

## Medications in osteoporosis



While there is an increasing number of medicines available for the treatment of osteoporosis, medication is not the only way to reduce fracture risk. It is also important to correct lifestyle factors (eg, smoking, high alcohol intakes) and to take measures to minimise the risk of falls (eg, exercise programmes, improving home safety, making sure glasses are appropriate, etc). These measures can be combined with one or more of the following types of medicine.

### Calcium

Calcium is an important constituent of bone. If the supply of calcium is inadequate to meet the body's needs, there will be resorption of bone to provide calcium for other purposes. A number of trials have demonstrated that increasing calcium intake by 500-1000 mg/day leads to a significant slowing of bone loss. Therefore, the optimal calcium intake in older people is probably in the range of 1000 - 1500 mg, which is equivalent to four to six servings of calcium-rich dairy products per day. The dairy products that are good sources of calcium are milk, cheese, yoghurt and ice cream. Many older people are uncomfortable taking this quantity of dairy products, and so use calcium supplements to bring their intake up to the target levels. Most authorities recommend that older people at risk of osteoporosis who do not already have a high calcium intake, take 500 - 1000 mg/day as a supplement.

### Vitamin D

Vitamin D is very important in allowing the body to absorb calcium from the diet. In individuals who are vitamin D deficient the rate of bone loss is higher and the formation of normally mineralised bone is reduced. Despite its name, vitamin D does not principally come from the diet but is made in the skin as

a result of direct sunlight exposure. As a result, vitamin D deficiency is most common in frail elderly people who seldom venture outside. Levels of vitamin D are easily measured with a simple blood test and it is wise for this to be checked in older people at risk of osteoporosis.

If vitamin D supplementation is necessary, then a typical dose is 500-1000 units daily. This is available in the form of cod liver oil or halibut liver oil, in the form of multivitamin tablets.

### Hormone Replacement Therapy (HRT)

The decline in bone density that occurs in all women after the menopause is attributable to the decrease in sex hormone production from the ovaries. Hormone replacement therapy involves administration of ovarian sex hormones or compounds very similar to them, to restore the levels of hormones in the body to those that existed before the menopause. If hormone replacement therapy is started at the time of menopause, postmenopausal bone loss is prevented, the height loss that occurs in older women is also prevented and the number of fractures developing over the next five to ten years is substantially reduced.

However, hormone replacement therapy can also be started many years after the menopause, when it will produce substantial increases in bone density and also appears to reduce the numbers of fractures. However, no really large study able to assess the impact of HRT on all the main types of fractures in elderly osteoporotic women has been carried out. In older women, the development of breast tenderness or vaginal bleeding can limit its use, and there remains concern that it may increase the risk of breast cancer.

## Medications in osteoporosis cont'd...

Raloxifene mimics the effects of oestrogen on bone, though the increases in bone density which it produces are not as great as those of oestrogen itself. However, it acts on the breast to oppose the effects of oestrogen and in a recent trial over four years, it substantially reduced the number of new breast cancers which developed. It has few side-effects but it does not have the beneficial effects of oestrogen on hot flushes. It has been shown to reduce the number of fractures in the bones of the spinal column but it does not appear to influence the number of fractures at other sites (eg, the hip).

### Bisphosphonates

The bisphosphonates are phosphate salts that bind to the surface of bone and inhibit the activity of the bone resorbing cells. In this way, they prevent further bone loss, and in fact tend to cause increases in bone density over the first few years of use. They are the most intensively studied group of treatments for osteoporosis and have been shown to decrease the incidence of fractures throughout the skeleton.

**Etidronate** was the first bisphosphonate to come into clinical use, and is the least potent. It causes increases in bone density in the spine of 2-3%. Trials have indicated that it reduces the incidence of spinal fractures, but there is no definite evidence that it reduces the incidence of fractures at other sites. It is taken in tablet form in courses lasting two weeks which are repeated every three months.

**Alendronate** increases bone density in the spine by 5-6% in the first two years. In patients with osteoporosis, it has been shown to halve the number of new fractures in the spine, hip and forearm. In the past, it has usually been administered daily, but appears to be just as effective if taken in a larger dose once a week. It sometimes causes heartburn or other forms of indigestion, particularly if the dosing instructions are not followed carefully.

**Risedronate** is the most recent bisphosphonate to come into clinical use. Its effects on bone density and fracture numbers are very similar to those of alendronate. It is taken in the form of a

daily tablet. It has caused few side effects during its developmental trials, but has only been in general clinical use for a short time, so its side-effect profile outside the trial situation is yet to be fully determined.

Bisphosphonates are very insoluble, so it is important that they are taken first thing in the morning with a full glass of water, at least half an hour before any food. They should not be taken with fluids other than water, since milk, tea, coffee or fruit juice all interfere with their absorption. With alendronate in particular, it is important to remain upright (either sitting or standing) for at least half an hour after the tablet is taken. This is to prevent the tablet from sliding back up into the gullet (oesophagus) where it may cause irritation resulting in heartburn.

### Calcitriol

Calcitriol is the most active naturally occurring form of vitamin D. It is normally produced in the kidneys. Its principal role is to regulate absorption of calcium from the diet. For a number of years, it has been used in Australia for the treatment of osteoporosis, though it has been little used for this purpose elsewhere. Some trials have shown it to produce small beneficial effects on bone density, though these are consistently much less than those resulting from the use of hormone replacement therapy or the bisphosphonates. Its effects on fracture numbers are unclear, one trial suggesting that it decreased the number of fractures and a second trial suggesting that it actually increased the number of new fractures occurring. Since there are now more effective therapies available, these are generally preferred.

There is now a range of treatments available for osteoporosis, and it is almost always possible to find one or more medicines that will provide safe and effective treatment for a given individual.

*Professor Ian R. Reid  
Department of Medicine  
University of Auckland  
New Zealand ■*