Prevention of osteoporosis*

Osteoporosis is a major and growing health problem. At least 1.3 million fractures in the United States each year are attributable to osteoporosis, including roughly 250,000 hip, 250,000 wrist and 500,000 vertebral crush fractures.[1] As many as 2.5 million Canadians and 25 million Americans have a sufficiently low bone mass to be at high risk of fracture. The national cost of osteoporosis in Canada was estimated at $300 million in 1988 compared to $7 to $10 billion in the U.S.[2]

Osteoporosis and its complications produce considerable morbidity and mortality resulting in very high socio-economic costs. Hip fracture has become so common, particularly in elderly people, that affected individuals now occupy 20% of orthopaedic beds in many countries. Mortality is high, approximately 10–25% within the first year. Over 50% of older hip fracture victims will never be able to perform all the activities of daily living unaided, and 15 to 25% will require a prolonged, and often permanent, stay in a skilled nursing facility.[2]

Prevention of bone loss remains the most effective approach to therapy. In fact, it is far easier to prevent bone loss than to restore bone mass and to repair the alterations in architecture that have already occured once osteoporosis is fully developed. This article will focus on the prevention of primary osteoporosis. The prevention of osteoporosis can be achieved either by the maintenance of adult bone mass through the prevention of bone loss, or by the enhancement of peak adult bone mass by increasing bone mass during childhood, adolescence and young adulthood.

Identification of candidates for prevention

Any prevention strategy in health care requires the identification of those particularly at risk of a condition. Since bone loss is an asymptomatic process, the practitioner will need some clues to select those individuals who are most likely to fracture in the future. These clues may be divided into risk factors and estimates of bone mass.

Risk factor assessment is a possible approach for predicting the likelihood of developing osteoporosis. Epidemiological studies have contributed substantially to our understanding of the risk factors. Some risk factors influence peak bone mass, others bone loss. Some are well-established, whereas many others are inadequately documented. The well-established ones are advanced age, female sex, an early menopause or premenopausal oophorectomy, or other kinds of premenopausal estrogen deficiency like strenuous exercise and anorexia nervosa leading to anovulation.

However, the risk factors that have been identified account for only about one third of the variability in bone mass and are insufficiently sensitive and specific to predict an individual's overall risk of developing osteoporosis. The analysis of multiple risk factors in perimenopausal women is an inadequate substitute for bone mass measurement, correctly identifying only 70% of women with low bone mass compared to nearly all women when direct measurments are done.[3] Nonetheless, in the absence of better methods, those indicator risk factors are often used as a first step in the process of decision-making about an individual's prophylactic intervention.

Bone mass and bone quality

Bone mass measurement is the only way to stratify patients by fracture risk. Two major factors determine bone mass: peak adult bone mass, which is the highest value that an individual attains during her lifetime; and subsequent bone loss. Hereditary and racial factors are probably the most important determinants of peak bone density. Whereas negative environmental and lifestyle factors (malnutrition, immobility, cigarette smoking and alcohol intake) may prevent a woman from reaching her genetically predetermined peak bone density, there is no evidence that the opposite is true. That is, "mega-nutrition" or excessive exercise does not increase peak bone mass much beyond the genetic limit.[4]

Recent data indicate that the probability for fracture in the future can be estimated with bone mass measurements of the spine and femur at the age of menopause.[5] Clinical indications and techniques for bone mass measurements were reviewed by Dr. R.G. Josse in the October 1991 issue of the *Osteoporosis Bulletin for Physicians*.

Although bone mass accounts for 75 to 85% of the compressive strength of bone tissue and is easy to measure with precision, we should not forget that other factors, at present more difficult to measure, contribute to bone fragility. The skeletal factors include bone architecture and bone quality. Thinning and loss of trabeculae both occur with aging. Decreasing the cross-sectional area of a vertical trabeculae by 50% reduces its compressive strength by 75% (square ratio) as does doubling the effective length of the column through loss of horizontal support trabeculae. Transmission ultrasound methods measure the time required for ultrasound to be transmitted across bone (patella) and provide a measure of structural property, i.e. tridimensional architecture and bone mass. Until now, those techniques have not been clearly validated.

Age-related impairments in bone quality include decreased elasticity of the collagen matrix of bone, increased fragility of hypermineralized old bone, and reduced repair of microfractures. A novel ultrasound technique, ultrasound reflection, was designed and implemented to study the mechanical properties of bone mineral and preliminary results are very promising.[6]

Extraskeletal factors also contribute to osteoporotic fracture. These factors include falls, the circumstances producing falls – like psychotropic drug use, and the nature and efficiency of protective reflexes. However, the risk factors for falling are difficult to correct. Fortunately, only about 6% of falls result in fractures and only 1% in hip fractures.

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Prevention strategies

In premenopausal women, attention should be focused on the attainment of optimal peak bone mass.[7] Environmental and lifestyle factors should be modified to achieve the genetically predetermined peak bone density. For all women, a diet with the recommended allowance for calcium (700–1000 mg per day) and moderate exercise are reasonable. Long-term compliance to the exercise program is a major problem unless a recreational form of activity is suggested. Daily walking (30 minutes) is probably the most efficient exercise. Furthermore, walking is associated with good long-term compliance and might be easily adopted as a mode of physical activity by broad segments of the population.[8]

All women should be encouraged to avoid cigarettes and excess alcohol. For young women with irregular periods or amenorrhea, it seems logical to give exogenous estrogens (oral contraceptives), but we lack clinical trials that demonstrate benefit.

At menopause, similar modifications of risk factor profile are proposed as a population-based approach. For those particularly at risk for osteoporosis, as defined by low bone mass on dual photon or dual energy x-ray absorptiometry, pharmacological intervention will be added to behaviour modifications. However, bone mass measurement is not essential if a woman has already agreed to receive estrogen replacement therapy.

Calcium supplementation

Calcium is a readily available nutrient. Dairy products supply 75% of dietary calcium intake and, because they include lactose and vitamin D, provide the best overall source of calcium. Unfortunately, most individuals will not achieve their recommended daily calcium intake with their diet and this may require 500–1000 mg of extra calcium as calcium supplements. There are many forms of supplemental calcium and the most important consideration is the bioavailability. Because of a better solubility and higher concentrations of calcium per tablet, name brands of carbonate or citrate preparations are preferred. At these amounts, calcium is virtually free of side effects. However, special care should be given to patients with a history of kidney stones. The beneficial effect of calcium supplements is a very controversial issue. This does not mean that is has no effect, only that an effect has yet to be convincingly shown. Any effect is likely to be small but may not be insignificant on an epidemiological basis. Finally, it should be stressed that calcium supplements do not prevent estrogen-dependent bone loss.

Estrogen replacement therapy

Estrogen replacement therapy is without question the established preventive treatment for postmenopausal osteoporosis. Estrogen therapy reduces the risk of hip fracture by about 50% and the risk of vertebral fractures by 75% to 90%. Prevention of bone loss is most effective in the earliest stages of osteoporosis, before perforation and removal of trabecular elements lead to irreversible destruction of bone microstructure. Data support the practice of starting estrogen replacement therapy as soon as possible to achieve maximum beneficial effects. Because menopause-induced bone loss is greatest in the five to 10 years immediately after menopause and because estrogen will only prevent loss of bone mass, it is uncertain whether a woman should begin estrogen replacement therapy 10 to 15 years after menopause if osteoporosis is the only indication for its use. Quigley et al.[9] found that estrogen therapy retarded bone loss in postmenopausal women before the age of 70 but was ineffective thereafter.

The duration of therapy is less well-defined. Existing data suggest that estrogen's protective effects persist only as long as it is being taken. Discontinuation of therapy causes rapid bone loss. Epidemiologic data suggest that at least six years of therapy are needed to reduce the risk of osteoporosis fractures significantly. Postmenopausal women should receive estrogens for at least 15 years, and some investigators recommend longer-term therapy. The risk of long-term estrogen use must be balanced against the long-term benefits.

The optimal dose of estradiol to prevent osteoporosis is 1.5–2.0 mg (100 ug for patch) while the dose of conjugated estrogens is 0.625 mg per day. For all women who have an intact uterus, estrogen must be accompanied by a progestrogen. Cyclical estrogen-progestogen therapy causes monthly bleeding. Continuous estrogen-progestogen therapy brings about a constantly atrophic endometrium and therefore does not include bleeding, which some women find mandatory. Mammography before estrogen therapy is recommended. Contraindications and other aspects of estrogen replacement therapy were reviewed in the first issue of *Osteoporosis Bulletin for Physicians*.

Because the use of estrogen replacement therapy for preventing bone loss requires long-term dosing, patient education is essential. Only 30% of women comply with their prescribed estrogen regimen.[10] In one review, of those women receiving estrogen for the first time, 20 to 30% never had the prescription filled, 20% stopped therapy within the first nine months, and another 10% used it on an intermittent basis. Intermittent therapy may be sufficient to alleviate vasomotor symptoms, but it is not adequate for preventing postmenopausal bone loss. About 5% of all postmenopausal women get long-term estrogen replacement therapy.

Other antiresorptive drugs

Calcitonin is effective in the prevention of osteoporosis but has to be administered by subcutaneous injection, which makes its widespread use impractical. When nasal spray preparations become generally available they will form a realistic treatment strategy. Cyclical etidronate represents a new and promising therapeutic approach for osteoporosis. The drug has a long skeletal half-life, which could theoretically lead to increased amounts of "old" bone on the very long term because of reduced remodeling.

Conclusions

The purpose of treating osteoporosis is to intervene in the progression of the disease before fracture occurs. Using bone mass measurements at the age of menopause, we can identify those at risk of fracture and offer effective prophylactic strategies. Finally, we need to quantify the risks and benefits of osteoporosis prophylaxis and convey this information in a meaningful way to patients and physicians alike.

References

1 Melton LJ III. Epidemiology of fractures. In: Riggs BL, Melton LJ III, eds. Osteoporosis: Etiology, Diagnosis, and Management. New York: Raven Press, 1988; 133–154.

2 Peck WA. Osteoporosis, a major worldwide public health problem. Third International Symposium on Osteoporosis, Copenhagen, 14–18 October 1990: abstract #716.

3 Slemenda CW, Hui SL, Longcope C et al. Predictors of bone mass in perimenopausal women: a prospective study of clinical data using photon absorptiometry. Ann Intern Med 1990; 112:96–101.

4 McCulloch RG, Bailey DA, Houston CS, Dodd BL. Effects of physical activity, dietary calcium intake and selected lifestyle factors on bone density in young women. Can Med Assoc 1990; 142(3):221–227.

5 Johnston CC, Melton LJ, Lindsay R, Eddy DM. Clinical indications for bone mass measurements. A report from the Scientific Advisory Board of the National Osteoporosis Foundation. J Bone Min Res, 1989; 4 (suppl 2):1–28.

6 Antich PP, Anderson JA, Ashman RB, et al. Measurement of mechanical properties of bone material in vitro by ultrasound reflection: methodology and comparison with ultrasound transmission. J Bone Min Res, 1991; 6(4):417–426.

7 Ott SM. Editorial: Attainment of peak bone mass. J Clin Endocrinol Metab 1990; 71(5):1082A–1082C.

8 Kriska AM, Bayles C, Cauley JA, et al. A randomized exercise trial in older women: increased activity over two years and the factors associated with compliance. Med Sci Sports Exerc, 1986; 18(5):557–562.

9 Quigley ME, Maretin PL, Burnier AM, et al. Estrogen therapy arrests bone loss in elderly women. Am J Obstet Gynecol, 1987; 156:1516–1523

10 Ravnikar VAS. Compliance with normal therapy. Am J Obstet Gynecol, 1987; 156:1332–1334.