Strontium and osteomalacia in renal failure patients

Sir,

We read with interest the article by Cohen-Solal et al. [1] on the accumulation of strontium and fluoride in dialysis patients. The authors’ findings agree well with previous reports from our group [2,3] as they also found bone strontium levels to be increased in patients with osteomalacia as compared with those presenting other types of renal osteodystrophy, i.e. hyperparathyroidism, adynamic bone disease and controls. Moreover, since in Cohen-Solal and colleagues study only French patients were included, evidence was presented that increased bone strontium levels and therefore increased exposure to strontium may also occur in haemodialysis patients treated in developed countries. This puts the issue of the potential role of strontium in the development of particular types of renal osteodystrophy in a broader perspective. Indeed, in our studies patients with increased strontium levels mainly came from developing regions [3,4]

As we showed previously, our data [3] as well as those of the present study do not allow one to draw final conclusions on the unique role of the element in the development of osteomalacia in dialysis patients. Nevertheless, we have some difficulties with the way the authors present and interpret their data and compare them with those of our studies. It is at least surprising that in the title of their paper the authors omit to mention the most important finding of their study, i.e. that ‘the bone strontium status is significantly increased in dialysis patients with osteomalacia’. They instead stress the ‘non-correlation between strontium (and fluoride) and osteoid tissue’, which in our opinion and in view of the data presented in the text is meaningless. A correlation may, but should not necessarily, be expected in a population presenting various types of renal osteodystrophy that are diagnosed according to particular criteria which may overlap with each other. First, taking into account the histological classification of Cohen-Solal and colleagues study, a substantial number of patients with hyperparathyroidism (criteria: bone formation rate > 0.08 μm/day; marrow fibrosis > 0.5%) have a moderately to distinctly increased amount of osteoid which at least in part will neutralize the possible association between strontium and osteoid accumulation in the context of osteomalacia. Secondly, adynamic bone disease (which in this study is mainly related to aluminium accumulation in the presence of normal strontium levels), as osteomalacia (associated with a high bone strontium), is typically characterized by a low bone turn-over. Keeping this in mind, making correlations between the bone strontium content and bone formation rate for the whole group again is of little sense and does not allow one to draw any conclusion on the potential effect of strontium on the bone turn-over. Thirdly, if the same approach were to be used by the authors to define a role for aluminium in the development of either osteomalacia or adynamic bone disease in their study the conclusion would be negative as well, although we believe, presumably among others, that a relationship between aluminium exposure and the development of both these diseases has been proven [5,6].

Moreover, when comparing their series with our patients’ data in the discussion session the authors suggest that the discrepancies between their and our study might be due to the different degree of bone strontium accumulation between both studies. To support this statement they mention that the bone strontium level in our osteomalacic subjects was 3-fold higher as compared with only 1.5 times in their patients. This is not correct, since in our study there was only a 2-fold increase (91 ± 51 vs 45 ± 31 μg/g) [2] and as such is consistent with their findings.

With regard to the authors’ opinion on the clinical relevance of our experimental data [7] and their statement that mineralization defects should only be observed at very high doses, we would like to stress that in a recent study from our group a distinctly increased mineralization lag time, hence reduced bone formation rate, was seen in chronic renal failure rats receiving doses 10 times lower [0.3 g/l in the drinking water (corresponds with a dose of ± 15 mg/kg)] than those used in the paper the authors refer to [7-9].

An annoying detail throughout the text is that reference is often made to inappropriate papers (e.g. references 13 and 15 in the Discussion session).

Finally, we have an additional major concern that should be considered in the context of the upcoming commercialisation of a particular strontium-based compound (strontium ranelate), which is being promoted as a new agent in the treatment and prevention of osteoporosis and osteoarthritis [10-12]. These diseases mainly develop in elderly people who already have a moderately decreased renal function (creatinine clearances < 60 ml/min) [13], comparable with that obtained in the ‘remnant kidney’ rat model. This implies that administration of the compound at doses up to even 4 g/day (± 60 mg/kg) may lead to a distinct accumulation of the element in bone up to values that will be comparable with those seen in our uraemic rat studies (doses varying between 12 and 60 mg/kg) and plasma levels (up to 15 mg/l) in which the development of osteomalacia could clearly be established.

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