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ORIGINAL ARTICLE

Testosterone-deficiency as a risk factor for hip fracture in elderly men☆

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KEYWORDS
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Abstract
Objetives: Progressive loss of bone mineral density weakens the bones and increases the probability of osteoporotic fractures. It is well known that sex steroids play a role in the maintenance of bone density. This fact makes us think there might be a correlation between sex steroid levels and osteoporotic hip fractures.
Materials and methods: A case–control study was performed. The cases were 54 men who suffered from hip fracture. They were compared with 54 age-matched male control subjects. Levels of total testosterone, sex hormone binding globuline, albumin and estradiol were measured in all subjects in order to calculate free testosterone and bio-testosterone levels.
Results: Men who suffered from hip fracture had lower serum total testosterone (8.74 nmol/l vs. 11.16 nmol/l; $p = 0.116$) and lower free testostenone (155.1 pmol/l vs. 204.4 pmol/l; $p = 0.02$) than control subjects. Bio-testosterone levels were lower in patients with hip fracture (2.69 nmol/l vs. 3.89 nmol/l; $p = 0.002$), being the latter the best fracture predictor (OR: 1.58).
Conclusions: In our study population, men with hip fractures had significantly lower levels of calculated free testosterone and bio-testosterone. These findings suggest that free testosterone and bio-testosterone levels are independent predictors for osteoporotic hip fracture in elderly men.

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PALABRAS CLAVE
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Fracturas de cadera

Déficit de testosterona como factor de riesgo de fractura de cadera en hombres de edad avanzada

Resumen

Objetivos: La pérdida progresiva de la densidad mineral ósea debilita los huesos y aumenta la probabilidad de fracturas osteoporóticas. Es conocida la acción de los andrógenos en el mantenimiento de la densidad mineral ósea. Este hecho nos hace pensar que podría existir una relación entre los niveles de esteroides sexuales y la fracturas osteoporóticas de cadera.

Material y métodos: Se realiza un estudio caso-control, donde los casos correspondieron a 54 varones con fractura de cadera que se aparearon por edad con 54 controles varones. A todos los pacientes se les determinó niveles de testosterona total, globulina transportadora de hormonas sexuales, albúmina y estradiol para el cálculo de la testosterona libre y la testosterona biodisponible.

Resultados: Los pacientes con fractura de cadera presentaron unos niveles de testosterona inferiores a los controles (8,74 n/mol/L frente a 11,16 nmol/L; p = 0,116) al igual que de testosterona libre (155,1 pmol/L frente a 204,4 pmol/L; p = 0,02). Los niveles de testosterona biodisponible fueron inferiores en pacientes con fractura de cadera (2,69 nmol/L frente a 3,89 nmol/L; p = 0,002) siendo esta última el mejor predictor para fractura (OR: 1,58).

Conclusiones: Los pacientes con fractura de cadera presentan unos niveles significativamente inferiores de testosterona libre calculada y biodisponible en nuestra población a estudio. Estos hallazgos sugieren que los niveles de testosterona libre y biodisponible son predictores independientes de fractura de cadera osteoporótica en pacientes de edad avanzada.

Introduction

Progressive loss of bone mineral density weakens bones and increases the likelihood of fractures. These fractures increase with age and lead to significant morbidity and mortality in the population, being higher in men than in women.[1]

Multiple studies have demonstrated that androgens play a crucial role in maintaining bone mineral density. We know the loss of bone mass after castration or androgen deprivation therapy in prostate cancer.[2] Also, androgen replacement therapy is associated to an increased bone mineral density in the spine and hip.[3] However, to date, there is little published evidence linking the effect of testosterone therapy and the risk of osteoporotic fractures.[4,5]

The aim of this study was to relate the levels of androgens and the risk of osteoporotic hip fracture in men.

Materials and methods

We conducted a case–control study in the period between February 2010 and January 2011, where the study population were the individuals belonging to the *Costa Ponent-Metropolitana Sud* health area, whose referral hospital is the *Hospital Universitario de Bellvitge*. We defined case as any man diagnosed with hip fracture confirmed after radiological study in the Emergency Department at that time interval. The controls were male subjects of the same reference population who underwent a routine blood test in this period of time, without a diagnosis of hip fracture.

The exclusion criteria that were applied to both groups were: (a) previous diagnosis of osteoporosis; (b) high-energy fractures; (c) androgen deprivation in prostate cancer patients; (d) diagnosis of hypogonadism; (e) treatment with corticosteroids; and (f) metastatic bone disease (Fig. 1).

Altogether there were 54 cases and 54 controls, whose data were paired according to their age (pairing range of 2 years).

All the study subjects underwent a thorough medical history to identify the possible causes of secondary osteoporosis, a physical examination and a general blood analysis and a specific hormone one, made during the first 48 h after admission, between 7 and 9 am.

The variables selected were age, concomitant disease (diabetes mellitus, hypertension, dyslipidemia, ischemic heart disease, and other diseases), type of fracture according to its anatomic classification (subcapital, transcervical, basicervical, pertrochanteric, persubtrochanteric, and subtrochanteric), and the variables result of the analysis (hemoglobin, hematocrit, mean corpuscular speed, creatinine, cholesterol, triglycerides, albumin, total testosterone, sex hormone binding globulin, and total estradiol). Furthermore, we subsequently calculated free testosterone (FT) and bioavailable testosterone (BioT) according to the formulas proposed by Vermeulen et al.[6] and accepted by the main scientific societies.[7]

The statistical analysis was carried out in different phases. First we carried out the descriptive analysis of the variables, according to their category. The quantitative variables were defined, according to their normality (Kolmogorov–Smirnov test), using measures of central tendency (mean or median) and of dispersion (standard deviation or interquartile range). The qualitative variables were described by means of frequencies and proportions. Then, we proceeded to perform the bivariate analysis. For the quantitative variables with normal distribution, we used the Student's ''*t*'' test, and for those who did not have a normal distribution, the Mann–Whitney U test. In the case of qualitative variables, we used the Chi square test, or Fischer's exact test when the conditions were not met for