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Letters

Incomplete Renal Tubular Acidosis in 'Primary' Osteoporosis

SIR – We read with interest and satisfaction the article by M. Weger et al. recently published in the Journal [1]. The authors have been able to ascertain the prevalence of mild or 'incomplete' forms of distal renal tubular acidosis (RTA) among patients with apparently 'primary' osteoporosis. Their work confirms and expands our findings, published in 1995 [2].

In that paper, we described 6 patients with osteoporosis and without nephrolithiasis (one man, five women), in whom renal acidification defects were suspected due to: a) alkaline urine pH in freshly voided morning samples (2 cases); b) low serum bicarbonate (3 cases); c) severe vertebral osteoporosis in a young male without any apparent risk factor; d) lack of a positive densitometric response to anti-osteoporotic treatment (3 cases). Of the 3 women with low serum bicarbonate but normal venous blood pH, 2 were shown to have high fractional excretion of bicarbonate. Two of the women and the male patient (all with normal serum bicarbonate) failed to properly acidify the urine after oral furosemide or ammonium chloride. We suggested that mild forms of RTA (both distal and proximal) might cause or aggravate involutional osteopenia, and that this entity should be added to the long list of diseases known to cause secondary osteoporosis.

In the last four years we have made the diagnosis of incomplete RTA in several other patients. Now we learn from Weger et al. that the prevalence of this disorder is high among osteoporotic subjects, especially males (44%) and premenopausal women (20%). This is important, because it is amenable to effective treatment with alkali: in our experience, bone mineral density measured by DEXA can show significant increments after one year: 2–4% at the hip, 5–10% at the lumbar spine and in the whole skeleton (unpublished observations).

We would greatly appreciate the publication of this letter, considering that our paper was not included by Weger et al. in their list of references, although it appeared in an indexed journal and had a detailed abstract in English.

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The author replies:

SIR – Immediately before we submitted our paper on renal tubular acidosis and osteoporosis [1] to Osteoporosis International in September 1998 we had again performed a search of the English literature on tubular acidosis and osteoporosis trusting that any relevant original investigations would be published in English. Since then we have learned that isolated case reports on the association of renal tubular acidosis had been published previously in the French and Spanish literature [2,3]. We consider the description of isolated cases of the association of a very common disease such as osteoporosis with a disease such as renal tubular acidosis (which occurs also quite common secondarily as a consequence to other diseases such as diabetes mellitus, interstitial nephritis, analgesic abuse, Sjögren syndrome, autoimmune thyroid disease etc) not convincing since it would make a chance occurrence of the association very likely. Therefore, from a few case reports of the association of the two diseases it would be very difficult to prove a causal relationship. This was the reason that we systematically investigated all consecutive patients referred for the investigaton of osteoporosis for the occurrence of renal tubular acidosis and found the reported high incidence of RTA I in patients with osteoporosis [1]. This high incidence remained even when we excluded all secondary forms of renal tubular acidosis due to the above named diseases. It must be stressed that in our experience dip sticks for urinary pH are useless for the detection of incomplete renal tubular acidosis but that it needs an exact pH-meter.

Since then, in another study, we have compared 20 other patients with osteoporosis with 20 subjects matched for age, sex and body mass index but with high bone mass densities (z-scores above zero). Again we have found a high incidence of incomplete renal tubular acidosis in patients with osteoporosis but have found normal renal acidification in 20 out of 20 subjects with high bone densities [4]. This further strongly supports our conclusion, namely that the association of osteoporosis and RTA is not a chance occurrence but probably represents a causal relationship as discussed in detail in our study [1].

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Evaluation of a Gel-coupled QUS Device

SIR – We have read with interest the excellent article by Frost and colleagues [1]. As pointed out in this article, there are a variety of quantitative ultrasound (QUS) devices commercially available. These devices have significant differences among them due to a number of reasons including coupling methods, transducer sizes, and implementation of SOS and BUA algorithms [2]. The paper by Frost et al. has addressed important issues related to the clinical applications of the Sahara (Hologic, Bedford, MA) QUS device, namely: daily quality assurance (QA), precision, age decrement, fracture discrimination and the application of World Health Organization (WHO) criteria for osteoporosis diagnosis. There are further issues that could be useful for the better application of the Sahara device that were not explicitly discussed.

It was reported in this study that a drift was observed with the daily phantom measurement. The drift was attributed to the deterioration in the transducer pad. The questions we would like to ask are: How useful is the regular phantom measurment for detecting machine malfunction? How significant was the correction of the measurement done during the drift period? Do the authors advocate correction of the data of patients (who are in a longitudinal study) following a drift using the phantom data? These have been points of debate for dual-energy X-ray absorptiometry (DXA).

The high odds ratio (OR) for vertebral fracture discrimination for a 1 SD decrease in QUS variable compared with axial bone mineral density (BMD) is surprising. These very positive results are in the face of higher reference SDs and lower age regressions for QUS than for DXA. Perhaps high ORs are a result of very low prevalence, hence low sensitivity but high specificity at the 1 SD threshold. Give prevalence for OR by site. Most studies have reported similar ORs for QUS and BMD. However, there are very limited data assessing the vertebral fracture discrimination of a gel-coupled device such as the Sahara. Again, comparison of cross-sectional studies in problematic since cause cannot be separated from effect. This is related to one of the hypotheses put forward for the high ORs for QUS compared with BMD: the immobility due to the chronic stage of the vertebral fracture. However, in a recent study by Laugier et al. [3] using a water-coupled imaging QUS device, only SOS was affected by 120 days of continuous bed rest. It would be useful to give further information on how vertebral fractures were defined and also the mean number of fractures per patient. Considering that the vertebral fracture patients were shorter and lighter than the control group, we wonder about the impact on the OR and suggest adjusting the ORs for BMI. BMI probably affects QUS of the calcaneus more than central BMD.

Another question that affects the clinical application of QUS is the appropriate *T*-score threshold for QUS. It is clear from the study by Frost et al. [1] and that by Faulkner et al. [4] that a *T*-score of -2.5 is not appropriate for QUS. However, no suggestion was given in the study by Frost and colleagues of an appropriate *T*-score for Sahara devices. It might be useful to report the *T*-scores for both BUA and SOS that gave osteoporosis prevalence similar to that of the femur at a *T*-score of -2.5. It was disappointing that some of the results on the WHO criteria were reported for the estimated BMD only. Considering the fact that SOS and BUA are due to different interaction mechanisms, it will be useful to report them separately.

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