Pulse

Menopause and osteoporosis

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GPs and menopause specialists Dr Alice Scott and Dr Louise Newson on managing osteoporosis in menopausal women

What you should already know

Osteoporosis is a disease of low bone mass, deterioration of bone tissue and disruption of bone microarchitecture, causing compromised bone strength and increased susceptibility to fracture. It is estimated that 536,000 new fragility fractures were sustained in the UK in 2010 causing an economic burden of nearly £4.4 billion, and this is predicted to rise.[1] Women are affected more than men due to increased bone loss postmenopausally. The prevalence of osteoporosis in women is 2% at 50 years and 25% at 80 years.[2]

Osteoporosis is preventable and treatable but asymptomatic until fracture occurs, therefore it is important to identify at risk patients in order to intervene before this happens. It is diagnosed based on bone mineral density (BMD) assessment by dual X-ray absorptiometry (DXA) and is expressed as a T score and/or the presence of fragility fractures. The T-score is the number of standard deviations (SD) above or below the mean BMD for young adults. Normal BMD is defined as a T-score between +2.5 above the young adult mean and -1.0 SD below the young adult mean. Osteopenia 'low bone mass' is a T score between -1 and -2.5. Osteoporosis is a T score of <-2.5 SD.[3] Severe or established osteoporosis is a T-score of -2.5 and a history of fragility facture.[4]

More from this series: Safe HRT prescribing (URL=http://www.pulsetoday.co.uk/clinical/clinical-specialties/womens-health/safe-hrt-prescribing/20039119.article)

The use of BMD alone to assess fracture risk has a high specificity but low sensitivity, meaning that a number of fractures occur in women who do not have osteoporosis as defined by T-score <2.5. Fracture risk calculators can be used to identify high risk patients who may benefit from preventative treatment and who should have a DXA scan to accurately assess their BMD. The two most widely used ones in the UK are FRAX (www.shef.ac.uk/FRAX (URL=http://www.shef.ac.uk/FRAX)) or Qfracture (www.qfracture.org (URL=http://www.qfracture.org/)).

NICE guidelines recommend calculation of fracture risk in all women over the age of 65, all men over 75, and in people under these ages in the presence of risk factors including: previous fragility fracture, current or frequent use of glucocorticoids, history of falls, family history of hip fracture, low body mass index of less than 18.5 kg/m^2, smokers, high alcohol intake, and in people with comorbidities which may cause secondary osteoporosis.[2] Following assessment with FRAX (without a BMD value) or QFracture, BMD with DXA should be measured in patients whose fracture risk is in the region of an intervention threshold and then the risk recalculated using FRAX with the BMD value.[2]

Primary prevention of osteoporosis in at-risk people includes lifestyle measures such as increasing physical activity, weight-bearing and muscle-strengthened exercises, stopping smoking, reducing alcohol to less than 2 units a day, taking measures to reduce the risk of falls and ensuring adequate calcium and vitamin D.[5]

What isn't as widely known, but you should think about

Around the time of menopause declining oestrogen levels increases the rate of bone resorption. There are oestrogen receptors on both osteoblasts and osteoclasts and HRT has been shown to stabilise bone turnover.[6] HRT has been shown to reduce vertebral and non-vertebral fractures in postmenopausal women by 30%[7] and low dose HRT has also been shown to be effective.[8] Unfortunately, due to unfounded safety concerns about HRT that were raised by the Women's Health Initiative Study[7], HRT is not considered a first-line treatment for osteoporosis by several of the leading medical societies and therefore is not advocated as such in the 2017 NICE guideline on osteoporosis, which recommends bisphosphonates instead, unless treating premature ovarian insufficiency, in which case it recommends HRT.[10]

Fortunately, reanalysis of both of these HRT studies has been reassuring with regards to the safety of HRT if started before the age of 60 and within 10 years of the menopause.[11] The global consensus statement on menopausal hormone therapy (endorsed by bodies such as the International Menopause Society and the International Osteoporosis Foundation) states that HRT can be initiated to treat postmenopausal women at risk of fracture or osteoporosis before the age of 60 years or within 10 years after menopause. This document also states that HRT is the only therapy with RCT-proven efficacy of fracture reduction in women with normal to osteopenic range (de Villers).[12] This is important as most fragility fractures occur in women with osteopenia rather than osteoporosis.[13] The British Menopause Society consensus statement on prevention and treatment of osteoporosis in women states that HRT is effective and appropriate for prevention of osteoporosis in menopausal women, and can be considered a first-line treatment for these women.[14] Both former and current use of postmenopausal oestrogen are associated with decreased odds of osteoporosis.[15]

Bisphosphonates are incorporated into bone where they inhibit osteoclasts and reduce bone resorption. The use of bisphosphonates is often limited by side effects such as upper gastrointestinal symptoms, bowel disturbance, headaches and musculoskeletal pains.[5] Oral bisphosphonates are also laborious to consume, as they must be taken on an empty stomach after an overnight fast and at least 30-60 minutes before food and drink, with the patient needing to stay upright for 30 minutes afterwards, which affects compliance. They cannot be used in severe renal impairment or in conditions that delay oesophageal emptying. Rare adverse effects include osteonecrosis of the jaw and atypical femoral fractures.[5]

HRT is cost-effective compared with bisphosphonates and has beneficial extra-skeletal effects including improvement in menopausal symptoms and improved cardiovascular risk profile.[16] It also avoids the side effects associated with bisphosphonates. Depending on the women's risk factors and the choice of HRT used (transdermal body identical appears to be the safest[17], it is often appropriate to continue HRT long-term. However, if the risks of HRT outweigh the benefits and HRT is stopped, bone loss recommences at a natural post-menopausal rate, so consideration should be given to treatment with another agent (e.g. a bisphosphonate).

The advantage of using HRT first line is that it either avoids treatment with a bisphosphonate or delays treatment, therefore reducing exposure to bisphosphonates, the safety of which is unclear if used for over 10 years.[18] However, bisphosphonates and other treatments for osteoporosis have an important role in treating women in whom HRT is contraindicated or unacceptable.

Read more: Women's health (URL=http://www.pulsetoday.co.uk/clinical/clinical-specialties/womens-health)

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References

1. Svedbom A, Hernlund E, Ivergård M, et al. Osteoporosis in the European Union: a compendium of country-specific reports. *Arch Osteoporos*. 2013;8(1-2):137.
2. NICE Guideline CG 146 Assessing the risk of fragility fracture: 2012 https://www.nice.org.uk/guidance/cg146 (URL=https://www.nice.org.uk/guidance/cg146)
3. Sözen T, Özışık L, Başaran NÇ. An overview and management of osteoporosis. *Eur J Rheumatol*. 2016;4(1):46–56. doi:10.5152/eurjrheum.2016.048
4. Gambacciani M, Levancini M. Hormone replacement therapy and the prevention of postmenopausal osteoporosis. *Prz Menopauzalny*. 2014;13(4):213-20.
5. NOGG 2017: Clinical guideline for the prevention and treatment of osteoporosis. https://www.sheffield.ac.uk/NOGG/NOGG%20Guideline%202017.pdf (URL=https://www.sheffield.ac.uk/NOGG/NOGG%20Guideline%202017.pdf)
6. Eriksen EF, Langdahl B, Vesterby A, Rungby J, Kassem M. Hormone replacement therapy prevents osteoclastic hyperactivity: a histomorphometric study in early postmenopausal women. J Bone Miner Res. 1999;14:1217–21
7. Writing Group for the Women's Health Initiative Investigators. Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial. *JAMA.* 2002;288(3):321–333.
8. Lees B[1], Stevenson JC. The prevention of osteoporosis using sequential low-dose hormone replacement therapy with estradiol-17 beta and dydrogesterone. Osteoporos Int. 2001;12(4):251-8.
9. Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. Lancet 2003; 362: 419-427.
10. NICE Guideline CG149 Osteoporosis: 2017 https://www.nice.org.uk/guidance/qs149 (URL=https://www.nice.org.uk/guidance/qs149)
11. Hodis HN, Collins P, Mack WJ, Schierbeck LL. The timing hypothesis for coronary heart disease prevention with hormone therapy: past, present and future in perspective. *Climacteric*. 2012;15(3):217–228. doi:10.3109/13697137.2012.656401
12. De Villiers, T.J. et al. Revised global consensus statement on menopausal hormone therapy. Maturitas , Volume 91 , 153 – 155

13. Eriksen EF. Treatment of osteopenia. *Rev Endocr Metab Disord*. 2011;13(3):209–223. doi:10.1007/s11154-011-9187-z
14. Stevenson, J. C. (2018). Prevention and treatment of osteoporosis in women. *Post Reproductive Health*, *24*(4), 167–170.
15. Siris ES, Miller PD, Barrett-Connor E, et al. Identification and Fracture Outcomes of Undiagnosed Low Bone Mineral Density in Postmenopausal Women: Results From the National Osteoporosis Risk Assessment. *JAMA.*2001;286(22):2815–2822.
16. Lobo RA, Pickar JH, Stevenson JC, Mack WJ, Hodis HN. Back to the future: Hormone replacement therapy as part of a prevention strategy for women at the onset of menopause. Atherosclerosis 2016; 254: 282-290.
17. L'Hermite M. HRT optimization, using transdermal estradiol plus micronized progesterone, a safer HRT. *Climacteric* 2013; **16**: 44–5
18. Hollick, R. J., & Reid, D. M. (2011). Role of bisphosphonates in the management of postmenopausal osteoporosis: an update on recent safety anxieties. *Menopause International*, *17*(2), 66–72.