The epidemiology, treatment and prevention of osteoporosis in Hong Kong Chinese

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There is an epidemic of osteoporosis and hip fracture in the Hong Kong Chinese population. The main risk factors for osteoporotic hip fracture in Hong Kong Chinese are a low calcium intake, a lack of load-bearing activities and hormonal deficiency. The therapeutic agents for the treatment of established osteoporosis include calcitonin, bisphosphonates, sodium fluoride and vitamin D. However, primary prevention by maintaining an adequate calcium intake, performing regular load-bearing exercise, and hormone replacement therapy represents the only cost-effective approaches in the management of osteoporosis.

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Introduction

Osteoporosis is a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.[1] Although osteoporosis is in itself asymptomatic, it results in fractures of the forearm, vertebral bodies and hip in the elderly. Among these fractures, hip fracture is the most disabling and is associated with the highest health care cost. For instance, the annual cost of osteoporosis to the health care system in the United States has been estimated to be at least US$10 billion.[2]

There are two main determinants for the development of osteoporosis in old age. These are the peak bone mass attained in young adulthood, and the rate of bone loss with ageing.[2] Articles in this seminar series contain essential information on bone accretion and bone loss in childhood, young adulthood, postmenopausal women, and patients treated with steroids. The epidemiology, prevention and treatment of osteoporosis in Hong Kong Chinese is reviewed here.

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Osteoporosis in Hong Kong Chinese: a modern epidemic

In keeping with its rapid pace of urbanisation, Hong Kong has seen an epidemic of osteoporosis and hip fracture in the last decade. As the population ages, the magnitude of the problem will continue to increase. Strategies for the treatment and prevention of the condition are essential.

There was a definite geographical pattern to hip fracture in the 1960s, with the incidence being highest in Caucasians and lowest in Chinese and Blacks (Table 1).[3] At that time, the age-adjusted incidence of hip fracture in Hong Kong Chinese was only approximately one-third of the rates found in Caucasians.[4] As Hong Kong underwent dramatic urbanisation between the 1960s and 1980s, a rapid increase in hip fracture incidence occurred. A territory-wide survey conducted in 1989 showed that the age-specific incidence of hip fracture had increased by 200% to 300% in elderly men and women of all age groups (Table 2).[5] By the mid-1980s, the incidence of hip fracture among Hong Kong Chinese people occupied an intermediate position at an international level (Table 1).

Similar to Hong Kong, the incidence of hip fracture has increased in other developed Asian countries

Table 1. Age-adjusted incidence rates (per 100 000) of hip fracture by sex in the population over 50 years of age, by geographical area

Geographic area, years of survey	Age-adjusted rates		Age and sex-adjusted rates: total
	Women	Men	
Norway, 1983-84	1293	551	968
Oslo, 1978-79	701	310	530
Stockholm, 1972-81	622	291	477
Denmark, 1973-79	620	203	437
New Zealand Whites, 1973-76	620	151	414
California Whites, 1983-84	559	207	402
Rochester, NY, 1965-74	510	174	364
Texas Whites, 1980	530	205	384
Hong Kong, 1985	353	181	277
Hong Kong, 1965-67	153	96	128
California Asians, 1983-84	338	104	235
Texas Hispanics, 1980	263	118	197
Yorkshire, UK, 1973-77	275	96	196
California Blacks, 1983-84	219	144	185
Kuopio, Finland, 1968	100	249	183
California Hispanics, 1983-84	197	90	151
New Zealand Maori, 1973-76	107	182	149
Singapore, 1955-62	75	100	86
Johannesburg Bantu, 1950-64	26	38	31

Source: Maggi S, et al. Osteoporosis Int 1991.[3]

Table 2. Age-specific hip fracture rates in Hong Kong per 100 000 population (1966, 1985, 1991)

Age group	Rates (per 100 000 population)					
	Men			Women		
	1966	1985	1991	1966	1985	1991
40-49	6	13	9	7	11	6
50-59	16	28	27	22	32	26
60-69	67	54	73	54	135	122
70-79	224	339	321	173	501	581
> 80	321	1156	1191	716	1521	1916

Source: Lau E. Proceedings of the Fourth International Symposium on Osteoporisis 1993.[5]

such as Singapore and Japan.[6,7] While there are much less accurate incidence data in China, the results of a survey conducted in Chengdu in 1989 (Huang CY, unpublished data) showed that the crude incidence rate for hip fracture was 30/100 000 in both men and women, which is close to the rate observed in Hong Kong.

With an increasing incidence and a rapidly ageing population, hip fracture will become a major public health problem for all Asian countries. It has been estimated that 51% of all hip fractures (totalling 3.2 million) will occur in Asia by the year 2050.[8]

The determinants of bone mass in Chinese

As bony trabeculae which are lost cannot be replaced, the prevention of osteoporosis is of utmost importance. With the exception of heredity, the primary regulators of bone mass in the adult are calcium nutritional state, physical activity, and endocrine reproductive status. The relationship between dietary calcium intake, physical activity, hormone replacement therapy (HRT) and osteoporosis in Hong Kong Chinese is reviewed here.

Calcium

The relationship between dietary calcium intake and osteoporosis has been the topic of rigorous scientific debate for many years.[9,10] The real situation has been described as "... calcium deficiency, once variously regarded as a non-existent condition in human beings, and as the major cause of age-related bone loss, now occupies a middle ground as one of many contributors to fracture risk, not the most important but the easiest to correct".[11] Calcium deficiency is a unique problem in Chinese people due to their very low dietary intake. The results of two surveys have shown that the dietary calcium intake in Hong Kong Chinese is less than 500 mg daily, which is one of the lowest in the world.[12,13] The relationship between calcium intake, load-bearing activities and the risk of hip fracture in Hong Kong Chinese was studied in a case-control study involving 400 patients with hip fracture and 800 controls (Table 3).[12]

Table 3. Dietary calcium intake and the risk of hip fracture in 400 patients with hip fracture and 800 controls

Fifths of the distribution of calcium intake (mg/day)	Number of patients	Number of controls	Non-adjusted odds ratio	95% Confidence interval	Adjusted* odds ratio	95% Confidence interval
			Women			
< 75	93	137	1.9	1.2 to 2.9	1.9	1.2 to 2.9
75-	47	72	1.8	1.1 to 3.0	1.9	1.1 to 3.1
83-	42	105	1.1	0.7 to 1.9	1.1	0.7 to 1.9
129-	57	126	1.3	0.8 to 2.0	1.2	0.8 to 2.0
≥ 244	41	120	1.0		1.0	
			Men			
< 75	44	67	2.0	1.1 to 3.7	2.1	1.1 to 4.2
75-	14	30	1.4	0.6 to 3.2	1.4	0.6 to 3.4
83-	23	44	1.6	0.8 to 3.2	1.7	0.8 to 3.7
129-	20	40	1.5	0.7 to 3.2	1.5	0.7 to 3.2
≥ 244	19	59	1.0		1.0	

Source: Lau EM, et al. BMJ 1988.[12]

* Adjusted for cigarette smoking and alcohol consumption

The relative risk of hip fracture increased with a low calcium intake, so that the relative risk in subjects with the lowest quintile of intake was 1.9 compared with those in the highest quintile. Moreover, the effects of calcium intake were independent of physical activity and smoking. As will be reviewed in the various articles in this issue of the Journal, dietary calcium intake is an important determinant of bone mass in Chinese subjects of almost all age groups.

The results of clinical trials on the effects of calcium supplementation on bone mass in postmenopausal women have been contradictory. The results of one meta-analysis have shown that calcium supplementation of 1 g or more daily decreases postmenopausal bone loss by as much as 50% at non-vertebral sites such as the mid-radius and metacarpels.[14] The effects are most pronounced when the baseline calcium intake is low, in older women, and in women with osteoporosis. In a recent clinical trial, women who ingested less than 400 mg of calcium daily benefitted more from a 500 mg calcium supplement than did women consuming more calcium.[15] As the dietary calcium intake is low in Chinese, calcium supplementation is likely to be effective in preventing bone loss. Although more data on the optimal supplementation dose are needed, a total daily calcium intake of 1000 mg should be adequate.

Physical activity

It is well-established that immobilisation causes rapid bone loss, while excessive activity in young women may lead to amenorrhoea and bone loss.[16,17] Although the results of observational studies differ as to the effects of moderate exercise on bone mass, we have documented that frequent load-bearing exercise protects the elderly against hip fracture.[12] In this case-control study, the relative risk for hip fracture was significantly raised among women who reported walking outdoors, upstairs, uphill, or with a load less than once a day, compared with those who perform these activities every day (Table 4). The same trends were observed in men. Load-bearing activity was also found to be protective against hip fracture in a similar study conducted in the United Kingdom.[18] A reduction in physical activity with urbanisation may account for the recent epidemic of hip fracture in Hong Kong Chinese.

Randomised controlled clinical trials have been conducted on the effects of exercise on bone mass in Caucasians. Intense aerobic exercise was found to increase vertebral bone mass, while brisk walking was found to be ineffective.[19,20] In addition to its effects on bone mass, exercise may improve muscle strength and coordination, hence reducing the risk of falls in the elderly. As the liability to falls is a significant and independent risk factor for hip fracture in Hong Kong Chinese, regular load-bearing exercise is likely to benefit elderly residents who consume little calcium and live in high-rise apartments.[21]

Endocrine reproductive status

Bone loss begins soon after the menopause and is most rapid during the first three to six years.[22-24] If begun soon after the menopause, oestrogen therapy prevents the early phase of bone loss and decreases the incidence of subsequent osteoporotic fractures by 50%.[25-27] Original data on the protective effects of oestrogen therapy in Chinese women is presented by Haines in this issue of the Journal, suggesting that oestrogen therapy has the same protective effects against postmenopausal bone loss in Chinese women.[28]

The other important public health effect of oestrgen therapy is its protective effect on ischaemic heart disease in postmenopausal women. Long term oestrogen therapy may decrease the occurrence of ischaemic heart disease by up to 50%.[29,30] However, oestrogen therapy is also associated with an increased risk of endometrial cancer, and possibly breast cancer.[31,32] The overall risks and benefits of oestrogen therapy should be established unequivocally by the Women's Health Initiative, a prospective clinical trial involving more than 140 000 postmenopausal women in the United States.

Although the attributable risks and benefits of oestrogen therapy in Chinese people may differ from those in Caucasians because of differences in disease prevalence, oestrogen therapy is indicated in postmenopausal women with a known high risk for hip fracture and ischaemic heart disease. For postmenopausal and elderly women in whom the risk of fracture is unknown, bone mineral density (BMD) can be measured by dual X-ray densitometry. Hormone replacement therapy is indicated in women whose BMD is one standard deviation or more below that of the mean.[2] The normal ranges and pattern of bone loss in postmenopausal Chinese women has been established and is published in the paper by Lau et al in this issue of the Journal.[33]

The prevention and treatment of osteoporosis in Chinese

As mentioned earlier, an adequate calcium intake, adequate load-bearing activities and oestrogen replacement therapy are important in the prevention of osteoporosis. Several therapeutic agents are also available for the treatment of established osteoporosis, and their

Table 4. Current physical activity and the risk of hip fracture in 400 patients with hip fracture and 800 controls

Frequency * of activity	Women					Men				
	Number of patients	Number of controls	Non-adjusted odds ratio	Adjusted† odds ratio	95% Confidence interval	Number of patients	Number of controls	Non-adjusted odds ratio	Adjusted† odds ratio	95% Confidence interval
Walking outdoors										
- Less than once a day	105	151	1.7	1.7	1.2 to 2.3	25	40	1.3	1.3	0.7 to 2.4
- Once daily or more	175	409	1.0	1.0		95	200	1.0	1.0	
Walking upstairs										
- Less than once a day	182	323	1.4	1.4	1.0 to 1.9	71	133	1.2	1.0	0.6 to 1.7
- Once daily or more	97	235	1.0	1.0		49	107	1.0	1.0	
Walking uphill										
- Less than once a day	267	523	1.5	1.6	0.8 to 3.1	111	216	1.4	1.9	0.7 to 4.7
- Once daily or more	13	37	1.0	1.0		9	24	1.0	1.0	
Walking with a load										
- Less than once a day	268	513	2.1	2.3	1.2 to 4.7	111	218	1.3	1.4	0.6 to 3.3
- Once daily or more	11	45	1.0	1.0		9	22	1.0	1.0	

Source: Lau EM, et al. BMJ 1988.[12]

* Information was not available for all subjects

† Adjusted for cigarette smoking and alcohol consumption

mode of action is reviewed here.

Calcitonin

Calcitonin is a peptide hormone with analgesic properties and few side effects, but it is expensive and requires parenteral or intranasal administration.[33,34] Parenteral calcitonin transiently increases vertebral bone mass in women with postmenopausal osteoporosis, and intranasal calcitonin therapy retards the postmenopausal loss of cancellous bone.[35-37] However, calcitonin may not reduce cortical bone loss, and its effect on fracture is unknown.[37]

Bisphosphonates

Bisphosphonates such as etidronate are carbon-substituted analogues of pyrophosphate, an endogenous physiologic inhibitor of bone mineralisation. Bisphosphonates are potent inhibitors of bone resorption. The dosage of etidronate that inhibits bone resorption also impairs the mineralisation of newly synthesised bone matrix, so that its long term continuous administration is not feasible. However, in two recent clinical trials, an intermittent regimen of two weeks of etidronate followed by 11 to 13 weeks of calcium supplementation alone led to a small increase (approximately 2.5% annually) in spinal bone mass and may also have decreased the occurrence of vertebral fracture during the first two years of treatment.[38,39] Bisphosphonates have the potential to become a relatively low cost, orally administered alternative to oestrogen for the treatment of osteoporosis.

Fluoride

Sodium fluoride stimulates bone formation and increases bone density in women with osteoporosis by 8% annually in the lumbar spine and by 4% in the proximal femur, but it decreases cortical bone density in the radius by 2% annually.[40] Bone with excess fluoride content has an abnormal structure, and its fragility may be increased.[41] The results from two recent studies have shown that fluoride prescribed in lower dosages (50 mg daily) decreases the vertebral fracture rate significantly.[42,43] Further results from clinical trials are needed to support the routine prescription of fluoride to patients with osteoporosis.

The active form of vitamin D and its analogues

A recent study conducted in Europe found that 800 IU of vitamin D3 was effective in preventing hip and vertebral fractures.[44] In Hong Kong, the 25-hydroxyvitamin D levels in hip fracture patients have been found to be significantly lower than those in community-dwelling individuals.[45] However, vitamin D deficiency is not a common problem among the Hong Kong elderly and low vitamin D levels are prevalent only in the institutionalised elderly.[46] While routine vitamin D supplementation is not indicated for all elderly individuals in Hong Kong, adequate vitamin D nutrition is particularly important for those who may be housebound, sunlight-deprived, nutritionally deficient, and vitamin D-resistant.

Conclusion

Osteoporosis and hip fracture are major public health problems in Hong Kong. A variety of therapeutic agents are available for the treatment of established osteoporosis. However, primary prevention by maintaining an adequate calcium intake and regular load-bearing exercise, and by HRT represent the best therapeutic approach to this modern epidemic.

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