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Original Article

Cost-Minimization Study Comparing Annual Infusion of Zoledronic Acid or Weekly Oral Alendronate in Women With Low Bone Mineral Density

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Abstract

Cost-minimization study to assess the annual direct costs of 2 antiresorptive strategies in postmenopausal women with low bone mineral densities (BMDs). Patients were randomly assigned to receive 70 mg of oral weekly alendronate or a 1-time 5 mg of intravenous zoledronic acid. All medical and nonmedical direct costs were recorded for 1 yr. Student's *t*-test or the Chi-squared test was used. A total of 101 postmenopausal women were enrolled with a mean age of 58.3 ± 7.6 yr and a postmenopausal period of 13.5 ± 8.3 yr. A total of 50 patients completed 1 yr of alendronate and 51 patients received zoledronic acid. At baseline, no differences were seen between the 2 groups in anthropometric measures, comorbidities, and bone mineral density. The costs for medical attention for low bone mass were $81,532 (US Dollars) for the alendronate group and $69,251 for the zoledronic acid group; the cost per patient was $1631 in the alendronate group vs $1358 in the zoledronic acid group ($p < 0.0001$). Therefore, zoledronic acid treatment provided an annual savings of 15% of the direct costs compared with oral alendronate treatment. Moreover, there was a significant increase in lumbar spine T-scores in the zoledronic acid group when compared with the alendronate group. Annual zoledronic acid infusion as an antiresorptive treatment in women with low BMD provides significant monetary savings when compared with weekly alendronate therapy for 1 yr. Zoledronic acid infusion is also linked to higher increase in BMD and compliance.

Key Words: Bisphosphonates; low bone mass; medical economics; postmenopausal osteoporosis.

Introduction

It has been estimated that 200 million people in western countries suffer from osteoporosis. In fact, approx 30% of postmenopausal women in Europe and the United States have osteoporosis. Of these individuals, at least 40%, plus 15% of men, will experience 1 or more factures that will affect their life span and quality of life to varying degrees *(1–4)*. In Mexico, 8.5% of women aged older than 50 yr have had a hip fracture, and hip fractures alone have an annual incidence of 169 per 100,000 women *(5)*. Osteoporosis and its related bone fragility fractures signify a considerable expense for society that continues to increase as the general population ages *(4)*. Moreover, the economic burden of both the diagnosis and treatment of osteoporosis, as well as the treatment of fractures because of bone fragility, has rapidly increased worldwide. For instance, a report from US investigators calculated a total cost of $13.7 to $20.3 billion in 2005 for the treatment of osteoporotic fractures *(2,4,6)*. If the number of postmenopausal women is considered, at least 6% of the national Mexican health budget would be required to provide minimum treatment and diagnostic strategies for this population *(7)*. Furthermore, in a

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1998 study from the United Kingdom, the social care and acute costs for all osteoporotic fractures were approx 727 million sterling pounds (nearly 1 billion dollars) (8).

The National Osteoporosis Foundation recommends initiation of pharmacologic treatment in patients with diagnosed osteoporosis (T-score: ≤−2.5), those with at least 1 osteoporotic vertebral or hip fracture, and those with low bone mass (LBM) and a US-adapted World Health Organization 10-yr probability of a hip fracture of 3% or higher or a10-yr probability of any major osteoporosis-related fracture of 20% or higher (9). Moreover, the American College of Physicians states that drugs indicated for osteoporosis prevention include alendronate, risedronate, ibadronate, raloxifene, estrogens, and zoledronic acid. Excluding estrogens, these same drugs along with calcitonin and teriparatide are recommended for the treatment of osteoporosis (10). Bisphosphonates, particularly alendronate and risedronate, which were made available over a decade ago, are the most commonly used drugs for the treatment of osteoporosis (11). Zoledronic acid has also been approved for osteoporosis treatment. Other drugs of the bisphosphonate class are seldom used in osteoporosis patients in Mexico. The clinical efficacies of alendronate, risedronate, and zoledronic acid for the treatment of low bone density and osteoporosis have been assessed in different randomized controlled trials, and when homogeneous endpoints are considered, the differences between these drugs appeared to be marginal (12−18).

Cost-minimization studies are a class of economic analysis in which 2 or more similar interventions are compared to determine money savings or differences in expenditures; the outcomes of these studies are expressed in monetary units (19) and all related costs should be included in the analysis. In most of these studies, cost calculations are performed from cases or data obtained in other investigations with different outcomes. However, we decided to perform a prospective trial with real patients to overcome this constraint.

Methods

All participants were invited female patients of the Postmenopausal Clinic in our Hospital. This clinic receives patients with oophorectomy, natural menopause, or other endocrine diseases; and board-certified gynecologists evaluate and treat climacteric symptoms and any anomalies in the breasts, cervix, or uterus. Densitometry is indicated every other year with a fast mode Performance HOLOGIC QB12-4000 densitometer (General Electric; Fairfield, CT) (20) to measure bone mineral density (BMD) region of interest according to International Society of Clinical Densitometry positions (21) of the lumbar spine (L1, L2, L3, L4, and total) and hip (femoral neck and total hip).

We enrolled women aged 45−79 yr with nonsurgical menopause, a Karnofsky index of 90−100 (Table 1), and low BMD in the lumbar spine and/or right hip according to current diagnostic criteria (21,22). We did not consider patients who were being treated for bone disease, had received bisphosphonates or hormone replacement therapy within the previous 12 mo, had a history of vertebral fracture, or had another cause of secondary osteoporosis. Other exclusion criteria included active smoking or a history of tobacco use with a cigarette consumption of 20 pack/yr or greater, a history of renal stones, serum creatinine level higher than 1.4 mg/dL, or any serum creatinine with a calculate glomerular filtration rate lower than 35 mL/min (Cockroft−Gault), gastrointestinal reflux grade II or greater, a history of ulcer disease, previous gastrointestinal bleeding or any gastrointestinal cancer, and failure to complete at least 80% of the scheduled medical visits or laboratory appointments within the previous year.

Table 1
Karnofsky Performance Status Scale (32)

%	Status
100	Normal, no complaints, no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or to do active work
60	Requires occasional assistance, but is able to care for most of his personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospital admission is indicated although death not imminent
20	Very sick; hospital admission necessary; active supportive treatment necessary
10	Moribund; fatal processes progressing rapidly
0	Dead

The Bioethics Committee of our institution reviewed and accepted our protocol, and informed consent was obtained from all participants. A team of internists completed a thorough assessment of each patient's clinical condition, including laboratory tests to rule out thyroid, renal, and liver diseases as well as determination of serum calcium, phosphorus and other electrolytes, and female hormone profiles; we also included the expenses of the densitometry and spine and hip X-ray films within the protocol costs. Once enrolled, women were allocated using a random numbers table into 2 different groups: patients in the A-group received 70 mg of alendronate (Fosamax; Merck & Co., Whitehouse Station, NJ) on a weekly basis plus a daily dose of 600 mg of calcium carbonate with 200 International Units of vitamin D (Caltrate 600 + D; Pfizer Pte Ltd, New York, NY); patients in the Z-group received an intravenous dose of 5 mg of zoledronic acid (Aclasta; Novartis, Basel, Switzerland) plus calcium and vitamin D, as mentioned above. Costs considered for medical attention for LBM were those related to the diagnosis and treatment of the low bone mineral disease and expenses for the treatment of adverse effects, including doctor appointments, laboratory