Release of Osteocalcin Fragments in the Serum of Dialyzed Patients during Desferrioxamine Treatment

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Dear Sir,

Aluminum seems to exert its detrimental effect on bone formation mainly by decreasing the number and activity of the osteoblasts [1]. Osteocalcin (bone Gla protein, BGP) is the main noncollagenous protein of bone matrix and it is synthesized exclusively by osteoblasts. A small fraction of this unique protein circulates in serum, where it is easily determined, reflecting accurately the osteoblastic activity [2].

Surprisingly, the effect of desferrioxamine (DFO) administration and subsequent Al removal on BGP values has not been investigated till now in dialyzed patients with Al toxicity, except for one report by Davie et al. [3] recently published in *Nephron*. According to this report an 'anomalous rise of serum osteocalcin' was observed in a conservatively treated patient with chronic renal failure after a short course of DFO therapy. Therefore, we studied BGP changes in 10 patients with a mean age of 56 ± 18 years, treated by hemodialysis (6 patients) or CAPD (4 patients) for 44 ± 32 months who received DFO for 9.5 ± 2.5 months. All patients were submitted to bone biopsy before and after the DFO treatment. The initial bone biopsies showed, besides Al bone deposition, secondary hyperparathyroidism in 3 patients, mixed bone disease in 5 patients and osteomalacia and aplastic bone disease in 1 patient each.

BGP was determined by two methods: first by conventional radioimmunoassay (RIA) which measures, besides intact BGP, its fragments as well; and second, by a new two-site immunoradiometric assay (IRMA) which measured only intact BGP. Given that BGP fragments derive both from degradation of intact BGP and from bone resorption, it is believed that BGP measured by RIA reflects not only osteoblastic activity but bone resorption as well, whereas BGP measured by IRMA reflects only osteoblastic activity.

After DFO treatment, bone biopsies revealed that Al removal had been achieved in 8 patients. However, osteoblastic activity was not significantly affected by DFO treatment, since histomorphometric indices of osteoblastic activity (i.e. osteoblast surface and bone formation rate) remained virtually unchanged. Moreover, BGP values measured by IRMA during DFO treatment remained stable at around 300 ng/ml.

In contrast, BGP values measured by RIA showed a sixfold increase (from 32 to 189 ng/ml, $p < 0.001$) during the first 2 months and subsequently dropped to values twice higher compared to the initial ones. This abrupt rise in BGP which, to our knowledge, has not been described till now in the literature was ascribed to osteocalcin fragments which were measured by RIA,

but not by IRMA. It seems likely that these fragments originated from bone resorption and not from degradation of newly synthesized BGP, since osteoblastic activity, as we mentioned, was not increased during DFO treatment. The mechanism by which Al is removed has not yet been clarified, but osteo-clastic resorption of bone also seems to play an important role [4]. Therefore, we can postulate that during DFO treatment, besides Al, fragments of BGP, previously incorporated in bone matrix, were released in serum possibly by bone resorption. In conclusion, our findings indicate that, during DFO treatment in dialyzed patients, besides Al, fragments of BGP are also released from bone. This observation, if further confirmed, along with the report of Davie et al. [3], suggests that there is a poorly defined association between Al removal by DFO and BGP metabolism.

References

- Goodman GW: Pathophysiologic mechanisms of aluminum toxicity: Aluminum-induced bone disease; in de Broe ME, Coburn WJ (eds): Aluminum and Renal Failure. Dordrecht, Kluwer Academic Publishers, 1990, pp 87-108.
- Malluche HH, Faugere MC, Fanti P, Price AP: Plasma levels of bone gla protein reflect bone formation in patients on chronic maintenance dialysis. *Kidney Int* 1984;26:869-874.
- Davie JWM, Worsfold M, Sharp CA, Perks J, Day JP: Anomalous rise of serum osteocalcin following desferrioxamine treatment in aluminium intoxication. *Nephron* 1993;65:245-248.
- Charhon SA, Chavassieux P, Boivin G, et al: Deferoxamine-induced bone changes in haemodialysis patients: A histomorphometric study. *Clin Sci* 1987;73:227-234.