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ORIGINAL PAPER

Is the fasting calcium/creatinine a bone resorption marker in patients with calcium renal stones?

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Abstract Osteoporosis and osteopenia are an important endocrine-metabolic disease that affect women and men from a certain age and it has a high risk and health cost. The aim of this short communication is to show that fasting calcium/creatinine ratio in patients with calcium stones is a marker of bone resorption.We studied 180 patients with renal stones with calcium composition and the relationship of them between the calcium/creatinine in urine after 8 h of fasting with bone densitometry (T-score) and values of bone resorption marker β-crosslaps (ng/ml). The Pearson correlation test was applied for the analysis of linear correlations between quantitative variables.We have observed a statistically significant positive linear correlation between the fasting calcium/creatinine and serum and β-crosslaps ($R = 0.534$, $p < 0.0001$) and a statistically significant negative linear correlation between fasting calcium/creatinine and T-score of bone densitometry in hip ($R = -0.237$, $p = 0.002$), femoral neck ($R = -0.217$, $p = 0.009$) and lumbar spine ($R = 0.292$, $p = 0.001$).The fasting ratio calcium/creatinine in urine is associated with increased levels of β-crosslaps marker and therefore may be useful as a marker of bone resorption in these patients.

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Introduction

Osteoporosis and osteopenia are an important endocrine-metabolic disease that affect women and men from a certain age and it has a high risk and health cost, hence the importance of adequate diagnostic and screening to facilitate the secondary prevention and treatment of this pathology [1]. The diagnosis of bone mineral density loss is carried out by bone densitometry [2, 3], which allows that patients are classified as normal, osteopenia, osteoporosis or established osteoporosis [4]. In addition to the diagnosis by densitometry, the increase bone activity can be measured by analyzing blood or urine markers of bone remodeling, including β-crosslaps, plasmatic marker of bone resorption [5]. Bone mineral density loss is present in patients with recurrent calcium kidney stones, who also show higher levels of specific markers of bone resorption and 24 h urinary calcium than patients without calcium kidney stones [6]. Other studies have found bone disorders and bone mineral density loss in patients with idiopathic hypercalciuria [7] and fasting hypercalciuria [8].

The aim of this short communication is to show that fasting calcium/creatinine ratio in patients with calcium stones is a marker of bone resorption.

Patients and methods

We studied 180 patients with renal stones with calcium composition and the relationship of them between the calcium/creatinine in urine after 8 h of fasting with bone densitometry (T-score) and values of bone resorption marker

Table 1 Correlation study between fasting urine calcium/creatinine with T-score bone densitometry, β-crosslaps bone resorption marker and age

	Fasting urine Calcium/Creatinine
Hip T-score densitometry	R = −0.237 (p = 0.002)
Neck femur T-score densitometry	R = −0.217 (p = 0.009)
Lumbar spine T-score densitometry	R = −0.292 (p = 0.001)
Serum β-crosslaps	R = 0.534 (p = <0.0001)
Age	R = 0.06 (p = 0.44)

Application of Pearson correlation test with statistically significant results if $p < 0.01$

β-crosslaps (ng/ml). We have analyzed, in two samples of fasting urine and serum analytics, the mean values of urine calcium/creatinine and serum β-crosslaps (determined by the "ECLIA" method, or electrochemiluminescence immunoassay, in an Elecsys MODULATOR ANALYTICS E170 automatic analyzer, Roche Diagnostics), besides studying the standardized values (T-score) of bone mineral density in the hip, femoral neck and lumbar spine with bone mineral densitometry (BMD) that was obtained using dual energy X-ray absorptiometry with Hologic QDR 4500 equipment.

A statistical analysis of the results was performed by applying the Student's t test and binary logistic regression, obtaining results through the OR and a 95% confidence interval. The Pearson correlation test was applied for the analysis of linear correlations between quantitative variables. The normality of the variables was checked by applying the Kolmogorov–Smirnov test, and the analysis of variance was checked with the Levene test. We established statistical significance when $p \leq 0.01$. The statistical analyses were performed with the program SPSS 17.0 for Windows.

Results

The mean age of patients included in the study was 49.9 ± 13.1 year. Mean values of β-crosslaps were 0.506 ± 0.194 ng/dL and for the fasting ratio calcium/creatinine 0.14 ± 0.05. Among the patients included in the study, 96 were men and 84 women, with no differences between them in relation to the levels of fasting ratio calcium/creatinine (0.141 ± 0.05 vs 0.148 ± 0.05, respectively, p = 0.64).

After analyzing the results of fasting calcium/creatinine ratio with Pearson's linear correlation test (statistical significance level of $p < 0.01$), we have observed a statistically significant positive linear correlation between the fasting calcium/creatinine and serum and β-crosslaps and a statistically significant negative linear correlation between fasting calcium/creatinine and T-score of bone densitometry (Table 1). These results mean that in patients with calcium kidney

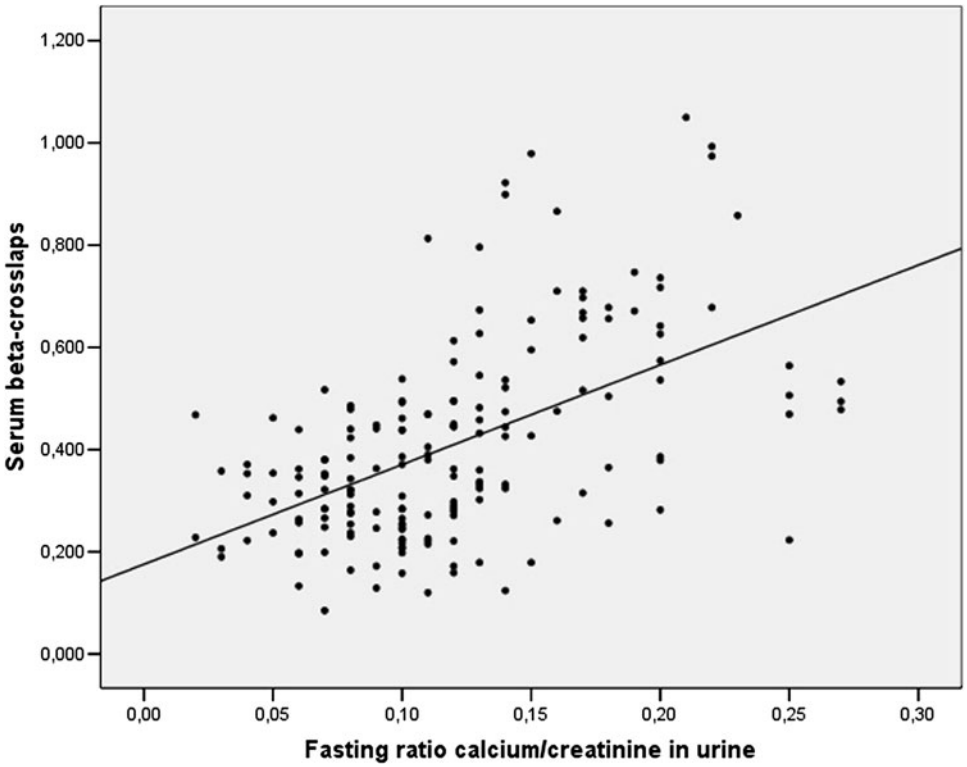

Fig. 1 Graphs in which we can observe the positive linear relation between levels of serum β-crosslaps and fasting ratio calcium/creatinine in urine

stones when the fasting calcium/creatinine is elevated, serum β-crosslaps is also elevated (Fig. 1), which is a marker of bone resorption and therefore there is a greater bone mineral density loss, which is reflected in more negative values in the T-score of bone densitometry, as we reflect in our results.

Discussion

The β-crosslaps is a marker of bone resorption derived from the carboxyterminal telopeptide, namely an octapeptide alpha-1 chain which is beta-isomerized [9]. It is now considered one of the most useful and reliable markers of bone resorption and it may be useful in monitoring antiresorptive treatment [5]. It has been observed in patients with calcium stones and fasting hypercalciuria that there is a significant negative linear correlation between bone marker levels of hydroxyproline and bone mineral density in lumbar spine and hip measured by densitometry [8]. However, although others authors have noted that hydroxyproline levels are higher in patients with idiopathic hypercalciuria, it is not correlated with bone density values in lumbar spine [10].

The correlation between osteopenia/osteoporosis and calcium nephrolithiasis has been recognized in a number of studies. Audran [11] and Zancheta [12] detected osteopenia in up to 55% of patients with hypercalciuria. Various studies have indicated that up to 60% of patients with calcium lithiasis have hypercalciuria, and many authors have observed a loss of bone mineral density in stone formers with hypercalciuria.

We agree with Letavenier [13] that the fasting hypercalciuria is a factor associated with bone mineral density loss in patients with renal stone disease, although we think that do not need to obtain a sample analytic after 2 days of non-calcium diet, being sufficient only an 8 h fast to establish that the higher levels in the fasting calcium/creatinine ratio show an increase of bone mineral density loss in these patients, so this ratio (fasting calcium/creatine in urine) is a reliable marker of bone mineral density loss in patients with renal calcium stones.

Furthermore, in our study, we have observed a strong statistically significant positive linear correlation between the values of this fasting ratio calcium/creatinine with serum levels of bone resorption marker (β-crosslaps).

As a conclusion to our study, we believe that in patients with calcium stones, the fasting ratio calcium/creatinine in urine is associated with increased levels of β-crosslaps marker and therefore may be useful as a marker of bone resorption in these patients.

References

1. Raisz LG (2005) Clinical practice. Screening for osteoporosis. N Engl J Med 353:164–171
2. Sosa Henríquez M, Díez Pérez A (2009). Osteoporosis. Concepto. Etiopatogenia. Clínica. Rev Clin Esp. 209(Supl 1):3–9
3. Cummings SR, Bates D, Black DM (2002) Clinical use of bone densitometry. Scientific review. JAMA. 359:1761–1767
4. World Health Organisation. Assesment of fractures risk in screening for osteoporosis. WHO technical report series 843. Geneva: WHO; 1994
5. Del Pino Montes J, Corral Gudino L, Montilla Morales C, Gómez Castro S (2009) Métodos complementarios en el diagnóstico y seguimiento de la osteoporosis. Rev Clin Esp 209(Supl 1):23–28
6. Arrabal-Polo MA, Arrabal-Martin M, de Haro Munoz T, Lopez Leon VM, Merino-Salas S, Ochoa-Hortal MA et al (2011) Mineral density and bone remodelling markers in patients with calcium litiasis. BJU Int. doi:10.1111/.1464-410X.2011.10167.x
7. Heilberg IP, Weisinger JR (2006) Bone disease in idiopathic hypercalciuria. Curr Opin Nephrol Hypertens 15:394–402
8. Tasca A, Cacciola A, Ferrarese P, Ioverno E, Visona E, Bernardi C et al (2002) Bone alterations in patients with idiopathic hypercalciuria and calcium nephrolithiasis. Urology. 59:865–869
9. Woitge HW, Pecherstorfer M, Li Y, Keck AV, Horn E, Ziegler R et al (1999) Novel serum markers of bone resorption: clinical assessment and comparison with established urinary indices. J Bone Miner Res 14:792–801
10. Bataille P, Achard JM, Fournier A, Boudailliez B, Westeel PF, el Esper N et al (1991) Diet, vitamin D and vertebral mineral density in hypercalciuric calcium stone formers. Kidney Int 39:1193–1205
11. Audran M, Bataille P, Sebert JL, Crouzet G, Auvinet B, Laval-Jeantet M et al (1991) Bone density in idiopathic hypercalciuria in men. Study by dual photon absorptiometry, X-ray computed tomography and histomorphometry. Rev Rhum Mal Osteoartic. 58:747–750
12. Zanchetta JR, Rodriguez G, Negri AL, del Valle E, Spivacow FR (1996) Bone mineral density in patients with hypercalciuric nephrolithiasis. Nephron. 73:557–560
13. Letavernier E, Traxer O, Daudon M, Tligui M, Huber-Brierre J, Guerrot D et al (2011) Determinants of osteopenia in male renal-stone-disease patients with idiopathic hypercalciuria. Clin J Am Soc Nephrol. 6:1149–1154