2.5. Hence case finding methods are the preferred option above screening. BMD measurement is not recommended in young men (<50 years of age) or premenopausal women unless significant risk factors are present.

Advanced ageing and several clinical risk factors contribute to fracture risk independently of BMD (Figure 2). Hence inclusion of risk factors increases sensitivity of testing, without compromising specificity. The tool to calculate the fracture risk has been developed by the WHO Collaborating Centre for Metabolic Bone Disease at Sheffield as the "WHO Fracture Risk Assessment Tool" (FRAX), which computes a 10-year probability of major osteoporotic or hip fracture. NICE recommends the use of FRAX in post-menopausal women to assess fracture risk; thereby identifying high-risk patients for whom initiating treatment will prevent fragility fractures.

Other measures of risk assessment include vertebral imaging and bone turnover markers. Low trauma vertebral fractures are consistent with a diagnosis of osteoporosis even in the absence of low BMD and are an indication for pharmacological treatment. Most vertebral fractures are asymptomatic and remain undiagnosed for many years; they may only be detected on vertebral imaging (vertebral fracture assessment [VFA], available on most DXA machines). Their discovery can completely change fracture risk. VFA can be repeated in cases of vertebral height loss, new back pain or if there is consideration of a medication holiday.

Additionally, biochemical markers of bone remodelling (bone turnover markers) are divided into bone formation and resorption markers (Table 1). Bone formation markers are produced by osteoblasts or by bone procollagen metabolism; whereas resorption markers are produced by degradation of osteoclasts or collagen tissue in bone.

The bone markers are predictive of fracture risk or rate of bone loss. They can be used to monitor efficacy of, and compliance with, osteoporosis treatment and to help as determine the duration of a drug holiday.

Prevention of osteoporosis

Lifestyle advice and treating risk factors can reduce the likelihood of fracture in people at risk. General measures such as: increasing physical activity; cessation of smoking; moderate alcohol consumption; optimal dietary calcium intake (1000 −1200 mg daily) and vitamin D sufficiency at all ages reduces fracture risk. In the elderly population, addressing modifiable factors has a major role in preventing osteoporotic fractures. These factors include visual impairment, medications that alters alertness and balance, home environmental hazards and falls risks. Post-menopausal osteoporotic patients, regardless of history of bone fragility fractures, should be treated with pharmacological therapy.

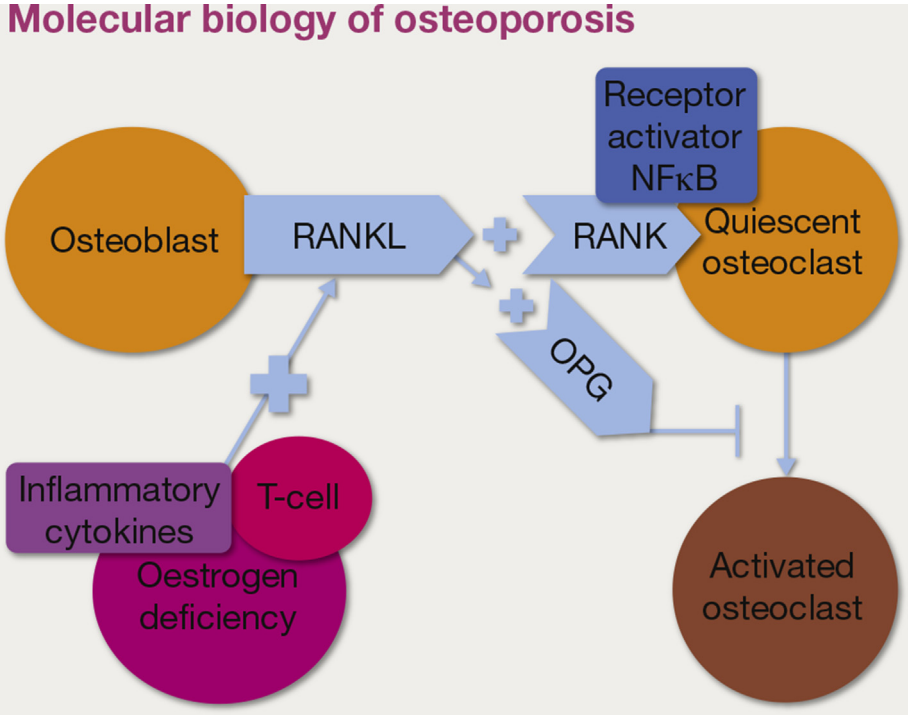

Figure 1

Pharmacological treatment of osteoporosis

Pharmacological treatment is either anti-resorptive (targeting osteoclasts) or anabolic (targeting osteoblasts). All of the recommended medications have been shown to increase the BMD and reduce the risk of fracture.

The anti-resorptive medications are: bisphosphonates (alendronate, risedronate, ibandronate, zoledronate, etidronate) and denosumab. The anabolic medication is parathyroid hormone peptide (teriparatide).

Medications that are also useful in postmenopausal women include hormone replacement therapy and selective oestrogen-receptor modulators.

Bisphosphonates

Bisphosphonates (BP) interfere with the biochemical processes of bone resorption, acting on osteoclasts and also inducing their apoptosis. They are adsorbed into the bones surface and remain embedded in the mineralized bone surface. This allows them to continue to exert their effects even after cessation of the medication. BP can be administered orally or intravenously. The oral BP are alendronate, risedronate, ibandronate and etidronate (once a week or monthly). Intravenous BP are zoledronic acid (once a year) and ibandronic acid (once every 3 months). BP are no longer on patent and are widely available and cost-effective medications. NICE recommends the use of oral BP as the first line treatment for post-menopausal osteoporosis. In patients who

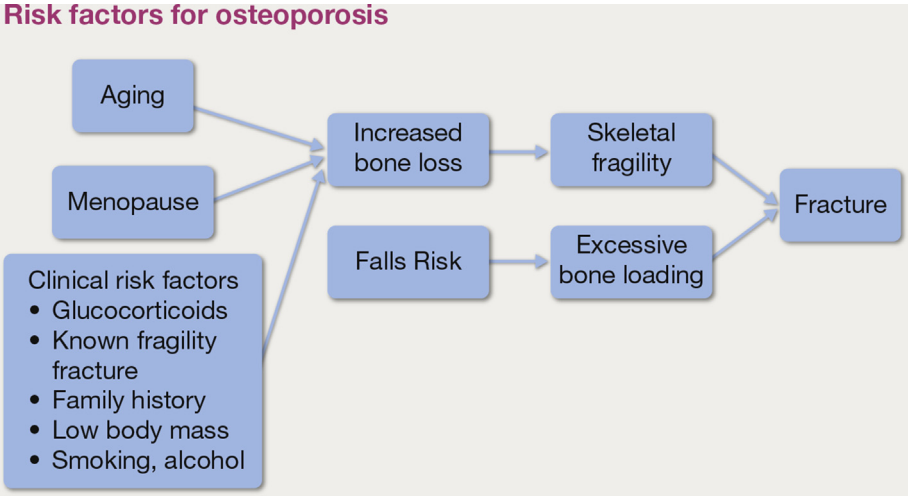

Figure 2

Markers of bone remodelling

Bone Formation Markers	Bone Resorption Markers
Procollagen type 1 N terminal propeptide (P1NP)	N terminal C peptide (NTX)
Procollagen type 1 C terminal propeptide (P1CP)	C terminal C peptide (CTX)Cross links (DPD: deoxypyridinoline; PYD: pyridinoline)
Bone specific alkaline phosphatase	Hydroxyproline
Osteocalcin	Hydroxylysine
	Bone sialoprotein
	Cathepsin K
	osteoprotegerin (OPG)
	receptor activator for nuclear factor kappa-B ligand (RANKL)

Table 1

are intolerant to oral BP or where BP are contraindicated, IV BP should be considered. BP are not licensed in patients with renal failure or those who have an estimated glomerular filtration rate (eGFR) of less than 45 ml/min/1.73 m^2 as they are considered to be nephrotoxic.

In the Fracture Intervention Trial, which involved 2027 women with known vertebral fractures at the start of the trial, evidence found that on completing four years of alendronate therapy new vertebral fractures were decreased by 47% and hip fractures by 51%.

The HORIZON-PFT trial included 7500 women with known osteoporosis. They were given 3 years of treatment with zoledronic acid and this reduced new vertebral fractures by 70% and hip fractures by 41%.

In summary, BP have been found to reduce vertebral, hip and non-vertebral fracture risk.

Oral and IV BP therapy should be reviewed after 5 years and 3 years respectively. The continuation of treatment should be assessed taking into consideration the following: patient age (75 years or above), T-score at the left femoral neck (2.5 SD or below), history of previous hip or vertebral fractures, recurrent fractures on therapy or receiving prolonged high doses of glucocorticoids. The National Osteoporosis Guideline Group, UK provides a decision algorithm at the end of 5 or 3 years of treatment with BP.

Denosumab

Denosumab is a human monoclonal antibody that inhibits the bone resorption by binding to the RANKL, thereby inhibiting the differentiation of osteoclasts and inducing their apoptosis. As a result of decreased osteoclastogenesis there is decreased bone resorption and increased bone mineral density. Denusomab is not renally cleared and can be safely administered in patients with low eGFR. NICE recommends denosumab treatment in patients with severe osteoporosis who are intolerant to initial BP therapy.

The "Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM)" trial, an international randomized controlled trial which ran over 36 months, found that women benefitted from denosumab therapy compared to placebo. Bone resorption was reduced by a median of 86% at 1 month, demonstrating superiority over all other bone antiresorptive medications. The 7868 women with a T-score of less than −2.5 but more than −4 at the lumbar spine or total hip involved in the study, were seen to benefit from twice yearly denosumab therapy, with 68% less vertebral fractures, 40% less hip fractures and 20% less non-vertebral fractures. A subsequent long-term denosumab trial extending up to 8 years (the FREEDOM extension trial) was associated with continued gains in BMD and persistent reduction in bone turnover markers with ensuing low fracture incidence. In contrast to BP, denosumab has a shorter retention time in bone and its effect disappears within 6 months of therapy cessation. The post hoc analysis after withdrawal of denosumab found significantly decreased BMD, with rebound increase in bone turnover and increased vertebral fractures within one year of discontinuation. What can be learned from this study is that BMD gains are lost if denosumab treatment is stopped without consolidation therapy.

Denosumab therapy is administered subcutaneously, 60 mg every 6 months. Patients should have optimal calcium and vitamin D sufficiency before and during the denosumab treatment as there is a risk of consequential hypocalcaemia. Side effects associated with denosumab therapy include hypocalcaemia, myalgia, diarrhoea or constipation, and an influenza-like illness.

Long term adverse effects of bisphosphonates and denosumab

Long-term treatment with BP and denosumab is associated with atypical femoral fracture and osteonecrosis of jaw. Atypical femoral fractures occur in the sub-trochanteric or diaphyseal shaft regions of the femur with minimal trauma and can be bilateral. The fractures are transverse and non-comminuted with lateral cortical thickening. It is imperative to advise patients about unexplained pain in the hips or lower limbs. On assessment of hip/thigh pain in patients on bisphosphonates or denosumab, imaging should be bilateral.

Osteonecrosis of the jaw is characterised by mucosal ulceration and exposure of necrotic bone. Management is usually conservative. Prior to initiating therapy, dental examination should be considered with preventative dentistry therapy if there are coexistent risk factors such as glucocorticoid therapy, poor oral hygiene or pre-existing dental disease. Cases of osteonecrosis of the jaw are rare and the benefits of therapy generally outweigh the risks. Invasive dental procedures should be avoided if possible, although bisphosphonate therapy is not a contraindication to dental work.

Hormone replacement therapy and selective oestrogen-receptor modulators

Hormone replacement therapy (oestrogen) inhibits bone resorption and maintains bone formation. Oestrogen receptors have been identified on osteoclasts, osteoblasts, osteocytes and bone marrow stromal cells. Oestrogen causes a decrease and reduction in the lifespan of osteoclasts resulting in decreased bone resorption. It also stimulates the activity of osteoblasts and influences calcium homeostasis. Because of its notable side effects, particularly increased risk of breast cancer and cardiovascular morbidity, it is not recommended in the elderly population. Early post-menopausal women are shown to have beneficial effect in terms of osteoporosis prevention and menopausal symptoms.

Selective oestrogen-receptor modulators, such as raloxifene, activate tissue receptors for oestrogen in bone, preventing bone loss and increasing bone mineral density. Raloxifene has been shown to reduce the vertebral fracture risk but not the hip or non-vertebral fracture risk. It is recommended in post-menopausal women who do not have history of menopausal symptoms.

The Women's Health Initiative was an observational study involving 120,566 women aged 50–70 years old between 1993 and 1998. The results found a significant reduction in new vertebral, non-vertebral and hip fractures with hormone replacement therapy in postmenopausal women.

Hormone replacement therapy is available as oestrogen or as an oestrogen plus progestogen combination, either orally or via transdermal patches. Raloxifene is an oral medication taken daily at a dosage of 60 mg and has been found to decrease the risk of breast cancer. Selective oestrogen-receptor modulators are contraindicated in women of childbearing age, previous history of venous thromboembolism, unexplained uterine bleeding, and renal or hepatic impairment.

Parathyroid hormone peptides

Teriparatide is a recombinant human parathyroid (PTH 1–34 amino acids) compound licensed for use in severe post-menopausal osteoporosis in Europe, containing the first 34 "active" amino acids. Teriparatide or intermittent PTH (1–84 amino acids) administration increases bone formation (anabolic effect) and is recommended by NICE in the management of severe osteoporosis in patients 65 years or above with intolerance, contraindication or unsatisfactory response to BP. The most marked effects are seen on cancellous bone. The benefits of teriparatide are lost quickly after cessation so it is often succeeded by an antiresorptive agent such as BP or denosumab. A randomized trial found a significant increase in bone mineral density when 1 year of teriparatide therapy was followed by 1 year of alendronate therapy. Due to the high cost of this medication, it is indicated for patients at very high risk of fracture, namely vertebral fractures. A randomized 21-month trial, which included women with low bone mineral density that had suffered previous vertebral fractures, found a reduction in vertebral fractures by 65% and non-vertebral by 35% compared to placebo. However, there was no reduction in risk of hip fracture. Teriparatide is administered subcutaneously, 20 μg, over a maximum period of 24 months. Only mild side effects have been seen with recombinant parathyroid hormone, with reports of occasional nausea and headache. The medication is generally well tolerated.

Teriparatide is contraindicated in the presence of hypercalcaemia, metabolic bone disease (other than osteoporosis), severe renal impairment; prior radiation to the skeleton or malignant disease of skeleton.

Miscellaneous therapy

Strontium ranelate was discontinued in the UK in 2017 due to increased cardiovascular risk in users. Calcitonin is no longer licensed in Europe to treat osteoporosis as the European Medicines Agency discovered an increased risk of developing cancer with calcitonin use over a prolonged period, and it was decided that the limited benefits were outweighed by the risks.

New therapies on the horizon

To date, anti-resorptive therapy is the most commonly used treatment for osteoporosis. Nevertheless, the prolonged use of this treatment results in suppression of osteoclasts as well as osteoblasts, resulting in reduced bone remodelling. This impairs the repair of micro-cracks in bone and leads to atypical femoral fractures. In the recent years, osteonecrosis of jaw has been reported in patients on long term treatment with bisphosphonates and denosumab. The need for anabolic therapy has become prominent in the last few years as teriparatide is licensed only for 2 years during each patient's lifetime. Moreover, a need for anabolic therapy has been identified in patients with severe osteoporosis presenting with multiple vertebral fractures, failure of anti-resorptive treatment or steroid-induced osteoporosis. Anabolic therapy significantly increases bone formation, which is followed by a period of delayed bone resorption, called the "anabolic window". Hence there is a net increase in bone deposition and volume. To consolidate the effect of anabolic therapy, it should be followed by anti-resorptive treatment.

Abaloparatide is a synthetic analog of PTH-related peptide (PTHrP), is identical to PTHrP (1–22 amino acids) and acts through the PTH receptor. The intermittent administration of Abaloparatide has an anabolic action. A phase 3 clinical trial with Abaloparatide (Study to Evaluate the Safety and Efficacy of BA058 [Abaloparatide] for Prevention of Fracture in Post-menopausal Women, ACTIVE) reduced the vertebral fractures by 86% compared to placebo.

Romosozumab is a humanised monoclonal antibody to sclerostin (produced by osteocytes, inhibits the bone formation and induces bone resorption). The phase 3 clinical trial (Fracture Study in Postmenopausal Women with Osteoporosis, FRAME) showed a significant reduction in vertebral fractures by 75% in the Romosozumab group compared to placebo.

The combination treatment with teriparatide and denosumab showed a significant increase in BMD in combination group compared to either teriparatide or denosumab treatment alone after 12 months of treatment.

The sequential treatment where anabolic therapy is followed by anti-resorptive therapy consolidates the anabolic bone density gains. In a clinical trial, a switch from teriparatide to denosumab after 24 months of teriparatide resulted in substantial gain in BMD whereas the switch from denosumab to teriparatide resulted in loss of bone density.

This suggests that combination and sequential treatment with teriparatide and denosumab should be considered in the management of severe osteoporosis.

The case

This case demonstrates an example of secondary prevention in a postmenopausal woman. Her right neck of femur fracture is indicative of a characteristic osteoporotic fracture. As per NICE guidance, DXA scan to measure BMD (lumbar spine and left femoral neck T-score of -3.8 and -2.5 respectively), a detailed assessment of other risk factors such as use of systemic glucocorticoids, low weight, history of inflammatory disease and smoking and alcohol consumption, were carried out. In light of her age, fragility fracture and BMD (T-score of less than -2.5), she falls in the treatment interventional threshold.

First line treatment according to NICE such as Alendronate, an oral BP was commenced, following exclusion of contraindications. National Osteoporosis Guideline Group (NOGG) and NICE guidelines recommend ensuring Calcium and vitamin D levels are replete prior to pharmacological therapies. As exemplified in our case, supplementation of calcium and vitamin D is particularly recommended in older persons, but only as an adjunct to other treatments. There should be caution with calcium supplementation in those with cardiovascular risk. The Institute of Medicine (IOM) recommends that women over the age of 51 years consume 1200 mg of calcium per day and 800−1000 IU of vitamin D per day for those aged 50 or over. Along with this, modification of other supportive measures should be taken into regard. Falls prevention strategies and home safety assessments by occupational therapists, muscle strengthening exercises provided by physiotherapists, along with smoking and alcohol prevention strategies should all be considered.

NICE guidelines recommend Alendronate as a first line option. Before commencing Alendronate, the presence of oesophageal abnormalities and renal impairment should be ruled out. The risks of osteonecrosis of the jaw and atypical fractures should be discussed. It should be noted that these risks are significantly outweighed by the potential benefit of fracture risk reduction. Results from recent meta-analysis show a highly favourable benefit to risk ratio; treatment with up to 5 years in osteoporosis, with fewer than one event caused per 100 fractures prevented, with a similar incidence for osteonecrosis of the jaw.

As a result of gastrointestinal symptoms with alendronate, she was subsequently changed to IV bisphosphonate. Both Zoledronic acid and denosumab are administered parentally and are potential options in the case of gastrointestinal adverse effects. In this case, zoledronic acid was given, the HORIZON-PFT trial showed that after 3 years of treatment period, most of the benefits in regard to bone mineral density were maintained, even after treatment cessation. Multiple pooled analyses of long term trials involving bisphosphonates (FLEX, HORIZON-PFT, VFERT-MN trials) found patients who received 6 years or more of BP had a greater fracture rate than those compare to a placebo. The evidence points towards the use of a drug holiday, to minimise the adverse effects of BP. The adverse effects outweigh the antifracture benefits after a certain point. When BP are discontinued, the benefit of BMD persists for at least another 3 years.

The length of treatment prior to a drug holiday is case dependant, generally 3−5 years, depending on the fracture risk. Some guidelines suggest using the FRAX tool to recalculate risk and those at an increased risk of fracture are recommended continue treatment. In our case an increase in bone mineral density was noted at 3 years and a drug holiday commenced, as the patient was deemed low risk.

NOGG guidelines suggest that after bisphosphonates are discontinued, fracture risk should be re-evaluated; after every new fracture or after 2 years if no new fracture occurs. In our case, after 2 years a repeat DXA showed an apparent decrease in BMD and IV zoledronic acid was reintroduced. Despite this, she symptomatically represented with anterior wedging and fractures at multiple points of her thoracic and lumbar vertebrae. In addition she had a BMD of less than −2.5 at the lumbar spine and femoral neck, and a low bone turnover indicated by bone markers.

The presence of a vertebral fracture increases subsequent risk of fracture by five fold and the risk of hip or other fractures by 2−3 fold. Patients with multiple vertebral fractures, as in our case, have shown to benefit from the use of teriparatide. Teriparatide is a very potent medication that is useful in reducing vertebral fracture risk when compared to a placebo. BP, raloxifene and denosumab have also been shown to reduce vertebral fragility fractures. The benefits of Teriparatide are quickly lost once it is discontinued, so it should be followed by an antiresorptive agent. ◆

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