Ciclosporin and Calcium Metabolism in Renal Transplanted Patients

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Dear Sir,

The impact of ciclosporin on bone mineral metabolism in renal transplanted patients is still debated. High serum levels of bone alkaline phosphatases and osteocalcin in ciclosporin-treated renal transplanted patients are reported by several authors, but the clinical meaning of this finding is controversial [1–3]. Some authors suggest that the rise of alkaline phosphatases and osteocalcin in ciclosporin-treated patients reflects an increase of both osteoblast activity and bone formation rate. Therefore, ciclosporin should exert a beneficial effect on bone mineralization [3] and/or a potential protection against the corticoid-induced osteoporosis [4]. On the other hand, histomorphometric findings in man [5] and in rat [6] argue against the ‘increased repair hypothesis’, demonstrating a delayed healing of bone lesions in ciclosporin as compared to azathioprine-treated renal transplanted patients.

We studied 26 transplanted patients, 14 treated with ciclosporin and prednisolone (CS) and 12 treated with azathioprine and prednisolone (Aza). These two groups were homogeneous regarding age, sex, duration of transplantation, plasma creatinine, and maintenance daily dose of prednisolone. Significantly higher serum alkaline phosphatase levels were observed in CS patients (230 ± 55 vs. 160 ± 24 U/l; p < 0.005). A sodium (150 mEq/day)- and calcium (500 mg/day)-restricted diet was then given to all patients for 10 days. A reduced calcemic and calciuric response in the 4 h following an oral calcium load (1 g) was observed in CS vs. Aza group [7]. These findings suggested the prevalence of a reduced intestinal calcium absorption and/or a high turnover osteopathy with ‘hungry bone condition’ in the CS group.

100
2 h

Fig. 1. Mean plasma activities (± SD) of 47Ca at 1 and 2 h, expressed as percent of administered dose in 6 CS-treated renal transplanted patients (■, 1 h 30 ± 2%, 2 h 27 ± 3%), compared to 6 Aza-treated renal transplanted patients (●, 1 h 29 ± 7%, 2 h 27 ± 4%) (P = NS).

To test these hypotheses, we compared the intestinal 47Ca absorption measured by the method of Nordin et al. [8] in 6 patients of the CS and in 6 of the Aza group. In all patients we found a
normal $^{47}$Ca absorption, and no difference between the two groups in percent absorption of the administered $^{47}$Ca dose (fig. 1). These results suggest a particular avidity of the endogenous calcium pool for exogenous calcium in CS-treated patients, which explains the minor increase of calcemia and calciuria after the oral calcium load.

In conclusion, our results are in agreement with the hypothesis that a rise of serum alkaline phosphatases in CS-transplanted patients might reflect the prevalence of a high turnover osteopathy. Therefore these data further emphasize the need to better clarify the bone histology, calcium, phosphate and vitamin D metabolism to prevent the risk of osteopenia in ciclosporin-treated renal transplanted patients.

References