

RECOMMENDATIONS FOR THE MANAGEMENT OF OSTEOPOROSIS

The incidence of osteoporotic fracture in New Zealand is increasing steadily. Fractures now affect more than 50% of postmenopausal women and about 30% of men over the age of 60 causing considerable debility and reduced quality and length of life. Health professionals should therefore encourage patients of both sexes to consider prevention and active intervention strategies for osteoporosis.

These recommendations have been formulated by Osteoporosis New Zealand and are a revision of earlier guidelines produced at the 2005 National Osteoporosis Meeting.

The recommendations focus on the commonest causes of osteoporosis, namely postmenopausal osteoporosis, age-related osteoporosis in men, and corticosteroid-induced osteoporosis.

Suggestions for investigation of other secondary causes of osteoporosis are provided depending on clinical context.

The recommendations do not attempt to provide a comprehensive treatise on the subject, nor do they replace clinical assessment and individual judgement by the doctor and his/her patient in considering management.

The recommendations concentrate on therapies registered in New Zealand.

The funding and availability of diagnostic testing (DEXA scans), and the availability and cost-to-patients of treatments, differ from other countries and may influence treatment decisions.

BASIC MEASURES FOR MAINTAINING BONE HEALTH

- Maintain a normal body weight, e.g. >58 kg in women of average height.
 - Undertake regular weight-bearing and muscle strengthening exercises to reduce the risk of falls and fractures.
 - Maintain good dietary calcium intake > 1-1.5 g/day (4-6 servings' dairy products).
 - Avoid vitamin D insufficiency, i.e. maintain serum 25-hydroxyvitamin D between 50-150 nmol/l – especially a problem for frail elderly. In this high risk population empirical treatment may be indicated and is safe and more cost effective than laboratory testing.
 - Avoid glucocorticoid drugs (e.g. prednisone); administer locally if possible.
 - Avoid an alcohol intake of more than 2 standard drinks per day.
 - Stop smoking.
 - Create safe environments for older people with appropriate modifications for visual and hearing impairment, e.g. install hand rails, remove loose rugs and cords, etc.
 - Avoid medications that may increase fall risk, especially sedatives.
 - Consider hip protectors if the patient has a high risk of falling.
- Glucocorticoid therapy
 - Parental history of a hip fracture
 - Low body weight (< 58 kg) or BMI (< 20 kg/m²)
 - History of smoking or heavy alcohol intake
 - Premature menopause in women or hypogonadism in males
 - Rheumatoid arthritis
 - Malabsorption, chronic liver or renal disease.
 - Any woman over 65 years or man over 75 years considering specific measures to prevent osteoporosis.

Only measure bone density when the result will impact on decision making.

INDICATIONS FOR OTHER INVESTIGATIONS

- In an individual with low bone density or fracture history not explained by their known risk factors, including age, further investigation may be necessary. This should be guided by the severity of the osteoporosis and by the history and clinical findings.
- Investigations may include serum calcium, phosphate, creatinine, protein electrophoresis, liver function tests, full blood count, ESR, thyroid function tests, 25-hydroxyvitamin D and tests for coeliac disease
- In men, total and free testosterone levels should be included.
- Biochemical markers of bone turnover are research techniques only at this time.
- Specialist referral should be considered for severe osteoporosis if no known risk factors or cause is identified following standard investigations.

INDICATIONS FOR MEDICATION IN ADDITION TO PREVENTATIVE STRATEGIES

- A prior vertebral or hip fracture.
- T score ≤ - 3 in the absence of fractures.

INDICATIONS FOR BONE DENSITOMETRY

- Any individual prescribed glucocorticoids or other medications associated with osteoporosis, e.g. anti-convulsants.
- Women with a history of premature menopause.
- Postmenopausal women or older men with a history of minimal trauma fracture.
- Women over 60 years and men over 70 years with risk factors such as:

- T score < -2.5 and an osteoporotic fracture.
- T score < -1.5 and the use of significant doses of oral steroids.
- A Frax or Dubbo determined risk of a hip fracture of $\geq 3\%$ or of all major osteoporotic fractures of $\geq 20\%$.

TECHNIQUES FOR MEASURING BONE DENSITY

Dual energy x-ray absorptiometry (DEXA) scanning is the most widely used and internationally accepted standard for measuring bone density.

- The WHO definition of osteoporosis and Pharmac funding criteria are based on DEXA scores.
- DEXA generates measurements at the sites of major clinical relevance - spine and hip. The risk of fracture at any skeletal site is best estimated by measuring the BMD at that site.
- Spinal measurements are sensitive in detecting change (including response to treatment), but can be falsely elevated by degenerative change, vertebral fractures and aortic calcification.
- Since hip fractures are associated with significant morbidity and mortality it is chosen site for use with the FRAX tool.
- Wrist scanning is a useful additional area of assessment when spinal scanning is affected by artefact and or hip scanning not possible due to previous surgery.
- Guidelines for providing a densitometry service including quality control, interpretation and reporting standards, have been developed and workshops for reporting physicians and technicians have been provided in conjunction with Osteoporosis New Zealand. Details are available via e-mail to info@bones.org.nz.

Ultrasound of the heel is sometimes used as a screening technique.

- Is a good predictor of fractures.
- Results indicating a low bone density by heel ultrasound should be confirmed by DEXA scan before therapy is instituted.
- It cannot be used monitor treatment (slow rate of change at peripheral sites).

With the above provisos it is a reasonable option in regions where DEXA is not available.

EXERCISE RECOMMENDATIONS

- Regular physical activity is a determinant of peak bone mass. Exercise during childhood and adolescence is more effective for increasing bone mass and strength than exercise in adulthood.
- The primary benefit of exercise on the bones of adults is conservation, not acquisition.
- In older individuals exercise can reduce the rate of bone loss and improve fitness and muscle strength contributing to prevention of falls and therefore lowers the risk of fracture.
- Exercise goals for osteoporosis should include pain reduction, increased mobility and improvements in muscle endurance, balance and stability.
- Targeted exercise programmes have a greater impact than general programmes for preventing falls.

- Individuals with poor posture, frailty, pain, impaired balance and mobility, or other co-morbidities such as arthritis, may benefit from water exercise.

THE ROLE OF CALCIUM IN THE MANAGEMENT OF OSTEOPOROSIS

An adequate intake of calcium is necessary throughout life both to acquire peak bone mass and to maintain bone health. With age, calcium intake falls (on average to about half that of RDI for those older than 60 years) and both the ability to adapt to a low calcium diet and calcium absorption are decreased.

- Calcium is known to be weakly anti-resorptive and supplementation has been shown to slow the rate of bone loss by one half to two-thirds.
- Supplementation may decrease fracture risk in community based post menopausal women who take supplementation regularly. However, this is not recommended as an adequate strategy alone to either treat osteoporosis or reduce fracture risk.
- Calcium and vitamin D supplementation has been shown to reduce the risk of hip fracture by 30% in institutionalised frail elderly.
- **Anti-resorptive therapy for the treatment of osteoporosis should be combined with supplementation of 1000 mg elemental calcium daily, best given in divided doses.** As calcium binds with bisphosphonates, it should not be given on the same morning as oral bisphosphonates.
- Calcium supplementation should be used with caution in those with a history of calcium containing renal calculi or hypercalcaemia.

THE USE OF CALCIUM SUPPLEMENTS - ADVICE FROM THE BONE CLINIC, GREENLANE CLINICAL CENTRE

The recent evidence from the Auckland Calcium Study that a one gram calcium supplement in elderly women was associated with an increase in risk of myocardial infarction has caused many doctors and patients to request advice regarding their use of calcium supplements for the treatment and prevention of osteoporosis. There is no international consensus around the subject at present. Our data have been presented at an Australasian and an American Meeting, but are not yet published.

One possibility is that the high doses of calcium accelerate vascular calcification. Three other recent studies of calcium supplementation in older women show similar trends, but do not reach statistical significance. While further research is being done in this area, we suggest the following approach:

1. It is likely that this is primarily a problem for elderly women because they are more likely than younger subjects to have prevalent coronary heart disease. Therefore, it seems wise to advise against calcium supplementation in those over the age of 70 years and in those known to have coronary heart disease. Aiming at a total calcium intake of approximately 1 g/day (equivalent to 4 servings of dairy products) seems sensible in these subjects. For instance, in a person consuming a dietary intake of ~ 0.5 g, calcium supplementation should not exceed 0.5 g.
2. There is very little data relating to the cardiovascular effects of calcium supplements in older men, so it may be prudent to apply the same precautions.

3. We continue to recommend regular sunlight exposure or vitamin D supplementation in all people over age 70 years.
4. At present, there is no evidence of adverse cardiovascular effects of calcium supplementation in younger women, so the conventional use of calcium supplements seems reasonable in these subjects.
5. In patients taking bisphosphonates for osteoporosis or Paget's disease, there is a theoretical risk of mild hypocalcaemia. Again, ensuring a total calcium intake of 1 g/day should prevent this (as above).
6. There is no reason on the basis of the Auckland Calcium Study, to be advising reduced calcium intakes in children, adolescents or young and middle-aged adults.

THE ROLE OF VITAMIN D IN THE MANAGEMENT OF OSTEOPOROSIS

- Vitamin D plays a major role in calcium absorption and bone health. It regulates synthesis and secretion of PTH, stimulates osteoblast function and promotes mineralisation of osteoid, regulates calcium and phosphate absorption and has a probable role in muscle by promoting strength, tone and balance. International data consistently demonstrate that vitamin D deficiency is almost universal in hip fracture patients and worldwide, more than half of women diagnosed with osteoporosis are shown to be vitamin D deficient regardless of age, latitude or season.
- Adequate Vitamin D is generally not obtained in the diet of the elderly in whom additionally, sunshine exposure tends to be minimal.
- Adults under the age of 50 need 400-800IU of vitamin D daily and adults aged 50 and older need 800-1000IU. (National Osteoporosis Foundation: Updated Recommendations for Calcium and Vitamin D Intake, January 2010).
- In the elderly patient previously untreated, vitamin D insufficiency might be assumed, corrected by calciferol 50,000IU daily for 10 days, and maintained by 50,000IU monthly (with or without oral vitamin D 800IU daily as multivitamin or combined with alendronate). This regimen should maintain levels and is well within safety limits.
- Activated vitamin D metabolites (**calcitriol and alfalcidol**) are regarded as inadequate monotherapies for the treatment of osteoporosis and will not reverse deprivational vitamin D deficiency. Data regarding their efficacy is mixed and there is some evidence they accelerate bone resorption if used alone.

MEDICATIONS FOR THE TREATMENT OF OSTEOPOROSIS: BISPSPHONATES

- Bisphosphonates are first line treatment. Two oral tablet formulations are available in New Zealand, **alendronate** and **etidronate**. Alendronate is the more potent of these is fully subsidised and widely available with few access restrictions. Current availability criteria are:
 - T score \leq -3.0.
 - T score $<$ -2.5 plus fragility fracture.
 - History of two significant osteoporotic fractures demonstrated radiologically.
 - History of one significant osteoporotic fracture with x-ray confirmation in frail elderly unable to access DEXA scan.
 - Glucocorticoids $>$ 5 mgs daily either on, or intended to be on, for $>$ 3 months and either a T

score of \leq -1.5 or one significant osteoporotic fracture demonstrated radiologically.

- Bisphosphonates are effective strategies for preventing fracture and are generally well tolerated, although some people experience upper gastrointestinal side effects with the amino bisphosphonates (e.g. alendronate).
- **In people with osteoporosis, bisphosphonates combined with adequate calcium** and vitamin D, are clearly more beneficial than calcium and vitamin D alone.
- **Alendronate** has been shown to decrease the risk for fracture at all sites by up to 56% within a few months of commencing treatment.
- **Etidronate** has demonstrated a lesser level of efficacy in preventing vertebral fractures, but has no proven effect in reducing hip fracture.
- **Intermittent** parenteral administration of intravenous bisphosphonates is a further option with this class of medications. From 1 September 2010, **Zoledronate** will be registered for the treatment of osteoporosis in New Zealand. 5 mg IV 1-2 yearly has now been shown to be at least as effective as alendronate in fracture risk reduction in both hip and spine. IV therapy might be considered for the severely osteoporotic intolerant of oral alendronate.
- The ongoing need for bisphosphonate therapy should be reviewed at intervals and in all patients at five years. Ongoing therapy decisions might be based on the severity of osteoporosis, response to therapy, presence of side effects and the potential for adverse effects associated with long-term use, e.g. the low risk of severe suppression of bone turnover.

MEDICATIONS FOR THE TREATMENT OF OSTEOPOROSIS: HRT and SERMS

- Treatment with **Hormone Replacement Therapy (HRT)** is complex and is no longer recommended as a general strategy for the treatment or prevention of osteoporosis. However, in healthy younger ($<$ 60 years) postmenopausal women, HRT is an effective alternative to bisphosphonates, and lowers the risk of osteoporotic fracture with similar efficacy.
- HRT has been shown to **reduce the rate of clinical** fracture in postmenopausal women (aged 50-79), not selected for high osteoporotic risk. The Women's Health Initiative (WHI) found that five years of **combined HRT** reduced the risk of clinical vertebral fractures and hip fractures by 34% and other osteoporotic fractures by 23%.
- Long-term use of HRT is associated with a range of other effects on health, including cardiovascular disease, stroke, pulmonary emboli and invasive breast cancer. The latter relative risk increase after a mean of 5.6 years use was 24% (2.9% versus 2.3% of women, i.e. an absolute risk increase of 0.6%) with the increase in risk emerging after four years use in the WHI. This increased risk of breast **cancer does not** apply to oestrogen alone therapy.
- In women with premature menopause or primary ovarian failure, use of **Oestrogen Replacement Therapy (ERT)** or Combined Hormone Replacement Therapy until average age of menopause should be considered, particularly in those who are demonstrated to have a low bone density/peak bone mass.
- **Selective oestrogen receptor modulators (SERMS)**. This is a class of medications that have oestrogen-like properties and effects on bone and lipids, but anti-

oestrogenic or antagonistic effects on breast and mixed effects on other organs, including the uterus.

- They have a role in breast cancer prevention in those at high risk.
- **Tamoxifen**, a first generation SERM, has been shown to decrease the risk of fractures of spine, hip and wrist by 32% in large breast cancer prevention studies. It is not recommended for the treatment of osteoporosis as it is associated with an increased risk of thromboembolism and endometrial carcinoma.
- **Raloxifene** is a second generation SERM registered, but currently not funded, for use in New Zealand at this time. It has a similar effect to Tamoxifen on decreasing the risk of breast cancer by 50%. It has a better safety profile with fewer cases of uterine cancer, PE and cataracts reported. Eight year data shows a significant reduction in risk for vertebral fractures. Raloxifene has a similar thromboembolism risk as oestrogen. **Raloxifene** may have a role in younger postmenopausal women who have an increased risk for breast cancer and have a low bone mass for age at menopause.

MEDICATIONS IN MANAGEMENT OF OSTEOPOROSIS: COMBINATION THERAPY

- Combination therapy, usually using a bisphosphonate with another anti-osteoporotic agent, can provide additional small increases in BMD when compared with mono-therapy. The impact of combination therapy on fracture rates is unknown. The added cost and potential side effects should be weighed against potential gains.

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Doctors Stella Milsom, Mike Nowitz, Elizabeth Spellacy and Professor I Reid.

MONITORING THERAPY

- As with any other chronic condition, lifelong management is important to ensure ongoing compliance with therapy. It is important to establish that the medication is being taken as directed. Less than 1% of oral bisphosphonates is absorbed and this will be negated by the medication being taken in conjunction with any food or fluid other than water.
- The interval between DEXA scans while monitoring therapy will vary according to age and the expected rate of bone loss, severity of osteoporosis and documented response to therapy. It is important to note that medication may decrease risk of fracture even when there is no apparent increase in BMD. As with most tests, BMD has some precision error such that changes of < 2-4% in the spine and 3-6% at the hip from test to test can be due to precision error of the method alone.
- Scanning at intervals of less than two years is recommended only for initial evaluation for response to treatment for those with severe osteoporosis, or in conditions of rapid or potentially rapid bone loss, e.g. monitoring of corticosteroid therapy in those not on bisphosphonates.

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