Osteoporosis: a look into the future from Primary Care

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Primary health care (PHC) is the first point of contact for patients in the health care system and is key to the suspicion of osteoporosis in postmenopausal women (PMO), as well as in the approach to its diagnosis and treatment and the establishment of the risk of fracture.

Osteoporosis is the most common bone metabolic disease in our environment, representing a serious public health problem world-wide[1], and specifically in our country[2]. The prevalence of osteoporosis determined by bone densitometry in the lumbar spine is especially high after the menopause[3,4]. It is estimated that in Spain, one in three women over 50 years of age suffer from osteoporosis, increasing to one in two for those over 70 years of age. Most of these patients are located in the 55-80 years age range[3,4], and it is estimated that 4% of those patients over 50 years of age with a hip fracture will die during hospitalisation, and 24% in the first year after fracture[5]. Vertebral fracture is the most common, and that of the hip the most serious and with a greater cost to the health system, while there may also be other fragility fractures such as the distal radius, humerus, rib and tibia[6].

The different guides consider those patients in whom two of the following factors exist, combined with low bone mineral density (BMD)[7], to be at high risk: being over 65 years of age; having family history, especially maternal, of femoral fracture; prolonged consumption of corticoids: and lastly, having had falls.

The aim of treatment is the prevention of fragility fractures, in both the short- and long-term. To achieve this, the correct identification of the origin of the fracture – traumatic or due to fragility – will enable the correct diagnosis and the correct clinical decision regarding treatment. In our setting, we simply calculate the risk of the main osteoporotic fractures, so-called major fractures (vertebral, hip, humerus and forearm), and of the hip at 10 years, using the FRAX tool[8]. These do not indicate the decision as to who to treat, but are the clinical criteria which govern that decision, which may follow the decision thresholds proposed by the European Guide to Osteoporosis[9], and above all, the guides of the different scientific societies which better fit our work environment.

Thus, following the criteria of the Canadian Scientific Advisory Council on Osteoporosis[10], for whom the risk is defined on the basis of the FRAX scores as: low risk (risk of fracture after 10 years <10%), intermediate risk (10-19%) and high risk (≥20%) for the main osteoporotic fractures, and low risk (<3%) or high risk (≥3%) for hip fractures; or Qfracture®[11,12]. Both tools would both support clinical decisions by identifying patients at high/low risk of osteoporotic fracture, as well as decision to treat, thus improving the predictive parameters for Spanish women in a way which is more cost-effective than the traditional model based on a T-score of ≤-2.5 in the DXA[13].

In respect of the increase in bone mass measured through densitometry, frequently used the primary care system in patients over the age of 65, this is not a good variable with which to measure the efficacy of drugs[14], this being one of the tests identified as having little clinical value in a study in 2012[15]. In fact, a number of clinical trials have indicated that antiresorptive drugs continue to prevent the appearance of fractures, even though the BMD diminishes. Therefore, DXA should not be carried out in a generalised and indiscriminate way, not simply on the basis of the age of the patient or when a postmenopausal women presents herself, but rather it should be requested on the basis of the presence of risk factors[14].

Regarding the efficacy of drugs used in the treatment of osteoporosis we must consider this to be very limited in secondary prevention (previous

fragility fractures), and, practically-speaking, not demonstrated in primary prevention. There has recently been published a systematic review[16], comparing the effectiveness of drugs used for the treatment of osteoporosis, which updates the review carried out in 2012[15], whose objective was to review the evidence to determine the salient aspects of the efficacy and safety of drugs indicated for the prevention of fractures. A striking conclusion of the study was the existence of good quality evidence supporting the idea that some medicines reduce the risk of fractures in people with a BMD in the osteoporotic range and/or previous vertebral or hip fractures, with a great variation in in efficacy between bisphosphonates, denosumab and teriparatide, and with serious but very uncommon adverse effects, such as atypical subtrochanteric fracture or osteonecrosis of the jaw. Also highlighted is the lack of direct comparisons of the benefits, and the harm which results from indirect comparisons, which do not allow one to indicate which drug is more efficacious than another[17].

There is no evidence that early treatment in people below the age of 65 brings any benefits, nor is there sufficient evidence to recommend treatment from the age of 80[16,18]. So, in a study by Sanfélix-Genovés et al.[19], they draw attention to the contrast in the high levels of pharmacological treatment which exists in the region of Valencia and the low prevalence of risk factors in adults (50-65 years) which, coupled with an overuse of BMD, translates into a very significant impact on health spending. We should not forget that the treatment of first choice is still to consider changing harmful habits, taking physical exercise or avoiding falls, combined with a sufficient intake of calcium and vitamin D, which are as effective as the increase in BMD obtained through drug treatment, or even more so. Doctors in the Spanish health system are aware of the existence of the high comorbidity of osteoporosis with cardiovascular risk factors which could indicate a closer physiopathological relationship. For this reason, 9 out of 10 patients who attend a clinic for osteoporosis receive information on healthy life styles, balanced diets and on how to achieve a sufficient intake of calcium[19]. However, in spite of the low efficacy of these drugs their consumption has shot up, multiplying six-fold in the last ten years. A report by the national health service in the UK which examined the use of medicines for osteoporosis developed countries put Spain as the top country in the prescription of these treatments, which is seriously incongruous if we take into account the fact that the incidence of osteoporosis in Spain is the lowest, not only in Europe, but in the world[20]. This is why drug treatment should be limited to high risk patients who are going to be those who really benefit[16,18,20].

In all the guides to clinical practice consulted, the first choice pharmacological treatment, due to their efficacy, safety and efficiency, are the bisphosphonates, essentially alendronate and/or risedronate[2,9,10,17], which are those which have been shown to be the most efficient in the different types of fractures, with as a possible alternative the oral administration of zoledronate in patients at high risk, and/or with osteoporosis.

Given the controversy over safety in recent years, in addition to the studies of new drugs and their combinations, studies are also being conducted of efficacy[21], of efficacy compared with new molecules[22,23], of treatment in men[24] and of the optimum duration of treatments[25]. To date, the scientific evidence only justifies prolonged use over more than five years in highly selected patients.

In those patients with intolerance or contraindications for bisphosphonates, denosumab[26], a SERM or strontium ranelate may be recommended. All of these have safety problems notified by PRAC (the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency), such as the temporary suspension of the sale in January 2014 of strontium ranelate due to an increase in serious cardiac events, thromboembolisms and/or skin reactions, or the risk of atypical femoral fractures with the use of denosumab, following the critical review which was carried out of the FREEDOM study[26].

In short, once a new medicine is authorised by the regulatory agencies and more in this type of pathology, the information regarding its efficacy and safety comes from the baseline studies and, therefore, the data are very limited. This obliges us to limit its prescription or, at least be "conservative" and, consequently, before prescribing a new drug for this pathology a careful risk-benefit assessment must be carried out, as well as assessing its suitability for each patient as against alternative more efficient therapies, with critical reviews carried out by professionals which allow comparison of the available information. This is an approach which addresses the patients and not the disease.

One of the issues which most concerns medical staff is adherence to treatment by the patient. In the work of Martínez et al. two out of three participating doctors considered that there was a level of non-adherence of 20%. Hence, one of the major challenges which doctors face is to successfully increase the adherence of patients to the recommendations and treatments they provide[27], involving all those concerned: patients, pharmacists and doctors. Adherence is understood to be as defined by the WHO in 2003, for whom it is: "the degree to which the conduct of a patient, in relation to the taking of medication, the following of a diet or the modifications of lifestyle correspond with the recommendations given by health professionals".

It can be deduced from this definition that, apart from the professionals and their communication with their patients, adherence also depends on the psychological connotations, experiences and knowledge of the patients themselves. Those people at risk of fragility fracture should take the opportunity to take informed decisions about their care

and treatment, in collaboration with the health professionals treating them. If the patient is in agreement, the families and carers should have the opportunity to participate in the decisions about the patient's treatment and care. The families and the carers should also have the information and support they need.

Good communication between health professionals and their patients is essential. This should be supported by written information based on the evidence, which suit the patients' needs and which should be culturally appropriate. It should also be accessible to those with additional needs such as physical, sensory or learning disabilities.

In short, in primary health care new paradigms are being opened up in relation to the management of a chronic disease, as is osteoporosis, in which the patients, in their environment, and the professionals involved should be jointly responsible for the development of their disease. It is known that a well-informed patient and a high degree of empathy with their family doctor enables an improvement in the doctor-patient relationship and, therefore, brings better health outcomes[27].

The health professionals face new challenges in improving therapeutic efficiency at this first level of care. For this reason they must carry out an effective selection of patients according to their risk (we ought not to forget that most patients with fractures are older, polymedicated and with multiple comorbidities and, up until now, not included in clinical trials), as well as the costs associated with their treatment and hospitalisation. In view of what lies ahead, this requires the establishment of protocols and guides to clinical practice agreed among the scientific societies in primary and specialised care (called "guides to guides", given the multidisciplinary nature of treatment in this pathology) and based on scientific evidence, which provide those aforementioned elements, creating integrated multidisciplinary educational programmes for the management of osteoporosis which allow the continuous updating and perfecting of the skills of doctors in primary care through active training programmes based on[28]:

1. Diagnostic and therapeutic decision algorithms.
2. Criteria for referral/monitoring.
3. Instructions for improving compliance
4. Criteria for the quality of care, of treatments, of life.
5. Cost criteria with evaluation of information on the economic impact of osteoporosis and associated fractures on their revenue.

In the primary care sector we should be more active in the search for new diagnostics, essentially promoting the use of the FRAX® tool, in women who attend clinics with diseases in which there is documented a high comorbidity with osteoporosis. It would seem to be essential to improve the quality of treatments of pluripathological and polymedicated patients, in whom new approaches, which incorporate the use of new drugs with demonstrable action on the risk of fracture and with widely-spaced doses, may help to resolve problems of adherence.

Throughout this process there will be key aspects of the management of osteoporosis, recommendations related to healthy lifestyles, diet, physical exercise, prior to the initiation of drug treatment, together with the need to emphasise that patients should take the recommended daily doses of vitamin D and calcium.

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Bibliography

1. National Osteoporosis Foundation. Clinician, guide to prevention and treatment of osteoporosis. Washington, 2010.
2. González J, Guañabens N, Gómez C, Del Rio L, Muñoz M, Delgado M, et al. Guías de práctica clínica en la osteoporosis posmenopáusica, glucocorticoidea y del varón. (SEIOMM) Rev Clin Esp 2008; 2008 (suppp1):1-28.
3. De Felipe R, Cáceres C, Cima M, Dávila G, Fernández S, Ruiz T. Características clínicas de los pacientes con tratamiento para la osteoporosis en un centro de Atención Primaria. ¿A quien tratamos en nuestras consultas? Aten Prim 2010;42:559-63.
4. Díaz Curiel M. Actualización de osteoporosis Madrid, FHOEMO; 2001.
5. Osteoporosis en Atención Primaria. Anónimo. Protocolos 4/2011 FMC 2011:7-32 Disponible en: http://www.elsevierinstituciones.com/ficheros/pdf/45/45v18nProtocolo_4a90034624pdf001.pdf [Accedido 06/12/2014].
6. Sosa M, Hernández D. Protocolo de actuación ante dos situaciones en osteoporosis frecuentes en Atención Primaria: Cuándo tratar siempre y cuándo evitar tratamientos innecesarios. Medicine 2014;11:3567-70.
7. Pérez Edo L, Alonso A, Roig D, García A, Guañabens N, Peris P, et al. Actualización 2011 del Consenso Sociedad Española de Reumatología de Osteoporosis. Reumatol Clin 2011;7:357-79.
8. Prieto-Alhambra D, Pagés Castellá A. Estimación del riesgo de fractura mediante la Escala FRAX®. FMC 2010;17:473-4.
9. Kanis JA, Burlet N, Cooper C, Delmas PD, Reginster JY, Borgstrom F, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2008;19:399-428.
10. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, et al. 2010 clinical practice guideline for the diagnosis and management of osteoporosis in Canada: Summary. CMAJ 2010;182:1864-73.
11. Hippisley-Cox J, Coupland C. Derivation and validation of updated QFracture algorithm to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study. BMJ 2012;344:e3427.
12. Hippisley-Cox J, Coupland C. Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of Qfracture Scores. BMJ 2009;339:b4229.
13. Azagra R, Roca G, Martín-Sánchez JC, Casado E, Encabo G, Zwart M, et al. Umbrales de FRAX® que identifica personas con alto o bajo riesgo de fractura osteoporótica en población femenina española. Med Clin (Barc) 2014;144:1-8.
14. Jamart L, Herrero S, Barrera C. ¿Está justificado el gasto en fármacos contra la osteoporosis? FMC 2011;18:317-20.
15. Qassem A, Alguire P, Dalla P, Feinberg LE, Fitzgerald FT, Horwitch C, et al. Appropriate Use of Screening and Diagnostic Tests to Foster High-Value, Cost-Conscious Care. Ann Intern Med 2012;156:147-9.
16. Crandall CJ, Newbery SJ, Diamant A, Lim YW, Gellad WF, Booth MJ, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: An update

Systematic Review. Ann Intern Med 2014;161:711-23.
17. Montes E, Bruno S, Cantabrana A, Sosa M, Arnaíz A, Plasencia M, et al. Osteoporosis en la postmenopáusica. Boletín Canario de Uso Racional del Medicamento (Bolcan) 2012;41-8.
18. Effective health Care Program. Treatment To Prevent Fractures in Men and Women With Low Bone Density or Osteoporosis: Update of a 2007 Report. Disponible en: http://effectivehealthcare.ahrq.gov/ehc/products/160/1007/CER53_LowBoneDensity_FinalReport_20120823.pdf [accedido 06/12/2014].
19. Sanfélix-Genovés J, Sánfelix-Genovés G, Peíro S, Hurtado C, Fluixá C, Fuertes J, et al. Prevalence of osteoporotic fracture risk factors and anti-osteoporotic treatment in the Valencia región, Spain. The Baseline characteristis of the ESOSVAL cohort. Osteoporos Int 2013;24:1045-55.
20. Kanis JA, Johnell O, De Laet C, Jonsson B, Oden A, Ogelsby AK. International variations in hip fracture probabilities: implications for risk assesment. J Bone Miner Res 2002;17:1237-44.
21. McClung MR, Grauer A, Boonen S, Boloñesa MA, Marrón JP, Diez-Pérez A, et al. Romosozumab in postmenopausal women with low bone mineral density. N Engl J Med 2014;370:412-20.
22. Tsai JN, Uihlein AV, Lee H, Kumbhani R, Siwila-Sackman E, McKay EA, et al. Teriparatide and Denosumab, alone or combined, in women with postmenopausal osteoporosis: the DATA study randomised Trial DATOS. Lancet 2013;382:50-6.
23. Vertebral Fracture Treatment Comparisons in Osteoporotic Women (VERO) Bethesda, MD: Instituto Nacional de Salud; Octubre 16 2012 [actualizado 11 de julio 2014] [accedido 07/12/2014 http://clinicaltrials.gov/ct2/show/study/NCT01709110].
24. Combination Risedronate-Parathyroid Hormone Trial in Male Osteoporosis (RPM) Bethesda, MD: Instituto Nacional de Salud; 29 de mayo 2012 [actualizado 15 de enero 2014] [Accedido 07/12/2014 http://clinicaltrials.gov/show/NCT01611571].
25. Comparison of the Effect of an Ongoing Treatment With Alendronate or a Drug Holiday on the Fracture Risk in Osteoporotic Patients With Bisphosphonate Long Term Therapy (BILANZ) Disponible en: http://clinicaltrials.gov/show/NCT01512446 [accedido 06/12/2014].
26. Cummings S, San-Martín J, McClung MR, Siris ES, Eastell R, Reid AR, et al. Denosumab for prevention of fractures in posmenopausal women with osteoporosis. N Engl J Med 2009;361:756-65.
27. Vargas Negrín F. Adherencia al tratamiento: un reto difícil pero posible. Rev Osteoporos Metab Miner 2014;6:5-7.
28. Martínez D, Abad P, Orero A, Navarro A, González J. Olmo V. Estudio socio sanitario de la osteoporosis postmenopáusica en Atención Primaria. Estudio ESTOP-MAP. IMC International Marketing Communication. Madrid 2013..