

Calcium intake, hormone replacement therapy and osteoporosis in postmenopausal Chinese women

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Osteoporotic fractures of the lumbar spine, hip and distal forearm cause considerable morbidity and mortality amongst postmenopausal women. These fractures occur at least as frequently in Chinese women as in Caucasians. Factors such as oestrogen deficiency, a low dietary calcium intake and a lack of knowledge about the risk of postmenopausal bone loss contribute to the problem. The administration of hormone replacement therapy is effective in preventing bone loss and also provides cardioprotection and relief from menopausal symptoms. The use of calcium supplements allows a lower dose of oestrogen to be prescribed than when oestrogen is used alone. The combination of oestrogen and calcium may even be effective in replacing lost bone in cases of established osteoporosis.

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Introduction

Osteoporosis is a condition in which bone mass of normal composition is lost, with the result that fractures may occur after an episode of relatively minor trauma. It occurs in all individuals with advancing age, but most commonly affects postmenopausal women. It has been estimated to be present in 15 to 20 million individuals in the United States, and is the cause of more than 1.2 million fractures each year.^{1,2} The sites most commonly involved are the lumbar spine, the femoral neck and the distal forearm. These fractures are associated with significant increases in morbidity and mortality.³ Mortality rises by 12% to 20% within one year of hip fracture, mostly resulting from pneumonia and pulmonary embolus. In Hong Kong, the incidence of hip fracture is increasing, and the risk of fracture appears to be at least as great, if not greater, than it is in Caucasians.⁴

Both the peak bone mass and the factors which influence the rate of subsequent bone loss determine the severity of osteoporosis. It has been suggested that Asian women have a higher risk due to a racial predisposition, a thin build, and a low dietary calcium intake. Other important factors include age, family

history, an early menopause, and the consumption of alcohol and caffeine. Cigarette smoking and infrequent exercise also predispose to this condition. The likelihood of fracture is also influenced by various factors which predispose to falls, including lack of coordination and muscle strength, and certain other medical conditions and their treatments.

Drugs which have been shown to be of value in the prevention and treatment of osteoporosis include oestrogens, calcium, calcitonin, the biphosphonates, parathyroid hormone, and fluoride. While the role of oestrogens in preventing bone loss after the menopause is well established, the importance of an adequate dietary intake of calcium has, until recently, been controversial. This discussion will summarise the use of oestrogen and calcium in the prevention of osteoporosis with special emphasis on the treatment of postmenopausal Chinese women.

The menopause and osteoporosis in Hong Kong Chinese women

Ovarian failure occurring near the time of the menopause may cause a variety of acute, medium, and long term effects. The most commonly recognised acute symptoms are those of hot flushes and sweating, while oestrogen deficiency of a longer duration affects mainly the lower genitourinary tract, where atrophic changes may give rise to urinary frequency and urgency, or

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vaginal dryness and dyspareunia. As with acute menopausal symptoms, these problems may seriously diminish the quality of life of postmenopausal women. The long term consequence of low levels of oestrogen is an increased risk for both osteoporosis and cardiovascular disease. These are the most important complications of the menopause, as their onset is insidious and both conditions have the potential for reducing life expectancy.

Postmenopausal women in certain parts of Asia tend to suffer less from acute menopausal symptoms than do Caucasians. In a recent study conducted in Chinese women in Hong Kong, hot flushes and sweating were reported in only 24.2% and 18.2% respectively, following a surgical menopause.⁵ The comparative figures are approximately 70% and 84% in Caucasians.⁶ Although the relative absence of symptoms in local women may seem to be advantageous, those who do experience symptoms are more likely to seek medical advice and to receive treatment—thereby alleviating their symptoms, but more importantly, minimising their risk for osteoporosis. The majority of their contemporaries, however, accept the menopause uncomplainingly, and remain ignorant of their risk for developing osteoporosis and of other problems associated with menopause. A survey conducted by us in 200 women living in Hong Kong and southern China showed that while most women could correctly define the menopause (73% in southern China; 96% in Hong Kong), none were aware of the concomitant risk for osteoporosis (Haines CJ, unpublished data).

The combination of a lack of acute menopausal symptoms and ignorance of the complications caused by oestrogen deficiency are responsible for the relatively small proportion of postmenopausal women in Hong Kong receiving hormone replacement therapy (HRT). Recent data suggest that less than 3% of postmenopausal women are using this treatment.⁷ In addition, the paucity of symptoms may interfere with drug compliance for those taking HRT, although there are no data from the local population to support this theory. Postmenopausal osteoporosis is a largely preventable condition, but at present most women are not receiving appropriate counselling and treatment.

Osteoporosis and hormone replacement therapy

It is now more than 50 years since the link was first made between oestrogen deficiency, the menopause, and the development of osteoporosis.⁸ Following menopause, bone undergoes an increased rate of

remodelling, with resorption usually occurring at a slightly higher rate than does formation. Oestrogen receptors have now been shown in bone.⁹ Postmenopausal bone loss can be prevented, and the risk of fractures reduced in most postmenopausal women by the administration of HRT.¹⁰⁻¹² The positive effects of oestrogen appear to be independent of how it is given, as bone loss prevention has been confirmed using subcutaneous implants, transdermal patches and a percutaneous gel.¹³⁻¹⁵ The minimum effective daily oestrogen dose necessary to prevent bone loss varies, being 2 mg for oral oestradiol, 0.625 mg for conjugated equine oestrogens (CEO), 1.5 mg for percutaneous oestradiol and 50 µg for transdermal oestradiol, given twice weekly.¹⁵⁻¹⁸ However, the effect of oestrogens is only maintained while treatment continues, and following withdrawal, bone loss occurs at a rate similar to that found in women who have had a surgical menopause.¹⁹

While the most benefit in bone loss prevention is obtained in those who commence treatment within five years of the onset of menopause, a positive effect has also been demonstrated in women who have begun treatment later, after 65 years of age.²⁰

Progestogens are routinely administered in addition to oestrogens for those postmenopausal women who have not had a hysterectomy, as the use of unopposed oestrogens is associated with an increased risk of developing endometrial carcinoma.^{21,22} While there is evidence to suggest that progestogens alone reduce cortical bone loss, they appear to have little effect on trabecular bone.^{23,24} Progestogens used in combination with oestrogens seem to have a synergistic effect. It has been shown that bone loss can be prevented using either 0.625 mg CEO or 0.3 mg CEO with 10 mg medroxyprogesterone acetate.²⁴ In addition, the combination of oestrogen with 19-nortestosterone progestogens may be effective in replacing bone mass, although this may not apply to other progestogens.²⁵

When combined with oestrogens, progestogens are most commonly prescribed on a cyclical basis of at least 10 days each month, and this causes regular withdrawal bleeding in the majority of cases. The inconvenience caused by this may contribute to nonacceptance of prolonged HRT use; other methods of administration have been described to overcome this problem. The most popular alternative involves the continuous use of both hormones, which is a suitable approach for those women who have an established menopause. However, those who have only recently become menopausal will often experience erratic

bleeding on such a regimen. Consequently, various investigators have looked at the effect of having less frequent withdrawal bleeding—assuming that it may only be necessary to induce shedding of the endometrium every three to six months to guard against the development of endometrial carcinoma.²⁶

Osteoporosis and calcium intake

An adequate dietary intake of calcium is essential not only for skeletal development but also for the maintenance of bone mass. Normal calcium losses (intestinal, urinary, dermal) must be balanced by an adequate intake to prevent any bone resorption, which would be necessary to maintain calcium homeostasis. As both calcium absorption and renal calcium reabsorption decrease with advancing age, an adequate intake of calcium is a special consideration for postmenopausal women.

Although the recommended daily allowance (RDA) of calcium in women older than 18 years is 800 mg, it has been suggested that postmenopausal women actually need a daily intake of at least 1400 mg.²⁷ The daily intake of Hong Kong women has regularly been shown to be below this RDA. One study conducted in elderly Chinese women living outside of institutions showed a mean daily calcium intake which ranged from 354 to 382 mg.²⁸ In a study conducted by us in younger women, the mean intake using similar methodology was 397 mg daily.²⁹ The relatively low intake seen in Hong Kong may be of greater significance to postmenopausal women than has been suggested in studies involving Caucasians. This is suggested by two studies which found a low dietary calcium intake to be a risk factor for hip fracture in elderly Chinese women—but not for a comparable group of elderly Caucasians.^{30,31}

Although there have been a great many studies examining the effect of calcium supplements (CS) on bone mineral density (BMD), the results have often been contradictory—and in many cases may have been influenced by the study design. Of 43 studies on the subject published since 1987, a majority (27) have reported a beneficial effect for calcium on bone density.³²

Earlier reports were frequently observational, and either lacked randomisation, the inclusion of a placebo effect, or suffered from a small sample size. Opinion was divided, with some reviews concluding that CS have a beneficial effect on the BMD of postmenopausal women, while others concluded that it was of little or no benefit.³³⁻³⁶ However, a more recent series of

independent prospective randomised studies has yielded much more convincing evidence to support the use of CS.

The first of these examined the effect of a 1500 mg supplement in a randomised, double-blind, placebo-controlled cross-over study involving 169 women aged from 35 to 65 years.³⁷ A significant reduction in bone loss was found for those taking the supplement over the course of the four years of the study. Another placebo-controlled study assessed the effect of CS on the BMD of older postmenopausal women known to have a low dietary calcium intake.³⁸ For women more than five years past the menopause, bone loss was retarded in those taking calcium, but not in the placebo group.

One study looked at three groups of women who were randomised into either a no-treatment, 1000 mg supplement, or 2000 mg supplement group.³⁹ A significant reduction in lumbar bone loss was found in both calcium-treated groups, compared with the control group. Another study which compared the effect of a 1000 mg supplement against that of placebo in postmenopausal women with a mean dietary calcium intake of 750 mg daily, found that the mean rate of loss of BMD fell by 43% in the calcium-treated group, compared with those receiving placebo.⁴⁰ Further support in favour of calcium came from a study that examined the effect of CS in postmenopausal women known to have a low BMD. The combination of a CS with regular exercise was found to be more effective in slowing bone loss than a regimen of exercise only.⁴¹

Further evidence to support the use of CS in the local population has been provided by the results of a recent study in which we examined the use of CS in a population of postmenopausal Chinese women whose mean daily dietary calcium intake was low (under 400 mg). One group received only oestrogen for 12 months, the other was given a 1000 mg CS in addition to the oestrogen. While the first group (oestrogen only) maintained BMD at all sites, there was a significant increase in BMD at the femoral neck in the group receiving supplemental calcium (Haines CJ, unpublished data).

The same dose of oestrogen was used in both groups in this study, however, there is evidence to suggest that lower doses of oestrogens may be effective in preventing bone loss if calcium intake is increased. A dose of 0.3 mg of CEO combined with a 1500 mg CS has been shown to preserve bone as effectively as a 0.625 mg dose of oestrogen without a supplement.⁴² This finding has been confirmed by another study which used a similar dose of oestrogen and a supplement to ensure

a calcium intake of 1000 mg daily.⁴³

Conclusion

Although Chinese women suffer fewer postmenopausal symptoms than do their Caucasian counterparts, they have at least as high a risk of developing osteoporosis and subsequent fractures. The administration of HRT prevents bone loss in the majority of postmenopausal women, and the addition of CS may enable lower doses of oestrogens to be prescribed, and contribute to the replacement of bone in those cases where the condition is already established.

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