BONE DENSITOMETRY AND HORMONE (ESTROGEN) REPLACEMENT THERAPY – APPENDIX 3

Estrogen deficiency – occurring following the menopause and in hypogonadal women – causes an accelerated rate of bone loss (up to 5% per year), which leads to an increased risk of hip, spine and other osteoporotic fractures. Estrogen deficiency can be reversed with the use of hormone replacement therapy (HRT) which stabilises bone loss, improves the bone mineral density (BMD) of the skeleton and reduces fracture rate.

The Women's Health initiative (WHI) study of HRT [1] has been the largest randomised controlled study of the use of combination HRT in healthy post-menopausal women and has radically altered our approaches to the long-term use of combination HRT. This study demonstrated a 34% reduction in the rate of hip and vertebral fractures. Other randomised controlled trials have been smaller. A meta- analysis of these trials[2] has shown a trend for a reduction in vertebral fracture rate of 34% compared with placebo comparisons and a 13% reduction in non-vertebral fractures. The confidence intervals for both comparisons included one and thus were not statistically significant. Numerous studies have consistently demonstrated that HRT increases bone mass at multiple sites. The conclusions of WHI which are widely accepted were that there are no overall health benefits of combination HRT due to the higher rate of breast cancer, cardiovascular, and cerebrovascular disease and pulmonary embolism in the treated group. There was a reduction of hip fractures and colon cancer in the treated group. The combination trial was halted early by the safety monitoring committee when the above results became known. **In absolute terms, during 5 years of treatment combination HRT leads to an adverse event in 1/50 women and a beneficial event in 1/200 women**[3]. The results from use of estrogen alone in women who have had a hysterectomy have not been published and this trial continues, presumably because there is less evidence of adverse events to date.

Bone densitometry of menopausal women or women with one or more of the osteoporotic risk factors is critical for the diagnosis of osteoporosis or osteopenia. It can be used to assess whether there is a need for women who are on HRT, particularly those who have been on it for five or more years, to remain on it. **The measurement of bone density can greatly influence the patients' and doctor's decision on the use of HRT**. Based on WHI the only reason for women to remain on combination HRT for more than five years is if they are at increased risk of osteoporosis or have debilitating menopausal symptoms. The benefits and disadvantages of HRT need to be discussed with the individual patient so that they can make a considered choice. The alternatives to HRT for preventing or treating osteoporosis need to be put to the patient (see later).

Bone density as assessed by DEXA and age are the most important risk factor for fractures. Patients are considered to be osteoporotic if their BMD levels are below the fracture threshold of 0.90g.cm^2 (lumbar spine) or 0.70gm/cm^2 (femoral neck) for the Lunar machine. However, patients with BMD values between 0.9 – 1.0gm/cm2 or between 0.8 – 0.7gm/cm^2 for the spine and hip respectively are considered to have an elevated risk of osteoporotic fractures. HRT in these patients, within one year of menopause or when FSH levels indicate the menopause, prevents the rapid phase of perimenopausal bone loss.
Other patients who would benefit from the use of HRT include women with:

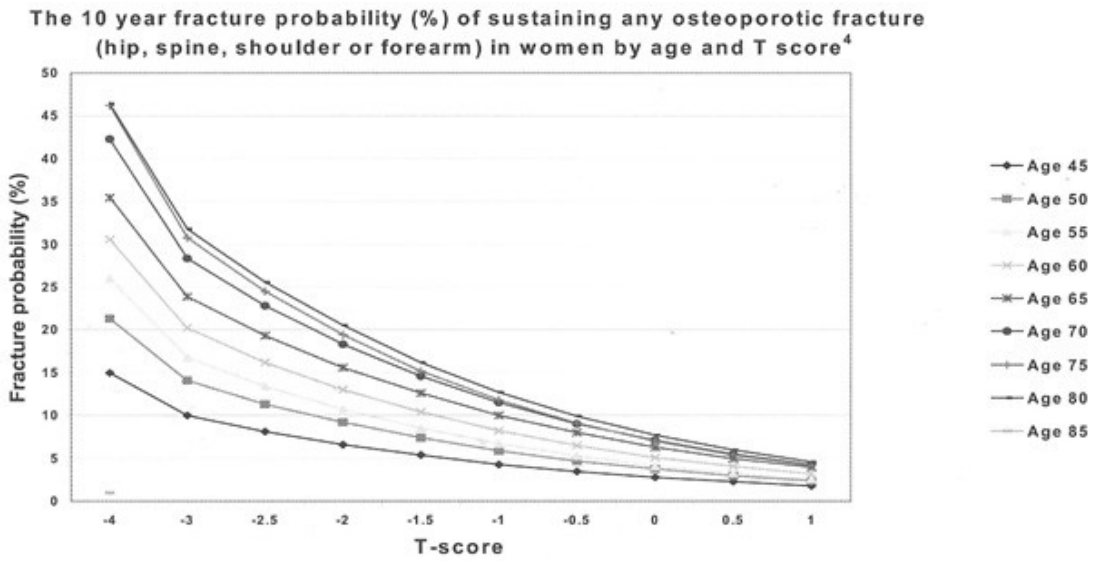
i. Early menopause (before 45 years)

ii. Bilateral oophorectomy or women who have had a hysterectomy and have a documented biochemical menopause (low estradiol or high RSH levels)
iii. Turners syndrome
iv. Exercise amenorrhoea
v. Anorexia nervosa or bulimia
vi. Past history of minimally traumatic fractures
vii. Post menopausal women receiving corticosteroids.

A very minority of women on HRT are considered to be “non-responders” in that bone loss continues despite therapy. However, most women on HRT demonstrate increased bone mass for a short period and then maintenance of bone mass. There is a demonstrated dose response with HRT. The use of bone densitometry in conjunction with biochemical markers for bone turnover allows for a more precise assessment of the skeletal response to HRT. Biochemical markers that can be used include pyridinoline (Type 1 collagen) breakdown markers in urine or serum bone alkaline phosphatase and osteocalcin. HRT leads to spinal and hip BMD increases by about 1 – 3% per year. Patients not on HRT lose spinal bone mass at a rate of 2% - 5% per year. The net difference in spinal BMD of 5% - 8% per year is a good indication of the efficacy of HRT. Subsequent monitoring of bone density every 2 to 5 years can determine the efficacy of HRT and indicate whether treatment can be stopped, commenced or the estrogen dosage altered.

A judgement needs to be made of the individual patients’ risk of fracture (see Figure). If she has a T score at the spine or hip , -1.5 and has had a prior fracture then treatment is indicated based on available evidence. Preferred treatment is a potent bisphosphonate such as alendronate or Risedronate. If she is receiving corticosteroids at a dose of prednisolone $\geq$ 5mg/day then her risk of fracture is increased and again treatment with a bisphosphonate is indicated. Women who have sustained a minimal trauma fracture are covered for one of the specific anti-osteoporotic treatments with Medicare however if a fracture has not occurred then treatment is not available through Medicare and may only be available through a public hospital outpatient clinic and this will vary from state to state. She can of course pay for treatment on a private script.

What is the risk of your patients fracturing? (see Figure)[4]. This is largely determined by bone density or bone content and age. Up until age 80 the best single predictor of fracture is bone density. The combination of age and bone density are a very strong combined predictor of fracture as demonstrated in the Figure. This date provides absolute estimates of risk of fracture, which **Bone Densitometry Australia will now provide for your patients.**



Preferred treatments now based on current evidence are alendronate, risedronate or raloxifene. The cost of treatments for the patient who has not fractured and can not claim under PBS will vary from pharmacy to pharmacy. Alendronate 40 mg per week will slow bone loss, however if there is ongoing bone loss as assessed by **DEXA** then the preferred treatment would be the 70 mg dose weekly or risedronate 35mg weekly. If the patient has predominantly spinal osteoporosis and wants to benefit from the lipid and breast benefits of raloxifene (Evista) then this treatment is indicated. The available treatments and their costs for 12 months of treatment excluding pharmacists' mark-ups are: Alendronate, 70mg weekly: $670.44; Alendronate, 10 mg per day: $714.36; Alendronate, 40 mg per week: $192.04; Risedronate 35 mg per week: $670.44; Risedronate 5 mg per day: $670.44; Raloxifene 60 mg per day: $726.72; Didrocal, 3 monthly course: $322.08. Some private health funds may contribute to the cost of these medications.

Doctor's requiring more information about these treatment approaches should contact Drs Will or Mastaglia or refer to Appendix 2.

References

1. Writing group of the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy post-menopausal women: principal results from the Women's Health Initiative randomised controlled trial JAMA 2002;288:321 – 33.
2. Wells G, Tugwell P, Shea B et al. Meta-analysis of the efficacy of Hormone Replacement Therapy in treating and preventing osteoporosis in post-menopausal women. Endocrine Reviews 2002;23:529-539.
3. Solomon CG, Dluhy RG. Rethinking post-menopausal hormone therapy. NEJM 2003;23:529-539
4. Kanis JA, Johnell O, Oden A et al. Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. Osteoporosis International 2001;12:989-995.