AUSTRALASIAN MENOPAUSE SOCIETY
EMPOWERING MENOPAUSAL WOMEN

Information Sheet

Osteoporosis

Key Points

- Osteoporosis is a common condition which increases the risk of fracture leading to significant morbidity
- The menopausal transition is associated with significant bone loss due to the decline in oestrogen
- Lifestyle management of osteoporosis includes ensuring adequate calcium intake, optimising Vitamin D levels, weight bearing exercise, reducing alcohol and smoking cessation
- Medical therapies include menopausal hormone therapy, SERMS, anti-resorptive medications (bisphosphonates and denosumab) and anabolic agents (teriparatide and romosozumab)
- The decision to initiate therapy depends on an individual's risk of fracture. The FRAX and Garvan risk calculators can be used as a guide to inform who should receive medical treatment

Background

Osteoporosis is a condition characterised by weakened bones that fracture easily. Worldwide, osteoporosis causes more than 8.9 million fractures annually (1) and one in three women over the age of 50 will experience a fracture (2). Osteoporotic fractures lead to significant morbidity and reduced quality of life. Because osteoporosis itself is asymptomatic, it is often only diagnosed at the time of a fracture.

Osteoporosis is diagnosed on dual energy X-ray absorptiometry (DEXA) when there is a T-score of ≤2.5 at the spine or hip, where T-score is the standard deviation based on normative data for a young healthy adult population. Alternatively, osteoporosis may also be diagnosed if an individual has a minimal trauma fracture, which is defined as a fall from a standing height (or equivalent trauma). Minimal trauma fractures most commonly occur in the hip, spine, forearm, humerus and pelvis. Fractures of the hands and feet are not considered minimal trauma. A prior minimal trauma fracture puts an individual at higher risk of further fractures.

Secondary causes of osteoporosis include hyperparathyroidism, coeliac disease, hyperthyroidism and glucocorticoid excess.

The role of oestrogen

Oestrogen plays an important role in maintaining bone strength. Bone density rapidly rises after puberty under the influence of oestrogen and peak bone mass is reached around age 30. After menopause, oestrogen levels drop and this results in accelerated bone loss. The average woman loses up to 10 per cent of her bone mass in the first five years after menopause (3). Data from Healthy Bones Australia suggest that 27% of women age ≥60 are osteoporotic and 51% of women ≥60 are osteopaenic. Women with premature ovarian insufficiency are particularly at risk of osteoporosis and it is recommended that these women are treated with hormone replacement therapy until the age of 50-51 (see AMS Information Sheet: *Spontaneous Premature Ovarian Insufficiency).*

Lifestyle management of osteoporosis

To reduce the risk of developing osteoporosis, a number of lifestyle factors should be addressed:

1. Ensure adequate dietary calcium. The recommended intake is1300mg/day for women over 50 (equivalent to 3-4 serves of dairy food per day). Some individuals are unable to reach this requirement and calcium supplements can be taken (see AMS Information Sheet: *Calcium Supplements*)
2. Maintain adequate Vitamin D levels. Vitamin D has a key role in calcium absorption from the gut. Normal bone mineralisation cannot occur if Vitamin D deficiency is severe. Healthy Bones Australia recommends a Vitamin D level of at least 50nmol/L at the end of winter.
3. Weight bearing exercise. Exercises which require the muscles and bones to work against gravity are effective in maintaining bone mass. This may take the form of weight bearing impact loading aerobic exercise (walking, stair climbing, jogging, volleyball, tennis and dancing) or strength/ resistance exercises (eg. free weights).
4. Smoking cessation. Smokers tend to be at higher risk of any fracture including hip fractures (4). Longitudinal studies show smokers to have accelerated bone loss compared to non-smokers (5,6).
5. Reduce alcohol intake. More than 2 standard drinks of alcohol per day is associated with an increased risk of fracture (7).

Fracture Risk Calculators

Although osteoporosis indicates a high risk of fracture, many fragility fractures occur in people with bone density levels above a T-score of -2.5. Fracture risk calculators such as FRAX and GARVAN help stratify fracture risk and are used to help guide clinicians as to which patients should be commenced on osteoporosis medications. These tools factor in a variety of established clinical risk factors including the bone density to calculate an individual's risk of developing a major osteoporotic and hip fracture in the next 5 and 10

years. An accepted recommendation is to initiate treatment if the risk or a major osteoporotic and hip fracture is ≥ 20% and 3% respectively (8).

Links to the fracture calculators can be found here: FRAX and GARVAN.

Medical therapies for osteoporosis

A number of medical treatments are available for the management of osteoporosis. Treatments aim to strengthen existing bone; help prevent further bone loss and most importantly reduce the risk of fracture.

Treatments include the following:

- Antiresorptive agents
    - Bisphosphonates
    - Denosumab
- Hormone therapy / SERMs
    - Hormone therapy (MHT) including Tibolone
    - Selective oestrogen receptor modulators (SERMs)
- Anabolic agents
    - Teriparatide
    - Romosozumab

Bisphosphonates

Bisphosphonates reduce bone resorption by inhibiting osteoclast action as well as increasing osteoclast apoptosis. They are effective in reducing vertebral, hip and other fractures. Oral bisphosphonates such as alendronate and risedronate may be taken daily, weekly or monthly. The intravenous form, zoledronic acid, is given every 12-24 months.

Possible side effects of treatment include gastrointestinal upset and reflux. A rare side effect is osteonecrosis of the jaw – the incidence is estimated to be 1 in 10,000 to 1 in 100,000 patient years for patients taking bisphosphonates for osteoporosis (11). Patients should be advised to have a dental review prior to commencement. Prolonged treatment on antiresorptive agents such as bisphosphonates increases the risk of atypical fractures. For this reason, some society guidelines recommend review after 3 years of intravenous and 5 years of oral bisphosphonate treatment (12). If the risk of fracture at this time is considered high then treatment should be continued; if the risk is low to moderate, then a drug holiday should be considered.

Denosumab

Denosumab is a monoclonal antibody against RANK ligand (RANKL); this prevents the development and maturation of osteoclasts and therefore slows bone resorption. It is given as a 6-monthly subcutaneous injection. It reduces the risk of vertebral, hip and other fractures. Like bisphosphonates, prolonged use can lead to atypical fractures. Importantly, denosumab cessation leads to a rebound effect where there is accelerated bone loss,

bone turnover markers are increased, and there is an increased risk of vertebral fractures. Many clinicians now recommend avoiding denosumab as a first line agent in younger patients requiring therapy because of the need to avoid very long term antiresorptive therapy and the rebound effect associated with denosumab discontinuation.

Menopausal Hormone therapy

Menopausal hormone therapy (MHT) relieves menopausal symptoms such as vaginal dryness, hot flushes and night sweats. When taken at the beginning of menopause, MHT can also prevent bone loss and should be started soon after menopause for maximum benefit. Some studies have shown that MHT can increase bone density by around five per cent in two years. On average, MHT reduces the risk of spinal and hip fractures by 40%.

MHT is most appropriate for use in women under age 60 who are at risk of fracture and especially those who have undergone early menopause (before 45 years of age).

It is generally accepted that the risks of MHT potentially begin to outweigh the benefit in women over the age of 60. However, some women may elect to continue hormone therapy beyond age 60 – this needs to be done in consultation with the woman's doctor and the woman needs to understand the risks and benefits of this therapy (see AMS Information Sheets: *Combined MHT* and *Oestrogen Only MHT*). It is also important to understand that bone loss will resume once MHT is stopped. The rate of bone loss is more rapid than normal for the first 4-5 years after stopping MHT. If an individual's bone density is already low before stopping MHT, alternative treatments to preserve bone density will be needed.

Tibolone

Tibolone is a synthetic steroid which has oestrogenic, progestogenic and androgenic actions. It is indicated for the treatment of symptoms associated with menopause and prevention of osteoporosis. The LIFT study showed that women using tibolone 1.25mg (standard dose 2.5mg) reduced the risk of both vertebral and non-vertebral fracture compared to placebo (9). Tibolone should be used in women at least 12 months after their final period (See AMS Information Sheet: *Tibolone as MHT*).

Selective Oestrogen Receptor Modulators (SERMS)

Selective oestrogen receptor modulators (SERMs) are medications that bind to oestrogen receptors and have an agonist effect at some sites (brain and bone) but are antagonistic at other sites (breast and endometrium). Raloxifene is available in Australia; it reduces the risk of vertebral fractures but not non-vertebral fractures (10). Women prescribed raloxifene should be warned that they are more likely to experience hot flushes and have a slightly increased risk of venous thromboembolism.

Bazedoxifene is a third generation SERM with oestrogen agonist effects on bone and antagonises the effect of oestrogen at the endometrium. In Australia, Bazedoxifene is combined with conjugated equine oestrogens in what is referred to as a tissue selective

oestrogen complex (TSEC). It is used to prevent osteoporosis and treat menopausal symptoms without the need for a progestogen, in women with a uterus and at least 12 months since last menses (see AMS Information Sheet *SERMS – their role in menopause management*).

Teriparatide

Teriparatide is a synthetic form of human parathyroid hormone. It works by stimulating osteoblastic activity leading to new bone formation. A meta-analysis comparing teriparatide with placebo showed a 74% reduction in the risk of vertebral fractures and a 39% reduction in the risk of nonvertebral fractures with teriparatide use (13). It is administered as a daily subcutaneous injection. Antiresorptive therapy should be continued after teriparatide treatment to maintain its effect. Only patients under the care of a specialist can be prescribed teriparatide and there are strict PBS and Pharmac criteria in Australia and New Zealand respectively.

Treatment is limited to one 18-month course per lifetime on the PBS and Pharmac. It is effective and safe to 24 months although patients would need to privately fund the additional 6 months.

Romosozumab

Romosozumab is a monoclonal antibody against sclerostin, an osteocyte-derived protein that inhibits bone formation. Inhibition of sclerostin leads to an increase in bone formation and a reduction in bone resorption. A meta-analysis of the studies examining the effect of Romozumab in post-menopausal women found a reduction in the rate of both vertebral and non-vertebral fractures (14). Like teriparatide, Romosozumab must be prescribed by a specialist.

Romosozumab is administered as two injections each month for a total of 12 months. The PBS indications for Romosozumab are also similar to teriparatide.

Where can I get more information?

https://healthybonesaustralia.org.au

www.bones.org.nz

www.jeanhailes.org.au

https://www.bonehealth.org.au

www.menopause.org.au

References:

1. Johnell O et al. Osteoporosis Int. 2006: 17;(12):1726-1733
2. Cheng XG et al. Bone. 1997;20(3):213-213
3. Greendale GA et al. J Bone Mineral Res. 2012; 27:111-118)
4. Kanis JA et al. Osteoporosis Int. 2005;16(2):155-162
5. Trevisan C et al. J Clin Densitom. 2020;23(3):381-389
6. Emaus N et al. J Bone Miner Res. 2014;29(9):2080-2089
7. Kanis JA et al. Osteoporosis Int 2005 Jul;16(7):737-42
8. Tosteson ANA et al. Osteoporosis 2008; 19(4); 437-447
9. Cummings SR et al. NEJM 2008; 359:697-708
10. Ettinger B et al. JAMA 1999;282(7):637-645
11. Khan AA et al. J Bone Miner Res 2015;30:3
12. Eastell R. JCEM: 2019; 104(5):1595–1622
13. Qaseem A. et al. Ann Intern Med. 2017; 166(11):818–839
14. Sing S et al. Osteoporosis Int. 2022; Jan;33(1):1-12