Abstract. – OBJECTIVE: The aim of this longitudinal retrospective ecological study was to evaluate the consumption of anti-osteoporotic medications and the evolution of pertrochanteric and femoral neck (FN), subtrochanteric and diaphyseal hip fractures between 2005 and 2010.

MATERIALS AND METHODS: Data were obtained from our Hospital Admissions Service (absolute number of fractures) and the Technical Directorate of Pharmacy (defined daily dose and absolute number of containers consumed of bisphosphonates (BP), raloxifene and strontium ranelate).

RESULTS: The overall incidence density of FN in 2005-2010 was 124.8 new cases per 100,000 persons per year. BP consumption increased between 2005 and 2010 to a peak of 70,452 containers consumed in 2010, while consumption of raloxifene declined. The number of subtrochanteric and diaphyseal fractures remained stable, but FN reached a peak in 2008 (N = 350) and fell thereafter (N = 284 in 2010). The percentage reduction in the number of FN in the period studied (2009: -14% and 2010: -11% compared to 2005) corresponds temporally with the increased consumption of BP (2009: +76% and 2010: +84% compared to 2005).

CONCLUSIONS: We found an inverse temporal association between the annual consumption of BP and the annual number of FN during 2005-2010. This is probably related to the cumulative effect of BP, although, given the limitations of the study design, other studies are needed to confirm our data.

Key Words: Bisphosphonates, Hip fracture, Osteoporosis

Introduction

Osteoporosis can be considered the silent epidemic of the twenty-first century, given the asymptomatic and progressive deterioration of bone quality. It is the most common metabolic bone disease, affecting 13% of the Spanish female population (26% of women aged > 50 years). Together with other complications, osteoporosis is characterized by low bone mass with microarchitectural deterioration and increased bone fragility with susceptibility to fractures1,3.

It is estimated that 25% of women aged > 50 years and 5% of men suffer one or more vertebral fracture throughout their lives. Likewise, the main cause of hip fracture in people aged > 50 years is osteoporosis, with mortality ranging between 5.6% and 8.3% in the acute phase and between 12% and 40% in the first year, with high morbidity (50% of patients left with some degree of disability)1,4.

The primary goal of osteoporosis treatment is to reduce or prevent the occurrence of fractures. Bisphosphonates have proven beneficial effects on bone mineral density and serum markers of bone remodeling, decreasing the risk of osteoporotic fracture5,6. They have proven to be cost-effective in the prevention and treatment of osteoporosis7,8 but their effectiveness in the general population is not well established9. Recent studies have evaluated changes in the prescription of anti-osteoporotic drugs and their relationship to hip fracture rates in recent years10,11.

Given the potential impact of the use of bisphosphonates in the prevention of osteoporotic fractures in the general population, the aim of our study was to evaluate the consumption of anti-osteoporotic medication and the evolution of pertrochanteric and femoral neck (FN), subtrochanteric and diaphyseal hip fractures during the period 2005-2010.

Materials and Methods

We carried out a longitudinal, retrospective ecological study in which the ecological unit was the population of the Valladolid-West Health Area (with a demographically-stable population of approximately 250,000) whose reference centre is the

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Rio Hortega University Hospital. Absolute numbers of annual pertrochanteric and femoral neck (FN), subtrochanteric and diaphyseal fractures during the period 2005-2010 were obtained from the Hospital Admissions Service. Data on the absolute number of containers of bisphosphonates (BP), raloxifene and strontium ranelate charge to the National Health System, which covers 99% of the population, were obtained from the Technical Directorate of Pharmacy, Regional Health Management. We did not include hospital consumption, private consumption, drugs without a prescription or drugs charged to mutual insurance companies. The variables studied were: incidence (new cases of fracture in our population in a year), incidence density (mean new cases of fracture in our study population in the study period) and consumption rate of drugs (number of packs consumed in a year per 100,000 inhabitants).

Statistical Analysis

Data were analyzed and graphics constructed using the Microsoft Office Excel 2003® Statistical Package.

Results

During the study period, there were 1872 cases of FN (318 in 2005, 301 in 2006, 345 in 2007, 350 in 2008, 274 in 2009 and 284 in 2010), 125 cases of subtrochanteric fractures (19 in 2005, 12 in 2006, 27 in 2007, 29 in 2008, 16 in 2009 and 20 in 2010) and 58 diaphyseal fractures (8 in 2005, 10 in 2006, 13 in 2007, 11 in 2008, 7 in 2009 and 9 in 2010). The overall incidence density per 100,000 persons per year for 2005-2010 was 124.8 new cases of FN, 8.2 new cases of subtrochanteric fracture and 3.8 new cases of diaphyseal fracture.

With respect to the use of anti-osteoporotic drugs, consumption of BP rose steadily from 19049 containers in 2003 to 50472 in 2010, while consumption of strontium ranelate reached a peak of 4326 containers in 2007 and decreased progressively to 2776 in 2010. The consumption of raloxifene fell from 13122 containers in 2003 to 5139 in 2010.

Figures 1 show the parallel evolution of the overall number of fractures and drug consumption expressed in number of containers throughout the study period.

The percentage reduction in the number of FN (2009: -14% and 2010: -11% compared to 2005) corresponded temporally with the gradual increase in the consumption of BP and their cumulative effect (2006: +11.5%, 2007: +34.5% 2008: +63.5% 2009: +76% and 2010: +84% compared to 2005) in our health area.

Discussion

Osteoporosis is a multifactorial disease that affects both sexes and whose prevalence varies between regions. Bone loss associated with aging is most evident from the fourth or fifth decade of life and, given the gradual aging of the Spanish population, osteoporosis is an increasingly prevalent disease. The annual estimated cost of all osteoporotic

Figure 1. Relationship between consumption of drugs (number of containers) and hip fractures.
fractures in Europe is 30 billion Euros\textsuperscript{12}. In Spain, BP represents 28\% of the global consumption of anti-osteoporosis drugs\textsuperscript{13}. Studies suggest that the decline in the absolute number of FN is due to increased consumption of BP, despite the influence of environmental factors in the appearance of FN and inadequate treatment adherence in the taking of BP in some cases\textsuperscript{10-14}.

Vicente Molinero et al\textsuperscript{13} evaluated the use of BP in the urban area of Zaragoza over a five-year period and found that alendronic acid was the most-commonly used BP with a global adherence to treatment of 80.6\% and that the incidence of FN remained stable after categorization according to therapeutic compliance. More recently, a study in Galicia\textsuperscript{11} evaluated the growing use of anti-osteoporotic medication over a five-year period and found no associated decrease either in the global incidence of hip fracture or in the incidence stratified by age and sex. Fisher et al\textsuperscript{10}, in a much larger Australian study, found an inverse relationship between anti-osteoporotic medication use, especially BP, and the rate of FN in both men and women over a 10 year period.

Our study provides relevant data on the incidence density of osteoporotic hip fractures, rates of anti-osteoporotic drug consumption and the parallel evolution of consumption of these drugs and their relationship with fractures. Unlike Guerra-García et al\textsuperscript{11}, we found that as BP consumption increased, the incidence of FN fell, while the global incidence of other hip fractures remained stable.

In addition to the limitations of studies using an ecological design, our study provides no information adjusted for sex and age (in contrast to other studies\textsuperscript{11,15}, since the data provided to us were in the form of absolute numbers.

In conclusion, this ecological study, a pioneer in our area, found an inverse temporal association between the annual consumption of bisphosphonates and the absolute number of FN during the period 2005-2010, and especially since 2008. This may be due to the cumulative effect of BP although, given the study design used, larger, specifically-designed studies are needed to confirm these data.

References