Early prevention of fracture in osteoporosis: new developments

Fractures in postmenopausal women are an important health issue in industrialized countries. Their cost to the NHS is believed to exceed £1 000 million per year. Postmenopausal osteoporosis is characterized by high bone resorption consequent upon oestrogen deficiency.

ASSESSMENT OF FRACTURE RISK

Bone densitometry measures existing bone mass, but this is not the same as bone resorption and bone density cannot identify individuals who will develop a fracture (Marshall et al, 1996). Indeed, for the same bone density, the fracture risk is some 8–10-fold greater in an 80-year-old than it is in a premenopausal female (Hui et al, 1988), and bone density in a multivariate analysis contributed little to the rising risk of fracture with age (DeLaet et al, 1997).

These limitations of bone densitometry have been recently debated (Wilkin, 1999). The notion that bone resorption, rather than bone density, may be the responsive element to modern treatments designed to prevent fracture is supported by a recent study of alendronate (Fosamax, Merck, Sharp & Dohme, Hoddesdon, Herts) in which substantial fracture prevention was achieved within 12 months (Pols et al, 1999).

The FOSIT (Fosamax International Trial) study was a double blind placebo-controlled study conducted over 12 months. It involved 1 908 osteoporotic, postmenopausal women recruited from 153 centres in 34 countries. Bone density was measured throughout the trial by dual energy X-ray absorptiometry (DEXA), and bone turnover by bone-specific alkaline phosphatase (a marker of bone formation) and urinary N-telo peptide crosslinks of type 1 collagen corrected for urinary creatinine (a marker for bone resorbtion).

FRACTURE INCIDENCE

The incidence of non-vertebral fracture over the 12-month study period was halved by the use of alendronate (19 *vs* 37 patients with fracture) representing a 47% risk reduction (95% confidence interval 10–70%; P=0.021). Bone density at the femoral neck rose by only 2.4% over the 12 months, whereas bone resorbtion fell by nearly 80% to premenopausal levels within 3 months. Bone-specific alkaline phosphatase levels fell by 50%, although rather more slowly, perhaps accounting for the small rise in bone density.

IMPLICATIONS

Protection of this degree within such a short period of time argues strongly for the use of alendronate in patients whose risk of fracture is high (i.e. the unstable and the infirm). Indeed, the benefits of antiresorbtive agents are known to accrue independently of age (Michaelsson et al, 1998). There is no evidence that bone densitometry can identify patients who will suffer fractures, but clear evidence from the FOSIT Study (Pols et al, 1999) that alendronate normalizes bone resorption and halves non-vertebral fracture risk within 12 months. HM

TJ Wilkin
Professor of Medicine
Plymouth Postgraduate Medical School
Derriford Hospital
Plymouth PL6 8DH

DeLaet CEDH, Van Hoet BA, Banger H, Hotman A, Pols HA (1997) Bone density and risk of hip fracture in men and women: cross sectional analysis. *Br Med J* **315:** 221–5

Hui SL, Slemenda CW, Johnston CC Jr (1988) Age and bone mass as predictors of fracture in a prospective study. *J Clin Invest* **81:** 1804–9

Marshall D, Johnell O, Wedel H (1996) Meta-analysis of how well measure of bone mineral density predict occurrence of osteoporotic fractures. *Br Med J* **312:** 1254–9

Michaelsson K, Baron JA, Farahmand BY et al (1998) Hormone replacement therapy and risk of hip fracture: population based case-control study. *Br Med J* **316:** 1858–63

Pols HAP, Felsenberg D, Wilkin TJ et al (1999) Multi-rational, placebo-controlled, randomised trial of the effects of alendronate on bone density and fracture risk in postmenopausal women with low bone mass. *Osteoporosis Int* **9:** 461–8

Wilkin TJ (1999) Changing perceptions in osteoporosis. *Br Med J* **318:** 862–5

KEY POINTS

- Alendronate halves the incidence of non-vertebral fracture within 12 months.
- The reduction in fracture risk is associated with the normalization of bone resorption, but minimal change in bone density.
- It is never too late to intervene — antiresorbtive treatment is equally effective in preventing fractures whatever the age it is started.
- Bone densitometry cannot identify individuals who will have a fracture.