Impact of Cyclosporine on bone metabolism in renal transplant recipients

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Background

Posttransplant bone disease is a common clinical problem that adversely affects the quality of life and must be of concern. High cumulative dosage of corticosteroids plays a main role in the pathogenesis of alterations of bone metabolism after renal transplantation. However, studies showed no correlation between bone mineral density (BMD) and steroid-cumulative dosage. As for the widely used calcineurin inhibitors (CNI) such as cyclosporine, studies investigating its impact on bone metabolism in vivo or in vitro yielded conflicting data. This study aimed to discuss the relationship between cyclosporin A (CsA) blood concentrations and bone metabolism status in renal transplant recipients.

Methods

37 renal allograft recipients who received a triple immunosuppressive therapy (steroids, CsA and Mycophenolate Mofetil) were included. Recipients were divided into high level group (CsA > 80ng/ml) and low level group (CsA≤80ng/ml) . Bone mineral densitometry at lumbar vertebrae L1-L4 and neck of the femur, as well as bone biochemical markers including osteoclast-specific tartrate-resistant acid phosphatase-5b (TRAP-5b), bone-specific alkaline phosphatase (B-ALP), total calcium (Ca), inorganic phosphate (PO4), 25-hydroxyvitamin D [25(OH)D], beta-CrossLaps (CrossL) and N-MID Osteocalcin (OSTEOC) were measured simultaneously.

Results

21 male and 16 female patients (44.0±13.3 years) were included with an average transplantation time of 25.44±17.10 months. There were no statistical differences in age, BMI, liver enzymes (ALT; AST), renal function parameters (serum urea nitrogen; uric acid; serum creatinine; Cystatin C), or cumulative dosage of steroids. Of all 37 recipients, 46.87% patients had bone loss (T score below -1.5 at any site of femoral neck and/or the lumbar) but there was no significant difference in the bone loss rate between two groups. Comparative analysis of bone biochemical markers showed that the level of PO4 in low CsA level group was higher than that in high CsA level group (1.05±0.15 mmol/L vs 0.90±0.26 mmol/L, *P*=0.031). Based on the reference range, an increase of PTH level and a decrease of 25-OHD level were detected in both groups, but no significant difference was found in PTH or 25-OHD between the two groups. In low CsA level group, the B-ALP level was lower (19.90±11.96μg/L vs 31.51±20.54μg/L , *P*=0.039)

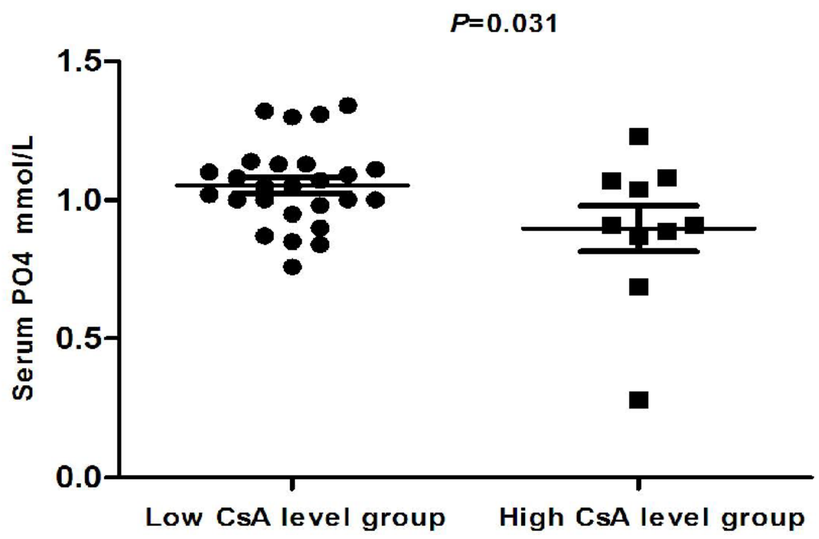

Fig1 The analysis of serum PO4 between low and high CsA level group

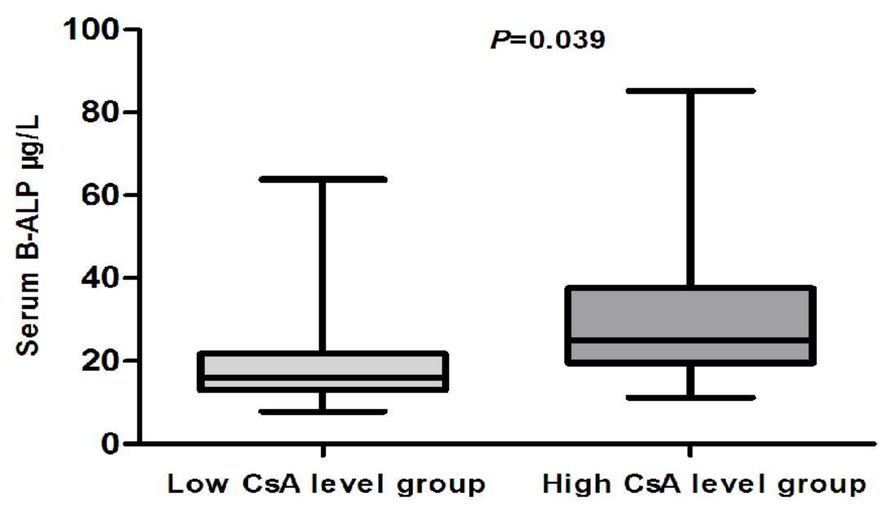

Fig2 The analysis of serum B-ALP between low and high CsA level group

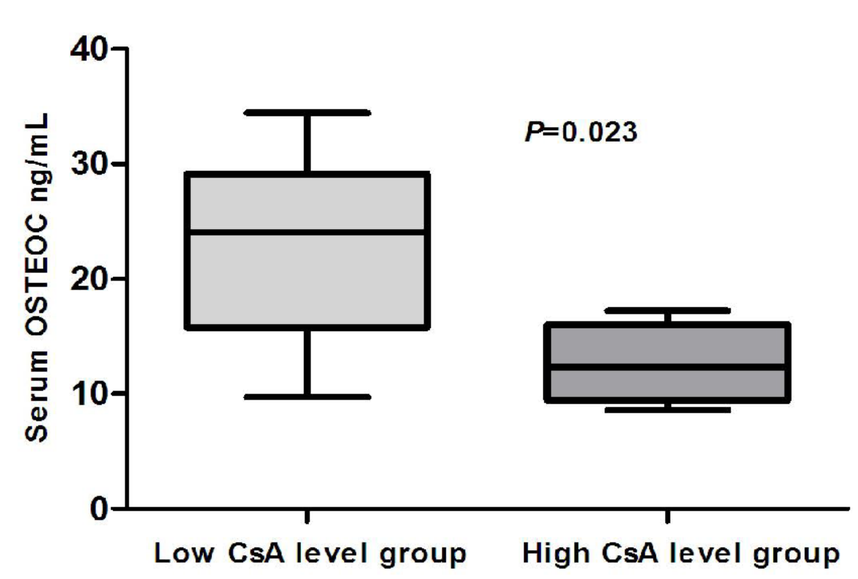

Fig3 The analysis of serum OSTEOC between low and high CsA level group

while the OSTEOC level was higher (23.19±7.99 ng/mL vs 12.62±4.34 ng/mL , *P*=0.023) than those in the high level group. Correlation analysis between CsA blood concentration and bone markers showed that CsA concentration was negatively correlated with OSTEOC (*r*=-0.529 , *P*=0.029).

Conclusions

Renal transplant recipients with an acceptable high level of CsA concentration showed a status of reduced bone turn-over and increased bone formation. CsA may play a protective role on bone metabolism in renal transplant recipients. And more studies should be performed to investigate the optimal target therapeutic concentration of CsA so as to improve the patients' outcome.

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