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Appropriate use in primary care of antiresorptive drugs against osteoporosis

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Summary

Background: To assess the appropriateness of the prescription of antiresorptive drugs according to the Guide to Osteoporosis of the Spanish Society for Family and Community Medicine (SEMFYC).

Material and methods: Descriptive transversal study carried out in two urban primary care centres. Out of all those patients who had taken an antiresorptive drug and/or had a diagnosis of osteoporosis, a sample of 411 patients was studied. Those who took the drug for other reasons (13), with diagnostic errors (8), *exitus* (3), or lacking clinical history (16) were excluded. Variables were recorded: age, sex, personal and family history of fractures, T and Z densitometric scores, type of antiresorptive drug, calcium and vitamin D supplements, and the specialist who initially indicated treatment. The appropriateness of the prescription was assessed according to whether or not it complied with the criteria in the SEMFYC Guide.

Results: 371 patients complied with the inclusion criteria. Of these, 96.5% were women. The average age was 68 years (standard deviation -SD-: 9.4). In 288 patients (77.6%) the personal antecedence of fractures was assessed, and in 21 (5.7%), that of the family. Densitometry had been carried out in 65.5% of patients. 65.2% had taken biphosphonates, and 14.8%, raloxifene. 72.8% were receiving vitamin D supplements, and 76%, calcium. In 30.5% of cases the treatment was initiated by the family doctor, in 21% by a traumatologist and in 14.3%, by a gynaecologist. In 204 patients (55%) the antiresorptive prescription was appropriate, in 113 cases (30.5%) it was not possible to determine the appropriateness, and in 51 (13.7%) it was inappropriate.

Conclusions: The prescription was inappropriate in fewer than 15% of patients, with biphosphonates the drugs most commonly used. In a third of patients densitometry was not carried out.

Key words: osteoporosis, Primary care, protocols, biphosphonates, strontium ranelate, raloxifene.

Introduction

Osteoporosis is a disease of the skeleton characterised by a reduction in bone resistance which exposes the individual to a higher risk of fractures¹. These fractures are the sole clinical consequence of osteoporosis, appearing in women from their fifth decade of life, and in men, later. In order of clinical importance, these fractures are those of the proximal femur, distal forearm and the spinal column^{2,3}.

It constitutes a major public health problem given its high prevalence (of 50% in women over 70 years of age)⁴ and the socioeconomic repercussions which these fractures have. In Spain, there are 30,000 hip fractures a year⁵, their incidence increasing exponentially and becoming a worrying problem in the elderly population. The treatment of these fractures carries a cost of some 720 million euros a year in our country.

We have available an arsenal of antiresorptive drugs (AD), such as the biphosphonates, raloxifene and strontium ranelate amongst others, which have shown a good cost-benefit *ratio*, taking into account the risk of fracture. Various works have shown that we seldom prescribe them in the presence of antecedent fragility fractures⁶, and that when we do indicate them, their prescription is not in accordance with the guidance⁷. We have available many recommendations from experts, both national and international, on when we should treat; some consider that the sole criterion is densitometric value, while others (the Spanish Society of Family and Community Medicine, the Spanish Society for bone and Mineral Metabolism Research, the National Osteoporosis Foundation, and many more) consider the diagnostic threshold to be different from the treatment threshold, and, as well as bone mass, consider the presence of other risk factors.

These drugs carry a high health cost. As an example, in Catalonia in the year 2008 the pharmacy costs of drugs for use against osteoporosis represented 35% of the cost of specialised drugs (some 485 million euros out of a total of 1,388 million euros).

For all these reasons, we would like to see to what extent the prescription of these drugs is appropriate to that set out in the Guide to Osteoporosis of the Spanish Society of Family and Community Medicine (SEMFYC) published in 2008⁸.

Material and methods

A transverse descriptive study was carried out in two health centres in the urban area of the city of Barcelona which serves a population of 45,851 inhabitants, of whom 22.7% are older than 65 years of age. Women of 50 years or more represent 44.9% of the total of women, and men of 60 years or more, 26.2% of all the men.

Using the computerised clinical history records system of the centre at the start of 2007, all those patients who had had a diagnosis of osteoporosis recorded (categories CIE 10 M80 and M81, M82 and their subcategories) were identified. Using the computerised prescription system, all the patients who had taken any AD (alendronate, risedronate,

raloxifene, strontium ranelate or calcitonin) were listed, obtaining a total of 1,806 patients with a recorded diagnosis of osteoporosis and/or currently using an AD. For the calculation of the sample size, in the absence of previous studies, a test pilot study was carried out, which observed an adequacy rate of 65%. Accepting an alpha risk of 0.5 in a bilateral contrast as a proportion, the sample size was calculated of 411 subjects, assuming that the population is the total, and a reposition rate of 0.25. Reasons for exclusion were considered to be diagnostic errors, absence of clinical history, those who took ADs for other reasons and those who were deceased. A simple random sampling was carried out.

The paper and computerised clinical histories were reviewed and the following data were gathered: age, sex, personal (PAF) and familial (FAF) antecedence of fracture, maximum values of T and Z scores (in the lumbar spine L2-L4, femoral neck and total hip) in the first bone densitometry carried out through dual X-ray absorptiometry, the specialisation of the doctors who initiated the treatment and who carried out the follow up, the type of AD, supplements of calcium and vitamin D and the appropriateness of the prescription. This last variable was defined as *appropriate* when it complied with the criteria of the Guide to Osteoporosis of SEMFYC (Figure 1) and an AD needed to be taken, *inappropriate* when they did not comply, and *indeterminate* when not all the data needed to evaluate it were available. The *inappropriateness* criterion included two subcategories: *a lack* (when an AD needed to be taken but was not prescribed) and *an excess* (when an AD was given but should not have been taken).

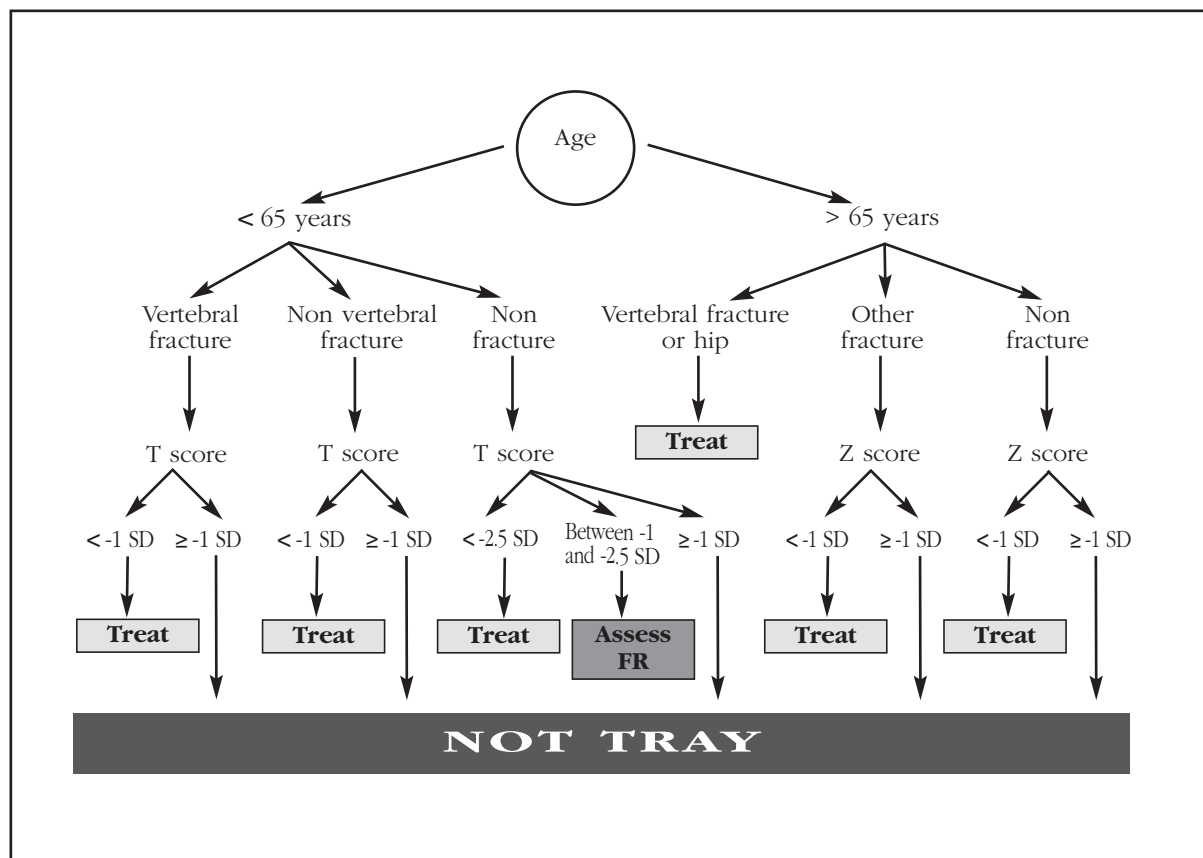
The SPSS.11 software package was used for the analysis. The results were presented with measures of central tendencies and with absolute and relative frequencies for the qualitative variables. To study the differences between the groups the chi squared (χ^2) test was used with $p < 0.05$.

Results

Of the 411 patients studied, 40 (9.7%) were excluded (8 due to diagnostic error, 16 for absence of history, 13 for taking ADs for other reasons and 3 due to *exitus*), leaving 371 patients.

The average age of the patients was 68 years (SD: 9.4); 96.5% were women. 247 patients (66.6%) had a diagnosis of osteoporosis recorded in its different CIE-10 categories: osteoporosis with pathological fracture (M80) in 53 patients (21.4%), osteoporosis without pathological fracture (M81) in 193 patients (78.1%), and osteoporosis in diseases classified in other places (M82) in one case (0.5%). Densitometry was performed in 243 subjects (65.5%), 167 cases of which complied with the diagnostic criteria for osteoporosis according to the definition of the WHO (Table 1). In 288 patients (77.6%) personal history of fracture had been recorded (Table 2), and in 20 (5.4%) a familial antecedent. The specialist who most frequently initiated the treatment and carried out the follow

Figure 1. Algorithm for therapeutic decisions in osteoporosis (adapted from the SEMFYC Guide 2000)



up was the family doctor (GP), followed by the rheumatologist (R), the traumatologist (T) and the gynaecologist (G) (Figure 2).

With respect to treatment, 242 patients (65.2%) took bisphosphonates 55 (14.8%) raloxifene, 11 (3%) strontium ranelate, 5 (1.3%) calcitonin and 1 patient (0.3%) was prescribed more than one associated AD. 57 patients (14.4%) took no AD. In terms of calcium and vitamin D supplements, 282 (76%) and 270 (72.8%) patients, respectively, received them.

In analysing by subgroups of prescribing doctor (Figure 3), bisphosphonates and raloxifene continued to be the most commonly used ADs, with statistically significant differences being observed between the gynaecologists and the other specialists ($\chi^2= 20.29$; $p<0.05$) in favour of a higher use of raloxifene on the part of the gynaecologist.

In 204 patients (55%) the prescription was defined as appropriate, and in 51 (13.7%) as inappropriate (31 by lack of AD and 20 due to its excess). By specialist, (Figure 4), no statistically significant differences were observed between appropriateness and inappropriateness ($\chi^2= 4.19$; $p>0.05$). 116 cases (31.3%) were indeterminate. In analysing the principal causes of indeterminacy it was observed that 83 patients did not have densitometry in their clinical history, and 45 had personal history of fracture.

Discussion

There are various consensus guides about when antiresorptive drugs should be used in osteoporosis in our ambit. The choice of the criteria proposed by the SEMFYC is due to the fact that it does not only consider the T- and Z-score densitometric values as the sole criterion for the recommendation of treatment, but it also values other risk factors, which are, principally, age and personal history of fracture. So not only is bone mineral density taken into account but other risk factors for osteoporosis, which allows the selection of a high risk population, thus increasing the positive predictive value of densitometry.

In analysing the appropriateness of the prescription we observe that in little more than 13% of cases was the prescription inappropriate, and if we considered only those patients who had been prescribed some antiresorptive drug (314 cases) we find that 6.4% should not have taken them. In our ambit there are few works which have assessed the appropriateness of prescription; Zwart et al.⁷ showed that in women between 50 and 80 years of age it is only considered to be justified in 8%, data disparate from those observed by us, where the appropriateness was 55%.

We find a high number of cases where the prescription was indeterminate. If we consider

Table 1. T-score and Z-score values observed by age subgroups in patients who had densitometries

		≤ 70 years (n=143)	> 70 years (n=100)	Total (n=243)
T score				
	< -2.5	94 (65.7%)	73 (73%)	167 (68.7%)
	Between -1 and -2.5	25 (17.5%)	8 (8%)	33 (13.6%)
	> -1	2 (1.4%)	1 (1%)	3 (1.2%)
	Not stated	22 (15.4%)	18 (18%)	40 (16.5%)
Z score				
	< -1	25 (17.5%)	9 (9%)	34 (14%)
	≥ -1	8 (5.6%)	16 (16%)	24 (9.9%)
	Not stated	110 (76.9%)	75 (75%)	185 (76.1%)

Table 2. Personal history of fractures noted in clinical history

		Absolute frequency	Relative frequency
Fracture		89	24%
	Vertebral	46	51.7%
	Hip	3	3.4%
	Multiple	12	13.5%
	Other	28	31.4%
Non fracture		199	53.6%
Not stated		83	22.4%

only those cases in which we have been able to determine the appropriateness (in 255 patients) we observe that in 20 patients (7.8%) who took an AD it would not be indicated. One of the principal limitations which we faced in designing this study was the known under-recording of computerised clinical histories. This was taken into account at the time of design of the study in the patient selection and data-gathering phases. In the selection, all those patients who had taken an AD were also reviewed so as not to miss patients who

had not been recorded correctly (in a third of those cases studied there was no diagnosis of osteoporosis). In the data gathering phase it was decided to review also paper-based clinical histories so as not to lose any information.

There were no significant differences in terms of appropriateness of prescription between specialists, and those that were seen were in terms of the use of ADs between gynaecologists and the other specialists, the former using raloxifene to a greater extent. In a study carried out in Navarra⁹

Figure 2. Medical specialisation of the professionals who initiated the treatment (prescriber) and who carried out the follow up

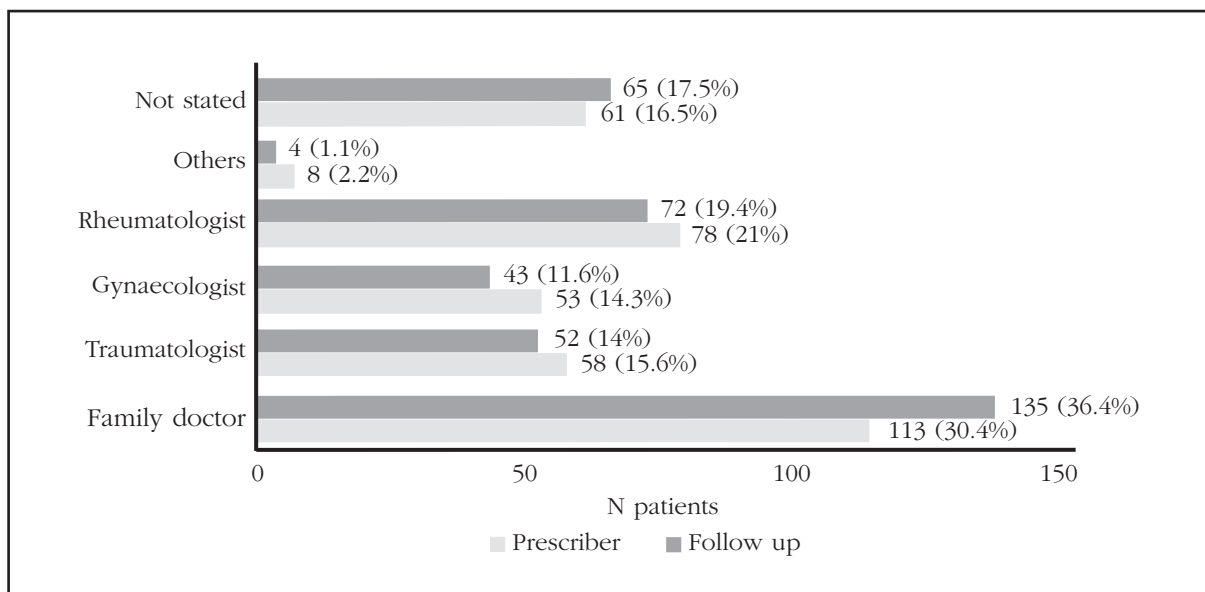
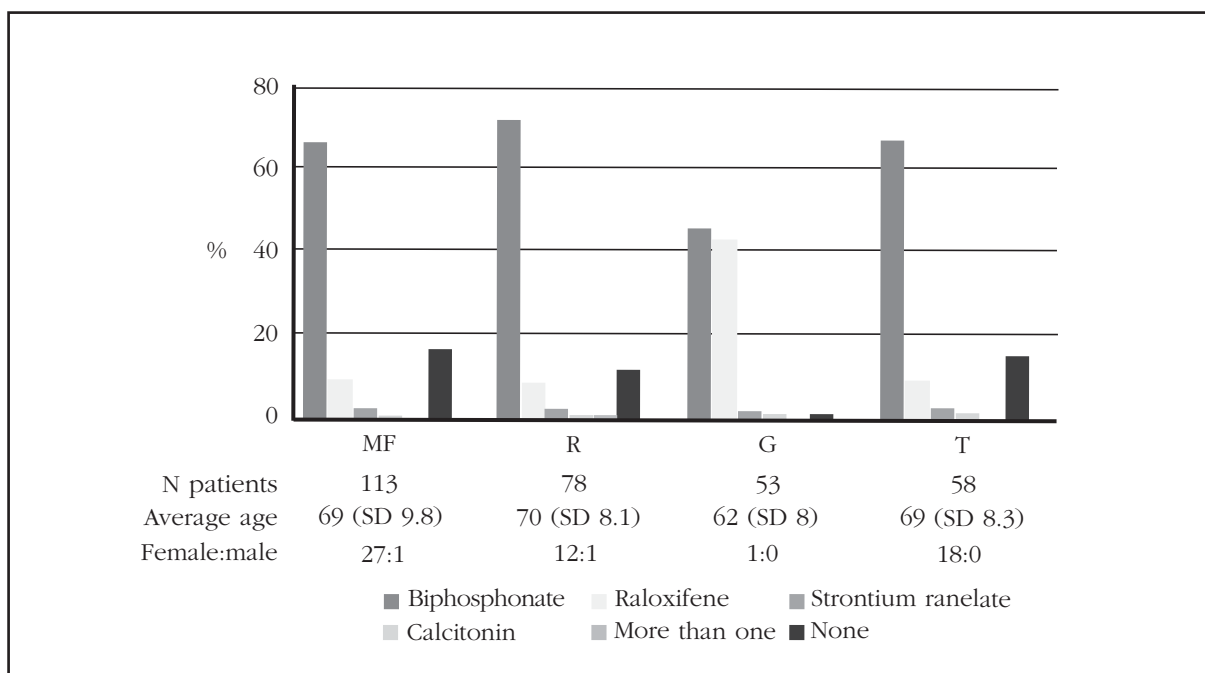


Figure 3. Types of antiresorptive drugs according to professional prescriber

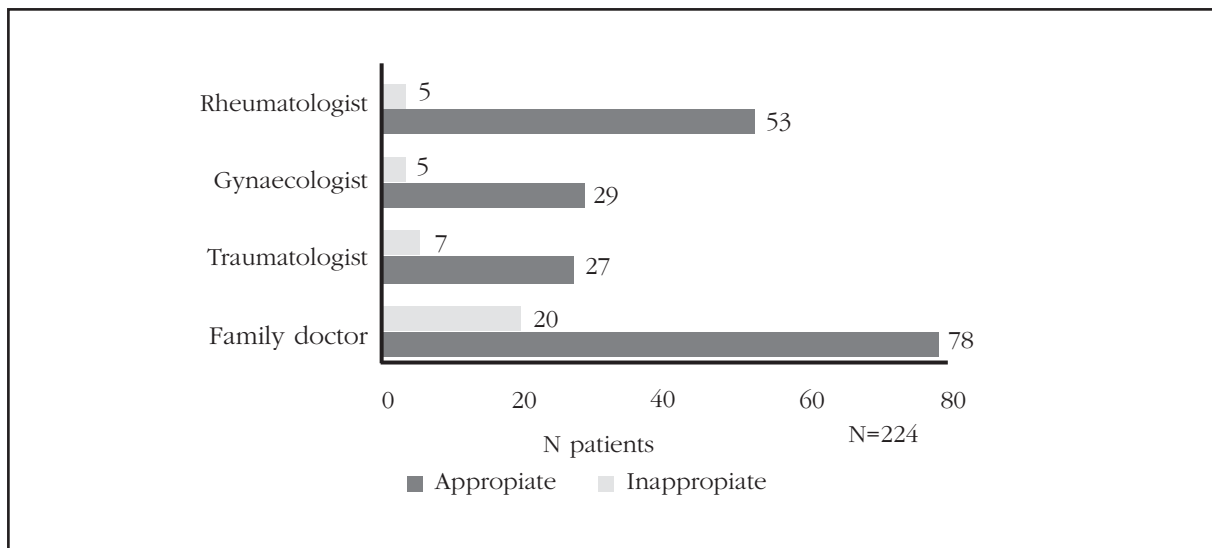


on the use of drugs for osteoporosis, a greater use of raloxifene was also observed on the part of gynaecologists. It may be possible to explain this by its role in the reduction in the incidence of oestrogen receptive positive invasive breast cancer in low risk women¹⁰, and for treatment of a younger population (average age 62 ± 8 years) where vertebral fracture is more significant than that of the hip¹¹. Raloxifene has been shown to reduce the risk of suffering vertebral¹², but not non-vertebral, fractures.

With respect to the use of calcium and vitamin D, three out of every four patients received supplements. This addresses two modifiable risk factors for osteoporosis^{13,14}, of which there is evidence that substitutive treatment in patients with a low intake of calcium and low levels of vitamin D would have a preventative effect on fractures, in particular in the population of elderly and institutionalised women^{15,16}.

In spite of the high level of accessibility of densitometry (100% in our centres) a low level of

Figure 4. Degree of appropriateness of the prescription according to medical specialism



actual performance of this procedure was found (in 6 out of every 10 cases), even though some societies such as the National Institute for Health and Clinical Excellence (NICE)¹⁷ are certainly recommending the use of bisphosphonates in secondary prevention to treatment of women of 75 years of age with previous fractures without the need to carry out densitometry. In our study this would mean 14 women out of a total of 128 not having densitometry. Recently PAPPS, in their recommendations¹⁸, propose an algorithm for taking decisions in the prevention of fractures in women, in which they also recommend initiating treatment before the presence of certain risk factors (personal history of peripheral fractures at over 50 years of age, history of morphometric vertebral fractures, family history of hip fracture and body mass index below 19 kg/m²), without the need for densitometry in women over 60 years of age. Since the carrying out of our work a new version of the SEMFYC Guide has been published¹⁹, which introduces as new elements in the therapeutic algorithm the consideration of treatment before the presence of earlier fractures, and, in their absence, consideration of the T values and other risk factors (maternal history of fracture, high risk of falls and low weight).

Finally, we mention that in this work appropriateness does not make reference to the fact that one or other AD may be more or less effective in the prevention of fractures, or may have a higher or lower level of cost-effectiveness, since there are already many studies^{12,20-22} which endorse these effects, which are not covered in the objectives of our work.

Thus we may conclude that, in spite of the problems we have found in the clinical history data records, in those cases in which we were able to determine the appropriateness of the prescription, this was high. The publication of new recommen-

dations raise, for us, the possibility of appropriateness at the present moment. We think that perhaps in the design of a future study it would be more interesting to contact patients to gather data on the different risk factors, thus minimising the loss of information. On reflection, it would also be interesting for each professional to think about the possible causes of the poor recording of data.

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