Densitometry trends in postmenopausal Asian women undergoing bisphosphonate treatment

Ang C L, Singh G, Goh A S W, Shen L, Tay B K

ABSTRACT

Introduction: Bisphosphonates have been shown to be effective in reducing the risk of fragility fractures in several landmark clinical trials conducted in Western populations. However, limited studies on bone mineral densitometry (BMD) trends have been conducted in Asian women. We conducted a retrospective review of electronic records to determine the actual BMD trends in a local population of postmenopausal women on bisphosphonate treatment.

Methods: The electronic records of all women over 50 years of age who had undergone BMD at Singapore General Hospital in 2004 were examined. Patients who were later started on bisphosphonates and continued the treatment for at least two years were selected for the study. Their subsequent BMD results were recorded, and longitudinal analysis was applied to determine the BMD trends as a cohort.

Results: A total of 254 postmenopausal women were included for analysis. Their mean BMD T-score was −2.70 before treatment, and improved to −2.56 and −2.27 one and two years after treatment, respectively. However, the score deteriorated to −2.50 and −2.62 three and four years after treatment, respectively. The difference between each year's results and those of the baseline was statistically significant.

Conclusion: In our study, the BMD scores in our local population showed improvement in the first two years of bisphosphonate treatment but declined subsequently. Our findings contrasted with those of studies conducted in Western populations. Further prospective studies are suggested so as to elucidate the actual BMD trends and fracture risk reduction in Asian women on bisphosphonate treatment.

Department of Orthopaedic Surgery, Singapore General Hospital, Outram Road, Singapore 169608

Ang CL, MBBS, MRCSE
Registrar

Tay BK, MBBS, FRCSE, FAMS
Emeritus Consultant

Department of Nuclear Medicine and PET

Goh ASW, MBBS, MSc, FAMS
Head and Senior Consultant

Department of Orthopaedic Surgery, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074

Singh G, MBBS, MMed
Associate Consultant

Biostatistics Unit, Yong Loo Lin School of Medicine, National University Health System, Block MD 11, #02-02, Clinical Research Centre, 10 Medical Drive, Singapore 117597

Shen L, PhD
Senior Biostatistician

Correspondence to:
Dr Ang Chia Liang
Tel: (65) 6321 6923
Fax: (65) 6224 8100
Email: med80199@yahoo.com

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INTRODUCTION

Osteoporosis is a disease of major health and socioeconomic significance.[1] An estimated 50% of women aged > 50 years would have an osteoporosis-related fracture in their remaining lifetime.[2] Osteoporosis-related fractures are most likely to occur in the spine, wrist or hip, but may affect any part of the body. They are associated with significant morbidity and mortality, with sequelae of chronic pain, disability and death.[3]

Bisphosphonates have been available for over a decade and are a mainstay among the various classes of drugs for the treatment of postmenopausal osteoporosis. Current bisphosphonates available in the market include alendronate, risedronate, ibandronate and zoledronic acid. Several landmark clinical trials have shown the efficacy of bisphosphonates in improving bone mineral densitometry (BMD) results, thereby reducing the risk for osteoporotic fractures.[4] In particular, the alendronate Fracture Intervention Trial (FIT) showed that patients treated with alendronate had a 51% reduction in hip fractures and a 44% reduction in vertebral fractures, with an increase in BMD of up to 6.2% over three years.[5] An extension of the FIT study, FIT long-term extension (FLEX), showed that patients treated with alendronate beyond five years had the same or increased BMD at the hip, femoral neck and lumbar spine compared with BMD decreases for patients who discontinued alendronate.[6] Risedronate has also been shown to reduce vertebral fractures by 41% and nonvertebral fractures by 39%, with an increase in BMD of up to 5.4% over three years.[7] A similar extension study on risedronate showed that the increases in spine and hip BMD were maintained or increased with two more years of treatment.[8]

These landmark clinical trials were conducted in Western populations with a Caucasian predominance.

Table I. Initial starting BMD T-scores of the patients.

Initial BMD T-score	No. (%)
< −1.0 to > −2.5 (osteopenia)	136 (53.5)
I ≤ −2.5 (osteoporosis)	80 (31.5)
Presence of a fragility fracture (severe osteoporosis)	38 (15.0)

BMD: bone mineral densitometry

Table II. Duration of bisphosphonate treatment in the patients.

Duration of treatment (yrs)	No. (%)
≥ 2	254 (100. 0)
≥ 3	187 (73.6)
≥ 4	121 (47.6)
≥ 5	33 (13.0)

However, in our anecdotal experience at a local institution, we observed many patients whose BMD results demonstrated significant deterioration despite being treated with bisphosphonates. A search of the available literature indexed on PubMed revealed one previously conducted study in a Chinese population, which showed BMD improvement after 12 months of alendronate treatment (4.87% increase at the lumbar spine).[9] The medium-to-long-term effects of bisphosphonate treatment on BMD results and the actual fracture risk reduction in Asian women have not specifically been identified. We conducted a retrospective review of patient records in order to determine the general BMD trends in local Asian postmenopausal women undergoing bisphosphonate treatment over a period of four years.

METHODS

This study was a retrospective review of the Sunrise Clinical Manager (version 5.8) electronic records of patients who were treated at Singapore General Hospital. A list of all women aged ≥ 50 years and who had undergone BMD imaging in 2004 was obtained from the Department of Nuclear Medicine. The electronic records of these patients were reviewed, and the data regarding age, race, duration of treatment with bisphosphonates, immediate BMD result before initiating bisphosphonates and subsequent BMD results was extracted. The exclusion criteria were patients on < 24 months of continuous bisphosphonate treatment, those who received other forms of osteoporosis treatment such as strontium or selective oestrogen receptor modulators and patients with no follow-up BMD images other than the initial one. Institutional Review Board approval was not required for the study.

At our institution, the decision to start bisphosphonate treatment would usually be based on the patient's BMD result and an assessment of the patient's risk factors for osteoporotic fractures, such as advanced age, a prior history of fragility fracture or a history of falls. Bisphosphonate treatment consisted of either alendronate or risedronate administered in standard weekly doses. Each patient who has undergone a BMD test would routinely be scheduled for a consultation with her doctor within 2–4 weeks after the test. The BMD test result would be reviewed, and the decision to commence osteoporosis treatment would be made during the consult. This initial BMD result would be recorded in our data collection. For patients who were treated with the minimum 24 continuous months of bisphosphonates, the final BMD result would be within a period of three months before or after stopping treatment. This was to ensure that the final BMD result would be a fair reflection of the patient's actual bone density around the time of stopping bisphosphonate treatment. Patients who did not have an available BMD result around the time of stopping bisphosphonate treatment were not included in the analysis. Each patient's BMD result was reported at two anatomical sites, the left femur and the lumbar spine. We recorded the worst result from either of the two sites for each BMD test. A statistical mixed model was constructed in order to evaluate the effects of bisphosphonate treatment on BMD trend. The Bonferroni correction was applied for multiple comparisons and the variable age was adjusted in the model.

RESULTS

A total of 254 women were included for analysis. These women had been treated with bisphosphonates for a minimum of 24 continuous months during the period from 2004 to 2009. Their mean age was 63.3 ± 7.7 (range 50–85) years. The majority were Chinese (94.0%), with Indians (2.8%), Malays (1.2%) and other races (2.0%) making up the minority. The distribution of initial starting BMD T-scores is shown in Table I.

Table II shows the different periods of bisphosphonate treatment within the cohort of 254 women. At the end of four years of treatment, 124 women had an available BMD result; 121 of these women were prescribed with bisphosphonates for at least four years. The mean starting BMD result was −2.70. This increased to −2.56 and −2.27 after one and two years of treatment, respectively. After three years of treatment, the mean BMD decreased to −2.5, and after four years, it was −2.62 (Fig. 1). This represented a 5.2% improvement in BMD after one year of treatment and a 15.9% improvement after two years of treatment

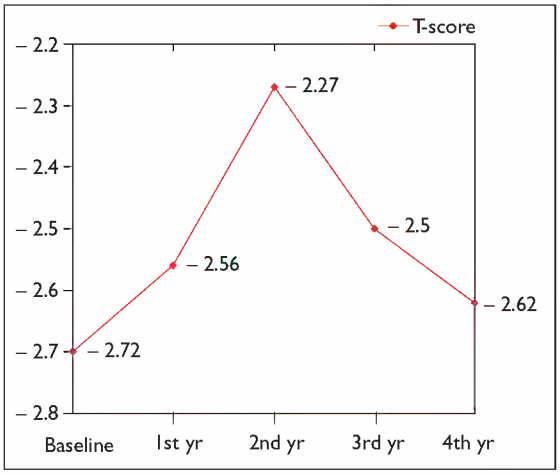

Fig. 1 Longitudinal analysis of bone mineral densitometry trend over a period of four years.

as compared to the baseline. After three and four years of treatment, the mean BMD result deteriorated to 7.4% and 2.9% above the baseline, respectively. The difference between each year's mean BMD result and the baseline BMD was statistically significant ($p < 0.0005$). The mean difference in each year's BMD result compared to the previous year was calculated from the mixed model and is not equivalent to the simple arithmetic difference between the mean BMD results. The mean difference between the baseline result and the first year was 0.26, followed by 0.10 between the first and second year, –0.05 between the second and third year, and –0.01 between the third and fourth year. The differences were statistically significant for the first two years ($p < 0.0005$), but not for the subsequent two years. Increasing age was found to correlate with decreasing BMD scores, which was statistically significant ($p < 0.0001$).

DISCUSSION

Bisphosphonate treatment has been shown to be effective in a number of landmark clinical trials conducted in Western populations. BMD improvement of up to 6.2% over three years was reported in these studies, along with a corresponding reduction in fragility fracture risk.[4,5,7] Moreover, extensions of these trials have shown maintained or increased BMD results with continued bisphosphonate treatment for up to five years.[6,8] Bisphosphonates have thus been widely established as the first-line treatment for the management of postmenopausal osteoporosis.

Our study aimed to identify the general BMD trend in a local population of Asian postmenopausal women. A PubMed search conducted at the time of writing this paper revealed only one study that documented BMD changes in a population of Chinese women who were being treated with bisphosphonates over a period of one year.[9] Our results showed that treatment with bisphosphonates increased the study cohort's BMD score by up to 15.9% above the baseline after two years of treatment. The BMD score subsequently deteriorated to 2.9% above the baseline after four years of treatment, but the deterioration was not statistically significant. Our results are primarily in concordance with landmark clinical studies conducted in Western populations in that a marked improvement in BMD score was seen with bisphosphonate treatment. However, contrary to a continually improving BMD trend shown in these studies, our findings indicate that the BMD results of local women may deteriorate despite continued treatment with bisphosphonates.

A review article by Lei et al[10] provided some insights into a potential difference in osteoporosis-related phenotypes between Asian and Caucasian women. These phenotypic differences may partially be the result of different genetic backgrounds, and included the pattern of bone loss and response to treatment. A separate review by Massart[11] found clues suggesting that race plays a major role in determining clinical response to treatment of osteoporosis with vitamin D and oestrogens. These previously published papers lend support to our finding that the clinical response to treatment of post-menopausal osteoporosis with bisphosphonates may be different in Asian and Caucasian women. The effects of bisphosphonates on decreasing bone resorption may 'wear out' much sooner in Asian women as compared to Caucasian women.

Our study was a retrospective review of electronic data, and the lack of specific information on patients' compliance to medications may thus be a potential confounder. Nevertheless, the patients' continued visits to the hospital with regular electronic prescriptions of bisphosphonates may be considered a soft indication of their likely compliance with medications, as non-compliant patients would likely not have returned for regular follow-ups. In cases where bisphosphonate treatment was discontinued even though BMD results were not yet optimal, the specific reasons would not be apparent to us, although it may conceivably be due to side effects of the medication or financial reasons.

In conclusion, our results suggest that Asian women may exhibit a different BMD response to bisphosphonate treatment compared to Caucasian women. Follow-up prospective studies may be useful in determining the medium-to-long-term response of BMD results to bisphosphonate treatment, which may impact the actual clinical practice in an Asian population.

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CME ACTIVITIES OCTOBER 2011

DATE & TIME	CME TOPIC	ORGANISER	VENUE	CME	SPECIALTY	CONTACT (TEL, EMAIL)
SMA Activities						
7 Oct 2.30 pm - 5.30 pm	Mastering Difficult Interactions with Patients	SMA-MPS	Sheraton Towers Singapore	2	All Specialties	Margaret Chan 62231264 margaret@sma.org.sg
5 Oct 6.30 pm - 9.30 pm	Mastering Adverse Outcomes	SMA-MPS	Sheraton Towers Singapore	2	All Specialties	Margaret Chan 62231264 margaret@sma.org.sg
5 Oct 6.30 pm - 9.30 pm	Mastering Professional Interactions	SMA-MPS	Sheraton Towers Singapore	2	All Specialties	Margaret Chan 62231264 margaret@sma.org.sg
8 Oct 2.30 pm - 5.30 pm	Mastering Difficult Interactions with Patients	SMA-MPS	Sheraton Towers Singapore	2	All Specialties	Margaret Chan 62231264 margaret@sma.org.sg
8 Oct 2.30 pm - 5.30 pm	Mastering Your Risk	SMA-MPS	Sheraton Towers Singapore	2	All Specialties	Margaret Chan 62231264 margaret@sma.org.sg
20 - 22 Oct 12.30 pm - 5.30 pm	Medical Ethics, Professionalism and Health Law Course	SMA	Safra Mount Faber	10	All Specialties	Loy Mong Shi 62231264 mongshi@sma.org.sg
Non-SMA Activities						
1 Oct 9 am - 4.15 pm	The 1st Respiratory Therapy Conference: The ARTS of Breathing	Singapore General Hospital	Health Promotion Board	4	Cardiology, Cardiothoracic Surgery, Internal Medicine, Respiratory Medicine	Maimunah Tahir 63214685 maimunah.mohd.tahir@sgh.com.sg
4 Oct 1 pm - 2 pm	Update on Atrial Fibrillation	NHG Polyclinics	Woodlands Polyclinic	1	Family Medicine	63553000
4 Oct 2 pm - 5.30 pm	Open Communication with Patients and Family after a Poor Outcome	National University Hospital	NUHS Tower Block	2	Others (Non-core)	Angie Ong 67726480 angie_ong@nuhs.edu.sg
6 Oct 1 pm - 2 pm	Managing Neck Lumps	NHG Polyclinics	Ang Mo Kio Polyclinic	1	Family Medicine	65547469
7 Oct 1 pm - 2 pm	Update on Acute Coronary Syndrome	NHG Polyclinics	Jurong Polyclinic	1	Family Medicine	66556040
8 Oct 2 pm - 5 pm	Pathology Today 2011: Chromosomes in Cancer and Prenatal Diagnosis	Singapore General Hospital	Singapore General Hospital	2	Pathology	Irene Lai 63214900 irene.alky@sgh.com.sg
8 Oct 9 am - 1.30 pm	Flexible Fiberoptic Workshop	Singapore General Hospital	Singapore General Hospital	7	Anaesthesiology, Emergency Medicine, Respiratory Medicine	Diana Lu 63214777 diana.lu.cw@sgh.com.sg
14 Oct 8.30 am - 5.30 pm	Quality Improvement (QI) Toolkit Workshop	National Healthcare Group	NHG College	4	Others (Non-core)	Choo Wei Yee 64782462 wei_yee_choo@nhg.com.sg
15 Oct 1 pm - 4 pm	GP Forum	Tan Tock Seng Hospital	Tan Tock Seng Hospital	2	Family Medicine	Sacha Bte Sadoon 63577877 sacha_sadoon@ttsh.com.sg

The above is a Continuing Medical Education (CME) Calendar, Category 1B.
Before attending any of these CME activities, please confirm event details with the respective course organisers. Information is correct at the time of printing.