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Study of bone mass in the alcoholic patient

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Summary
A prospective descriptive study was conducted to assess the alteration in bone mineral density (BMD) in alcoholic patients, under the age of 65 and free of non-modifiable risk factors for osteoporosis, who were admitted to the Clinical Toxicology Unit for detoxification and subsequent supervision, between January 2007 and May 2008. Nutritional profile and liver function were also analysed in order to establish a relationship with the BMD observed in subsequent studies. 36 male patients were studied with an average age of 51 years. Pathological levels of bone mass (in the spinal column and hip) were detected in 53% of patients (42% with osteopenia and 11% with osteoporosis), a much higher percentage than that expected in a male population of such an age. Vertebral fractures were observed in six patients (16%) and hip fractures in four (11%).
The care of alcoholic patients must be comprehensive and depends on the state of the addictive disorder, with the active treatment of the alcoholism being essential and a priority. However, given the risk of fractures associated with falls, once a metabolic abnormality is diagnosed, the appropriate treatment should be initiated as soon as possible.

Key words: *Osteoporosis, Osteopenia, Alcoholism.*

Introduction
Osteoporosis (OP) is a systemic disease of the skeleton characterised by compromised bone resistance, which predisposed an increased risk of fracture[1]. Bone resistance is related to two properties of the bone: the bone mineral density (quantity) and its quality.

Bone mineral density (BMD) is expressed in grams of mineral by surface or volume and can be estimated using different techniques, although double energy axial radiological absorptionometry (DEXA) is considered the standard reference for this purpose. Bone quality refers to the macro- and micro-architecture, accumulated microlesions, mineralisation and remodelling of the bone.

In 1994, the OMS[2] established some densitometric criteria which categorised the situations in which it is possible to measure the bone density using DEXA, and related this to the value of the peak bone mass (T-score). As much for carrying out densitometries (it is not viable to screen the whole of the population), as for the initiation of treatments, it is essential to evaluate the risk factors, which we obtain from epidemiological studies in which we confirm which factors coincide in more patients[3] (Table 1).

Since 2008 we have had available a tool, based on the work of Kanis 2005[4], which allows us to calculate the index of fracture. This is the FRAX Index, available on the internet (www.shef.ac.uk/FRAX/), which calculates the risk of fracture at 10 years, both vertebral and non-vertebral, and hip, fractures, assessing risk factors and BMD of the femoral neck. This can be calculated without the densitometric value, so allowing the establishment of a patient's treatment without being dependent on densitometry results. Among the risk factors included is alcohol intake, which

makes this approach more useful for the patients discussed here.

In Spain OP affects around 2 million women over 50 years of age and some 750,000 males[5]. However, it is an illness which is underestimated by the patients themselves, by the authorities, and by health professionals[6].

The excessive consumption of alcohol is an important risk factor for osteoporosis, above all in the male population, and is included, as we have just seen, in the FRAX Index. The consumption of alcohol reduces bone mass by modifying bone formation and remodelling[7-10]. In adolescence it reduces the peak bone mass, which increases the probability of osteopenia or osteoporosis in adulthood. A high intake of alcohol is associated with pathological and dietetic changes which can have a negative impact on bone metabolism causing osteoporosis, such as: malnutrition, vitamin D deficiency and parathormone (PTH), hypoproteinemia, hepatopathia, hypomagesemia, deficiency in Group B vitamins and folic acid, excess of iron, diminution f testosterone[11-14]. Other factors, such as a reduction in B12 and folates[15], or hyperhomocisteinemia[16], might also have a negative impact, although their importance is yet to be determined. These chronic changes will cause a loss of bone mass which will result in osteopenia and osteoporosis at a much earlier age[17-21].

In men, OP usually happens unseen, due to its scarce clinical symptoms and the deterioration which accompanies alcoholic patients at many psycho-organic levels (hepatopathies, neuropathies, etc). If fractures occur (and the frequent falls experienced by alcoholic patients increase their incidence) the suspicion of OP is more evident and facilitates the diagnosis.

The principal objective of our study was to asses the change in bone mass in male patients with alcohol dependency (according to the DSM-IV criteria)[22].

The secondary objectives were to assess the analytical study of phosphocalcic metabolism , the existence of bone fractures through anamnesis of the patient (extravertebral fractures) and radiological study of the dorso-lumbar spinal column profile (vertebral fractures). We also assess the deficiency of magnesium, proteins and vitamins in group B, hormonal changes (thyroid function and PTH), excess of iron and study of liver function.

Material and Methods

The study involved patients who had attended the Unidad de Toxicología Clínica from January 2007 t o May 2008, admitted for detoxification, followed by treatment to combat alcohol dependency, who were less than 65 years old and had extensive other non-modifiable risk factors for osteoporosis, who had been informed about the study, and who gave their informed consent.

We present a descriptive prospective study which brings together a total of 36 patients who meet the criteria listed.

On the patients selected a detailed anamnesis of their history of alcoholism (duration of the dependence, type of consumption, episodic or continuous, quantity of alcohol, maximum period of abstention), personal medical, psychiatric and bone fracture history, and body mass index (BMI), was carried out.

A standard analysis was carried out on all patients, which studied liver function, markers for hepatitis B & C & Mantoux viruses, also adding the factors to be assessed in our study calcium and phosphorus in blood and urine at 24 hours, PTH, vitamin D, osteocalcine, tartrate-resistant acid phosphatase (FATr), bone alkaline phosphatase, C-terminal telopeptide (CTX), magnesium, vitamin B12 and folic acid.

In addition to a radiological study of the thorax and abdominal echography, we also carried out a radiological study of the dorso-lumbar spinal column in profile, to detect fractures, which we took as the reduction of its anterior, middle and posterior height, above 20% (Genant index), as well as densitometry of the spinal column and hip, by means of double photon absorptiometry (Lunar).

The data were analysed statistically with the SPSS programme, version 15.

Results

36 male patients with an average age of 51 years were included in the study. The average body mass index was 25. The patients had an average duration of alcohol dependency of 26 years, with a continuous pattern of consumption in the majority of cases (72%) and an average daily consumption of 21 standard units of drink (UBE), with periods of abstinence of a maximum of 9 months.

30% of patients had psychiatric histories, most of which were anxiety-depressive disorder (25%). In terms of known medical history, predominant in order of frequency were: alcoholic hepatitis 47% (cirrosis 19.5%), ulcer 39%, diabetes 16%, pancreatitis 13%, polyneuropathia 11% and encephalopathia 11%. 94% of patients combined tobacco smoking with their drinking habit, and 6% consumed other drugs.

Liver affectation, as might be expected, is common, with the echographic study finding hepatic steatosis (enlargement and echogenicity) in 25% of patients and signs of portal hypertension in 44%. 42% of patients had altered coagulation, with Quick's diminution in 42% of patients. GOT was high in 36% of cases, with an average of 79 U/L (normal interval 10-35 U/L), GPT was high in 58% of patients, with an average of 58U/L (10-45 U/L), FA was normal in 92% of cases, GGT high in 94%, with 365 U/L as the average (8-55 U/L). Bilirubin was high in 42%, and amylase and lipase normal in 19%.

In terms of indices of nutritional profile, the following findings stand out: anemia in 50% of patients, macrocytosis in 47%, B12 deficiency in 14%, reduction in folic acid in 23% and of magnesium in 51%. 12% of patients had hypoalbuminemia. Ferritin was high in 48% of cases. Study of lipids: hypocholesterolemia in 12% and hypoglyc-

Table 1. Risk factors for osteoporotic fractures. SEIOMM Guides 2008[3]

	High risk	Moderate risk
Mixed factors (BMD + independent component)	- Advanced age - Previous personal history of osteoporotic fractures - Maternal history of femoral fracture - Low body weight* - Glucocorticoids** - High bone turnover	- Diabetes mellitus - Tobacco smoking
Associated with low BDM	- Hypogonadism in males - Primary hyperparathyroidism - Anorexia nervosa - Prolonged immobility - Anticonvulsants - Malabsorption syndrome	- Female sex - Early menopause*** - Primary and secondary amenorrea - Rheumatoid arthritis - Hyperthyroidism - Vitamin D deficiency - Low calcium intake****

High risk: when relative risk > 2
Moderate risk: relative risk > 1 and < 2
* Body mass index < 20kg/M^2
** Period greater than 3 months and more than 7.5 mg prednisone/day
*** Before 45 years of age
**** Lower than 500-800 mg/day
Factors related to the tendency to having falls and associated with the production of fractures, are considered independent factors. BMD: Bone Mineral Density

eridemia in 14%; hypercholesterolemia in 36% and hyperglyceridemia in 17%.

Bone metabolism study: no changes in values of calcium or phosphorus were detected. PTH was high in 5% of cases, with values 10% higher than normal in these cases. Osteocalcine and bone fraction of alkaline phosphatases were normal. FATr was high in 50% of cases (18 patients). CTX was increased in 36.1% of cases (13 patients).

According to the OMS' densitometric criteria, fifteen patients had osteopenia (41.6%) and four, osteoporosis (11.1%). Of the fifteen patients with osteopenia, in seven it was present in the spinal column and hip, in four only in the spinal column and in four only in the hip. Of the four patients with osteoporosis, in three cases this was detected in the spinal column and in one case, in the hip. The three patients with densitometric osteoporosis in the spinal column had osteopenia in the hip, and the case of osteoporosis in the hip had osteopenia in the spinal column.

We found vertebral fractures in 6 patients (16.6%) and hip fractures in 4 patients (11.1%). We did not find other extravertebral fractures. The existence of costal fractures, so prevalent in alcoholic patients, was not evaluated, since they frequently pass unnoticed clinically and radiologically, we would have required other complementary investigations (gammagraphy) to identify them with certainty.

Discussion

We have studied a group of patients with a history of severe alcoholism and secondary, alcohol related, organic damage in the main hepatopathy (69% steatosis and 44% portal hypertension) and ulcers. A high percentage presented with nutritional deficiencies: anemia, hypoalbuminemia and vitamin deficiencies. These were accompanied by active tobacco smoking in most of the patients (94%). Only 6% had an addiction to other drugs.

Pathological levels of bone mass were detected in 53% of patients (42% osteopenia and 11% osteoporosis), a percentage much higher than would be expected in a population of males of the same age[23,24]. This increase in oseopenia/osteoporosis concurs with that described in other studies of alcoholic patients[25].

In the parameters related to bone metabolism, we only detected an increase in the markers for bone resorption, both in FATr (50%) and CTX (13%), as a manifestation of an increase in bone resorption in these patients. PTH was high in 2 patients (5.5% of cases), with a minimum deviation from normal.

We detected vertebral fractures in 6 patients (16.6%) and of the hip in 4 patients (11.1%). Four patients with vertebral fractures had osteopenia in the spinal column and hip and two of those had osteoporosis in the spinal column. Of the four patients with hip fractures, one had osteo-

porosis in the hip (the only case), while the three remaining had osteopenia in the hip. We only considered fractures considered to be osteoporotic, that is, produced by low impact trauma or without known cause, discarding those caused by significant trauma. Other extravertebral fractures were not found and costal fractures were not studied.

The care of alcoholic patients needs to be comprehensive and we must study the impact of alcohol on the different organs and systems, whether the patient is admitted for detoxification, or due to alcohol-related secondary pathologies. The nature of this integrated approach will depend on the state of their addictive pathology, with the active treatment of the alcoholism being essential. However, given the importance of fractures associated with osteoporosis in the alcoholic patient, which diminishes their quality of life and increases mortality, above all through fracture of the hip, we believe it essential to assess the use of antifracture treatment in these patients. The application of the FRAX index could help us in this, since it already includes alcohol as a risk factor, and could help us take decisions in light of a prediction of a fracture in the next 10 years.

In treating patients with digestive intolerances, and possibly with little adherence to treatment, the current availability of new drugs such as zoledronic acid, which can be given intravenously and with an annual dose, could contribute to a reduction in fractures in these patients, as well as reducing their mortality, which is increased by fractures[26,27]. Since they are often in poor health, we must ensure that these patients do not have a septic mouth, to reduce the possibility of mandibular osteonecrosis[28].

Bibliografphy

1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA. 2001;285:785-95.
2. WHO Study Group. WHO Technical Report Series, 843. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Ginebra: World Health Organization, 1994.
3. González Macías J, Guañabens Gay N, Gómez Alonso C, del Río Barquero L, Muñoz Torres M, Delgado M, et al. (Comité de Redacción, en representación del Comité de Expertos de la SEIOMM para la elaboración de las Guías). Guías de práctica clínica en la osteoporosis posmenopáusica, glucocorticoidea y del varón. Sociedad española de Investigación Ósea y Metabolismo Mineral. Rev Clin Esp 2008;208 Supl 1:1-24.
4. Kanis JA, Borgstrom F, De Late C, Johansson H, Johnell O, Jonson B et al. Assessment of fracture risk. Osteoporosis Int 2005;16:581-9.
5. Díaz Curiel M. Prevalencia de la osteoporosis densitométrica en la población española. En: Rhöne-Poulenc Rorer, Ed. Edimsa. Madrid, 1996;95-117.
6. Calvo Catalá J, García-Borrás JJ, Campos Fernández C y grupo COSMIS: Conocimiento de la osteoporosis en los servicios de medicina interna. Resultados del proyecto COSMIS. Rev Esp Enf Metab Óseas 2004;13:1-4.
7. Grazio S, Korsic M, Jajic I. Effects of smoking and alcohol consumption on vertebral deformity in the elderly an epidemiological study. Coll Antropol 2005;29:567-72.
8. Naves Diaz M, O`Neill TW, Silman AJ. The influence of alcohol consumption on the risk of vertebral deformity. European Vertebral Osteoporosis Study Group. Osteoporos Int 1997;7:65-71.
9. Chakkalakal DA. Alcohol-induced bone loss and deficient bone repair. Alcohol Clin Exp Res. 2005;29:2077-90.
10. Turner RT. Skeletal response to alcohol. Alcohol Clin Exp Res. 2000;24:1693-701.
11. Kim MJ, Shim MS, Kim MK, Lee Y, Shing YG, Churg CH et al. Effect of chronic alcohol ingestión on bone mineral density in males without liver cirrosis. Korean J Intern Med. 2003;18:174-80.
12. Laitinen K, Lamberg-Allardt C, Tunninen R, Harkonen M, Valimaki M. Bone mineral density and abstention-induced changes in bone and mineral metabolism in noncirrohotic male alcoholics. Am J Med. 1992;93:642-50.
13. Klein RF. Alcohol-induced bone disease: impact of etanol on osteoblast proliferation. Alcohol Clin Exp Res. 1997;21:392-9.
14. Sampson HW. Alcohol`s harmful effects on bone. Alcohol Health Res World. 1998;22:190-4.
15. Herrmann M, Wildemann B, Wagner A, Wolny M, Schorr H, Taban-Shomal O et al. Experimental folate and vitamin B12 deficiency does not alter bone quality in rats. J Bone Miner Res 2009;24:589-96.
16. Herrmann M, Tami A, Wildemann B, Wolny M, Wagner A, Schorr H et al. Hyperhomocysteinemia induces a tissue specific accumulation of homocysteine in bone by collagen binding and adversely affects bone. J Bone Miner Res 2009;44:467-75.
17. Rider KM, Shorr RI, Bush AJ, Kritchevsky SB, Harris T, Stone K et al. Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects. J Am Geriatr Soc. 2005;53:1875-80.
18. Ilich JZ, Brownbill RA, Tamborini L, Crncevic-Orlic Z. To drink or not to drink: how are alcohol, caffeine and past smoking related to bone mineral density in elderly women?. J Am Coll Nutr. 2002;21:536-44.
19. Kanis JA, Johansson H, Johnell O, Oden A, De Laet C, Eisman JA et al. Alcohol intake as a risk factor for fracture. Osteoporos Int. 2005;16:737-42.
20. Tucker KL, Hannan MT, Qiao N, Jacques PF, Selhub J, Cupples LA et al. Low plasma vitamin B12 is associated with lower BMD: the Framingham Osteoporosis Study. J Bone Min Res 2005;20:152-8.
21. Schnitzler CM, MacPhail A, Shires R, Schnaid E, Mesquita J, Robson H. Osteoporosis in African hemosiderosis: role of alcohol and iron. J Bone Miner Res. 1994;9:1865-73.
22. DSM-IV. American Psychiatric Association. (1994). Diagnostic and Statistical Manual of Mental Disorders (4th ed.). Washington, DC.
23. Ebeling PR. Osteoporosis in men. N Eng J Med 2008;358:1474-82.
24. Calabuig E, Muñoz ML, Valero JL, García–Borrás JJ. Osteoporosis en el varón. En: Calvo Catalá. Osteoporosis. Ed. Aguilar. Valencia 2008.59-79.

25. Kathleen M, Sowers MFR, Dekordi F, Nichols S. Osteoporosis Int 2003;14:396-403.
26. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA et al. HORIZON Pivotal Fracture Trial. Once-yearly zoledronic acid for treatment of post-menopausal osteoporosis. N Engl J Med 2007;357:1799-809.
27. Lyles KW, Colón-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C et al, for the HORIZON Recurrent Fracture Trial. Zoledronic Acid in Reducing Clinical Fracture and Mortality after Hip Fracture. N Engl J Med. 2007;357:1799-809.
28. Bagan JV, Poveda R, Murillo J, Díaz Fernández JM, Carbonell E, Sanchis JM et al. Bifosfonatos y osteonecrosis de los maxilares. En: Calvo Catalá. Osteoporosis. Eds. Aguilar, Valencia 2008, pág 203-13.