Prevention and Treatment of Postmenopausal Osteoporosis
National Consensus of the “Belgian Bone Club”, November 1996


INTRODUCTION

Osteoporosis is a general disorder of the skeleton, characterized by a low bone mass and a progressive deterioration of bone microarchitecture leading to a decrease in skeletal resistance and an increase in fracture risk. Obviously, this definition does not exclude that extra-skeletal determinants, like frequency of falls or traumatisms, could also play a role in the occurrence of fractures.

In prevention of osteoporosis, the aim is to maintain the bone mineral density and biomechanical resistance of the skeleton at a level that enables the skeleton to sustain the forces to which they are exposed in daily life. The acquisition of an optimal peak bone mass and a maximal limitation of subsequent bone loss are important in this perspective.

In treating established osteoporosis, the objective is to prevent further skeletal deterioration and increase bone mass as much as possible to provide a documented reduction of the risk of vertebral and/or peripheral fractures. The fracture risk increases gradually as a function of decreasing bone mineral content or density. In current practice, interpretation of bone mineral density measurements is based on a comparison with the mean values of peak bone mass obtained in healthy young adults, between 25 and 30 years of age (i.e. the T-score). Based on these reference values, an operational definition of osteoporosis was proposed by the World Health Organisation applicable to Caucasian females. Based on the concept of T-score, two levels of severity for values of bone mineral density, are proposed. “Osteopoenia” is related to mean values of bone mineral density located between 1 and 2.5 T-scores below the mean value. Such an “osteopenia” requests a preventive strategy. “Osteoporosis” is present in subjects whose bone mineral density is at 2.5 or more T-scores below the mean value for young adults. Such an “osteoporosis” relates to major risk for developing further fractures. The wording “severe osteoporosis” describes an osteoporosis (defined on the basis of the T-scores) which is already complicated by non-traumatic fractures of the wrist, spine or hip.

For the positive effect of a drug on bone mineral content to translate into a decrease in fracture rate, it is mandatory that pharmacological intervention does not induce deleterious effects on the biomechanical properties of the skeleton.

In 1993, the Belgian Bone Club in a national consensus document, discussed the different preventive and therapeutic strategies of post-menopausal osteoporosis. The aim of the present document is to update this position paper. In this document, we will only consider the primary involutional osteoporosis in females, excluding secondary forms of osteoporosis, particularly those related to glucocorticoids.

Calcium

In peripubertal children and adolescents with a balanced diet, the daily nutritional calcium supply should be at least 1200 mg. The usefulness of systematic administration of pharmacological calcium supplements during the period of growth has not been established and should not be advocated. In eugonadal women, the daily calcium requirements is at least 800 mg. The daily calcium requirements in postmenopausal women under adequate hormonal therapy are similar to those recommended for eugonadal women. In eugonadal women, the daily calcium requirements is at least 800 mg. The daily calcium requirements in postmenopausal women under adequate hormonal therapy are similar to those recommended for eugonadal women. In postmenopausal women who are not currently receiving hormonal replacement therapy, a daily intake of at least 1500 mg of calcium (diet and pharmacological supplements combined) partially protects against postmenopausal bone loss. Such a partial protective effect has been documented mainly in women who are postmenopausal for more than five years. In the curative treatment of osteoporosis, calcium supplement should be regarded as an adjuvant ther-

*Department Endocrinology, University of Gent
**Department Rheumatology, University of Louvain
***Department Rheumatology, Jan Palfijn Hospital, Merksem
+Department Gynecology, University of Brussels
++Department Cancerology, University of Brussels
++++Department Rheumatology, University of Leuven
§ Department Physical Medicine, University of Liège, Belgium.
apy. Supplements are mandatory in some specific treatments (fluoride, calcitonin, bisphosphonates). Partition of the dose and intake during meals increase calcium bioavailability. Several calcium salts are available in different preparations for oral intake. It is important always to take into account the content in elemental calcium which varies considerably from one preparation to another. Prescriptions should be limited to preparations for which bioavailability has been documented although it has not been unequivocally demonstrated that a limited difference between calcium salts in terms of bioavailability might be related to significant long-term variations in clinical efficacy. Administration of calcium, alone, in doses up to 2-3 g per day does not present any major risk.

**Vitamin D**

Administration of vitamin D supplements to healthy children, adolescents, eugonadal women and postmenopausal women up to 70 years of age, has no place in the prevention of postmenopausal osteoporosis. Administration of vitamin D in doses approaching the daily requirements (400 to 800 IU/day or 2500 IU/month or every two months) concomitantly with calcium supplements (total intake of at least 1500 mg/day) is justified in elderly people living in nursing homes or community-dwellings, who are frequently vitamin D-deficient, mainly in winter. The 1-alpha-hydroxylated derivatives (alophacalcidol and calcitriol) have a limited positive effect on the bone mass. Inasmuch as a preventive effect on the occurrence of fractures has not been established, their use cannot be recommended. As to date, it is not possible to state that the therapeutic benefit of these derivatives on bone differs from that of vitamin D. One should also take into account the potential toxicity (hypercalciuria, hypercalcaemia) when pharmacological doses are being used.

**Hormonal replacement therapy**

Hormonal replacement therapy is effective in preventing osteoporosis. The mean effective daily dose is 0.625 mg conjugated equine estrogens or 2 mg 17-beta-estradiol administrated orally or 50 μg 17-beta-estradiol by transdermic route. Other estrogens or alternative routes of administration (e.g. percutaneous), resulting in an equivalent estrogenic environment, are also justified. To prevent postmenopausal bone loss, estrogen can be given either continuously or following an intermittent regimen during at least 20 days per month. Estriol has no protective effect on bone at doses currently used for climateric symptoms. Tibolone cannot be considered a postmenopausal hormonal replacement therapy and will be discussed with anabolic steroids. Moreover, hormonal replacement therapy has other beneficial effects (reduction of climateric symptoms, probable decrease of cardiovascular mortality). A slightly increased risk of breast cancer, as consequence of hormonal replacement therapy, with or without progestogens, is likely. The risk of endometrial carcinoma can be prevented by the association of a progestogen, at least 10 days per month but preferably 12-13 days per month. The practical modalities of the therapy can influence the compliance, which often causes problems for this kind of treatment. The duration of treatment should be at least 10 years if the aim is to reduce the risk of femoral neck fracture. To date, it is not even clearly documented that even such a prolonged estrogen replacement therapy can effectively protect against risk of hip fractures at elderly age. In the curative treatment, estrogen still exerts a protective effect on bone mass, but the risk/benefit ratio for this approach is not established.

**Salmon calcitonin**

Long-term administration of calcitonin by parenteral or nasal route, can prevent postmenopausal trabecular bone loss. The optimal therapeutic regimen is yet to be established. A therapeutic benefit of calcitonin at the level of the cortical bone has not been established in the prevention of osteoporosis. In the curative treatment, calcitonin prevents further bone loss. The latter effect is especially pronounced when the initial level of bone turnover is high. A role of calcitonin in preventing fractures has been reported on several occasions. Calcitonin has analgesic properties in patients with recent vertebral crush fractures where a duration of therapy of one month (50 or 100 IU/day subcutaneous) is recommended. In prevention of further bone loss, in women with established postmenopausal osteoporosis, a ratio of at least 50% between duration of treatment (50-100 IU/day) and follow-up is required. The proposed treatment duration is two years.

**Bisphosphonates**

The use of bisphosphonates in the prevention of osteoporosis remains experimental. In the treatment of osteoporosis, the effect of etidronate has been studied only in a population already presenting with prevalent vertebral compression fractures. In those patients, there is a positive effect on bone mass, but a reduction of the fracture incidence in the whole osteoporotic population has not been established. The suggestion, based on an “a