

Pharmaco-economic issues in the treatment of severe osteoporosis

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Summary

Introduction: clinical guidelines recommend to identify and treat people at high risk of fracture. **Methods:** we have carried out a simulation concerning pharmaco-economic issues in the treatment of severe osteoporosis and particularly those people with previous femoral fragility fractures, assuming that only 13.1% of hip fractured patients had started a proper antifracture therapy, as shown by the analysis of the Tuscany regional database. **Results:** Annual costs sustained by the Italian healthcare system for treating hip fractured patients all over Italy have been estimated to range from 2 560 000 in year 2000 to 3 291 750 in year 2005, representing only 0,3% of the overall costs sustained because of hip fractures in Italy. **Conclusions:** Sixty percent of the pharmaceutical costs can be considered as ineffective from a therapeutic point of view because patients were assuming their drugs only for 6 months. There is a need for specific codification of osteoporotic fragility fractures at hospital admissions and for implementing regional strategies aimed to reduce hip re-fractures by increasing the number of patients on treatment and incrementing adherence to treatment.

KEY WORDS: osteoporosis; fractures; costs.

Introduction

Osteoporosis is a common skeletal disease in older populations, leading to more than a million fractures annually in the United States (1) and Europe (2). Nonvertebral fractures represent 75% of osteoporotic fractures seen in clinical practice (3). The incidence of nonvertebral fractures, especially at the hip, increases rapidly with age (4). Fractures are a burden to society; in terms of costs, morbidity and mortality. In order to prevent these fractures, clinical guidelines recommend that candidates for osteoporosis therapy be identified by screening the bone mineral density of all woman ages 65 and over (or earlier for at risk populations) in order to plan proper treatment strategies (5). Italy has one of the highest life expectancies in the world: according to the Italian National Institute for Statistics (ISTAT), life expectancy at birth increased at a rate of 4 months per year from 1950 to 2005, reaching 77.8 years for men and 86.9 years for women (6, 7), but it is estimated to rise up to 78.4 and 87.4 years, respectively, by 2010 (6, 7). In Italy, 18% of the population is actually over 65 years of age (6); within the next decade, this age group may exceed 22% of the population (8). Moreover, 4% of this group is already ≥ 80 years of age (6). For these reasons, Italy represents an interesting international case study for determining social and economic burden of aging-related diseases, because of the increasing weight of older age groups within the general population (resulting in the inversion of the age pyramid), which is a general phenomenon observed in all industrialized countries. Therefore, observations made in Italy could be relevant for many other industrialized countries facing similar problems of ageing of the population. Increased life expectancy is associated with a greater frailty of elderly people and a higher prevalence of chronic and degenerative diseases. Osteoporosis and its complications - especially hip fractures - represent a challenge for health professionals and decision makers in the 21st century. The World Health Organization (WHO) considers osteoporosis to be second only to cardiovascular diseases as a critical health problem (9), and in our previous study we have shown that incidence and costs of hip fractures in Italy are already comparable to those of acute myocardial infarction (10). Furthermore, hip fractures have a 5% acute mortality rate and a 15-25% 1 year-mortality (11, 12). Once hip fracture has occurred, the ability to walk is completely lost in 20% of cases, and only 30-40% of patients recover a degree of autonomy comparable to the period before the fracture (13-16). The main Epidemiological Study on the Prevalence of Osteoporosis in Italy (ESOPO) reported a high prevalence of osteoporosis: 23% among all women, with age-specific rates ranging from 9% (40 to 49 year olds) to 45% (70 to 79 year olds), and almost 15% in men aged ≥ 60 years (15, 16). According to these percentages, about 4 million of Italian women and 800 thousand men are thought to be affected by osteoporosis (7). It is known that osteoporosis is a condition that enhances the risk of fracture, especially vertebral and hip fractures (17). Furthermore, one fifth of fractured patients will experience another hip fracture within few years, accounting for 20% of hip fractures costs (200 millions €/year in Italy). Despite that, only a minority starts any treatment, and a relevant size of patients stops therapy within 2-3 months (18). In this study we aimed to evaluate pharmaco-economic issues concerning the treatment of severe osteoporosis and particularly those people with femoral fragility fractures.

Methods

We analyzed the hospital discharge records, which are collected at the Italian Ministry of Health (national hospitalization database, SDO). These information are anonymous and include patient's age, diagnosis, procedures performed, and length of the hospitalization. The present manuscript focuses on the number of patients hospitalized because of hip fracture in Italy and subsequently treated with any antifracture drug during the years 2000 through 2005. First of all, we analyzed the national hospitalization database (SDO) maintained at the Italian Ministry of Health in order to determine the number of hospitalizations due to hip fractures in the Italian population aged ≥ 65 years old as we did in our latest paper concerning this topic (19). The study period (from year 2000 to 2005) was chosen because it reflects the most recently available nationwide clinical (hospitalization records) and demographic data. Population data were obtained from the National Institute for Statistics (ISTAT) for each of the considered years (1). Hip fractures were defined by the following ICD-9CM diagnosis codes (major diagnosis): 820.0-820.1 (femoral neck fractures), 820.2-820.3 (per-trochanteric femoral fractures) and 820.8, 820.9 and 821.1 (other femoral fractures). Data were stratified by gender and into three age groups (65-74 and ≥ 75 years) and were processed using Stata (StataCorp, College Station, USA) and Excel (Microsoft, Redmond, USA) softwares. Hip fractures in patients aged 45 to 64 represented about 8% of all fractures and were excluded from the analysis as conservatively considered as unlikely to be osteoporotic. We performed descriptive statistical analyses of the incidence in each gender and age subgroup across the 6 examined years. After having determined the number of hospitalizations due to hip fractures, we considered about 20% of these admissions as rehabilitation records of the same patients (8). Furthermore, we had to take into account a 5% acute mortality rate (within the first month) (8). Secondly, we aimed to estimate the number of hip fractured patients treated with any antifracture drug after having been discharged from the hospital. Therefore, we have analyzed the Regional Tuscany databases (hospital discharges records and pharmaceutical prescriptions records) in the latest available period (2005-2007) in order to calculate the incidence of hip fractures in people aged over 65 years old (both male and females) and medical prescriptions concerning those patients within one year after the fracture (18). We have used major diagnosis codes ICD9-CM 733.14, 733.15, 820 (all extensions), 821 (all extensions), 829 (all extensions). Persistence on treatment rate at 1 year was found to be $< 40\%$. Almost 7,000 elderly patients were found to have experienced a hip fracture per each considered year, but the number of hip fractured patients being treated with a drug effective in reducing the risk of fracture declined from 13.1% to 12.0% across 3 years (18). According to that, we have assumed that a proper

antifracture therapy has been prescribed only to 13.1% (referring to the highest rate of the regional analysis) of hip fractured patients all over Italy, in order to perform a pharmaco-economic simulation concerning the treatment of severe osteoporosis, which is actually the condition leading to femoral fractures in elderly people. According to the analysis previously carried out in Tuscany, we assumed that only 40% of hip fractured patients in Italy have continued their therapy for 1 year, with 60% of them remaining on treatment just 6 months (18). In order to be more conservative and to overcome possible inter-regional discrepancies, we have decided not to drop the 13.1% rate across the 6 years examined, although the analysis of Tuscany regional database had shown a 1.1% decrease across 3 years. Similarly, the average cost considered for an antifracture therapy with bisphosphonates for 1 year has been computed in 500 Euros per patient (250 Euros per patient if the therapy was withdrawn within 6 months), including supplementation with calcium and vitamin D, although some drugs could result in less expensive annual costs.

Results

Annual costs sustained by the Italian healthcare system for treating hip fractured patients all over Italy has been estimated in 2 560 000 in year 2000, 2 730 000 in 2001, 2 815 750 in 2002, 3 129 000 in 2003, 3 162 250 in 2004, 3 291 750 in year 2005 (Table I). The increasing costs are due just to the growing number of hip fractured patients. Sixty percent of these estimated costs can be considered as ineffective from a therapeutic point of view because patients were assuming their drug only for 6 months. Table I also shows the estimated number of hip fractured patients aged over 65 years old ranging from 58,794 to 75,577 between years 2000 and 2005, with an increase of 22.2% across six years. Table II shows the overall costs sustained for hospitalization, rehabilitation and pharmacological treatment following hip fractures in people aged ≥ 65 years old, from year 2000 to 2005 as reported in previous Italian national studies (19, 20), including costs of pharmacological treatments as resulted from our analysis. According to that, costs of hip fractures in Italy have reached 1 billion Euros in year 2005. As shown in Table II, costs sustained for pharmacological treatments effective in reducing the risk of subsequent hip fractures represent 0.3% of the overall costs related to hip fractures in Italy. Table III simulates the hypothesis of having treated with antifracture therapies for 1 year all the hip fractured patients in Italy. In this case, costs sustained for antifracture drugs would rise from about 27.9 to 35.9 million Euros across six years, thus accounting for 3.5% of the overall yearly direct costs of hip fractures occurring in Italy, actually corresponding only to 0.26% of the overall national pharmaceuticals expenditures.

Table I - Direct costs sustained for hospitalizations and rehabilitation following hip fractures in people aged ≥ 65 years old, from year 2000 to 2005.

	Patients (n) & costs (€) Year 2000	Patients (n) & costs (€) Year 2001	Patients (n) & costs (€) Year 2002	Patients (n) & costs (€) Year 2003	Patients (n) & costs (€) Year 2004	Patients (n) & costs (€) Year 2005
Hospitalizations due to hip fractures >65	73 493	78 354	80 804	89 796	90 753	94 471
Expected hip fractured patients >65 (no.)	58 794	62 683	64 643	71 837	72 602	75 577
<i>Pts (no.) discharged from the hospital*</i>	55 854	59 549	61 411	68 245	68 972	71 798
Patients starting any antifracture therapy	7 316	7 800	8 045	8 940	9 035	9 405
Costs of the therapies (Euro)[^]	2,560,600	2,730,000	2,815,750	3,129,000	3,162,250	3,291,750

* Assuming 5% acute mortality rate

[^] Assuming only 40% of treated patients to complete 1 year of treatment

Table II - Direct costs sustained for hospitalizations, rehabilitation and pharmacological treatment following hip fractures in people aged ≥ 65 years old, from year 2000 to 2005.

	Year 2000	Year 2001	Year 2002	Year 2003	Year 2004	Year 2005
Hospitalizations due to hip fractures	73 493	78 354	80 804	89 796	90 753	94 471
Expected hip fractured patients >65	58 794	62 683	64 643	71 837	72 602	75 577
Overall hospitalizations direct costs	343,000,000	373,000,000	394,000,000	433,000,000	448,000,000	467,500,000
Overall rehabilitation costs €	392,876,272	418,852,367	431,970,539	480,005,732	485,140,236	531,986,400
Costs of the therapies € [^]	2,560,600	2,730,000	2,815,750	3,129,000	3,162,250	3,291,750
Total estimated costs €	738,436,872	794,582,367	828,786,289	916,134,732	936,302,486	1,002,778,150

[^] Assuming only 40% of treated patients to complete 1 year of treatment

Table III - Simulation of pharmacological costs in the hypothesis of treating all hip fractured patients for 1 year.

	Year 2000	Year 2001	Year 2002	Year 2003	Year 2004	Year 2005
Hospitalizations due to hip fractures >65	73 493	78 354	80 804	89 796	90 753	94 471
Expected hip fractured patients >65 (no.)	58 794	62 683	64 643	71 837	72 602	75 577
Pts (no.) discharged from the hospital*	55 854	59 549	61 411	68 245	68 972	71 798
Costs of the therapies (euro)[^]	27,907,000	29,774,500	30,705,500	34,122,500	34,486,000	35,899,000

* Assuming 5% acute mortality rate; [^] Assuming 100% of treated patients to complete 1 year of treatment

Discussion

The burden of hip fractures occurred in the Italian elderly population is substantial and must be acknowledged as an important health problem. Osteoporosis-related hip fractures do not only lead to high medical care costs but also to high rehabilitation costs, which represent more than 50% of total costs in our analyses. Other authors have also reported rehabilitation costs as the most important cost category accounting for 66% of the total annual costs, followed by medical care costs (31%), informal care (2%) and indirect costs (1%) (21). It must be pointed out that the treatment would result not only in expenditures, but would reduce the number of subsequent hip, vertebral and other non vertebral fractures suffered from the same patients. Therefore, costs sustained for drugs generate a reduction of direct and indirect costs associated with fractures which would occur without treatment. Furthermore, the entire hip fractured population should have been treated with antifracturative drugs as stated by the Italian Pharmaceutical Agency. Our simulation concerning the treatment of the overall hip fractured population has shown that costs sustained for pharmacological treatments effective in reducing the risk of subsequent hip fractures would account for 0.26% of the overall national pharmaceuticals expenditures, which is a very low rate if compared with the expenditures sustained by the national healthcare service for cardiovascular-active drugs, actually representing 32% of the overall pharmaceuticals expenditures. Although in Italy is not currently available a codification for osteoporotic fragility fractures, the fact that more than 90% of hip fractures occurred among people aged >65 were actually suffered from people aged >75 years old (mainly women >75 with a rate of 82%) seems to prove the osteoporotic nature of these fractures. On the other hand, the 22.2% increase of hip fractured patients number between 2000 and 2005 strongly confirms the need for ensuring proper pharmacological treatments to this population, which has the highest risk of subsequent fragility fractures. However, there is a need for specific codification of osteoporotic fragility fractures at hospital admissions. Another important point to discuss is the therapeutical compliance. Almost 25% of the costs sustained to treat the general population (approximately 55 millions €/year in Italy) is wasted in too short treatment courses that unlikely reduce fracture risk. A good effort

would be to stop earlier short courses so to prolong them over one year. The analysis of regional databases would help for early identification of fractured patients with low adherence to therapies (18). The analysis of Tuscany database concerning hip fractured patients found a persistence on treatment rate at 1 year was found to be $< 40\%$ (18). This value is lower than that reported after the introduction of once-a-week drugs, which are nowadays widely used. Average Medication Possession Rate (MPR) was found to be 27%. Over 3 years, 77.9% of hip fractured patients had MPR $< 50\%$ vs. 55% of the general population on treatment. Only 2.0% of hip fractured patients had MPR $> 90\%$ (which is required to maximize risk fracture reduction) vs. 18.6% of treated patients in the general population (all people assuming antifracture therapies) (18). Hip fractured patients with MPR $< 50\%$ accounted for 44.3% of the Daily Defined Dose (DDD) vs. 24.1% of the general population (18). It must be noticed that $\frac{1}{4}$ of the costs sustained to treat the general population (approx. 55 millions €/year all over Italy) are wasted in providing very short treatment courses that unlikely reduce fracture risk (18). Therefore, relevant goals would be either to stop short treatment courses or to prolong them for more than one year. Regional databases would help for early identification of hip fractured patients without treatments or low compliance rates to therapies, in the frame of local strategies aimed to reduce hip re-fractures by increasing the number of patients on treatment and incrementing adherence to treatment.

Conclusion

Costs of hip fractures in Italy have reached 1 billion Euros in year 2005, but expenditures sustained for pharmacological treatments have been estimated in just 3 million Euros. Sixty percent of these pharmacological estimated costs can be considered as ineffective from a therapeutic point of view because patients were assuming their drug only for 6 months. Costs sustained for treatments effective in reducing the risk of subsequent hip fractures represent just 0.3% of the overall costs related to hip fractures in Italy. There is a need for specific codification of osteoporotic fragility fractures at hospital admissions and for implementing regional strategies aimed to reduce hip re-fractures by increasing the number of patients on treatment and incrementing adherence to treatment.

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