Association of Serum Cytokine Profiles with Tacrolimus-induced Chronic Nephrotoxicity in Chinese Liver Transplant recipients

Jiangtao Tang [1], Yunying Shi [2], Junlong Zhang [1], Yunfei An [1], Yun Liao [1], Yi Li [1], Lanlan Wang [1*]

1 Department of Laboratory Medicine, West China Hospital of Sichuan University, Chengdu, Sichuan, China
2 Department of Nephrology, West China Hospital of Sichuan University, Chengdu, Sichuan, China
Correspondence: Lanlan Wang, MD, PhD, Department of Laboratory Medicine, West China Hospital of Sichuan University, Chengdu 610041, Sichuan Province, P. R. China. Email: wangll87@126.com

Objectives

Calcinurin inhibitors (CNI) associated chronic nephrotoxicity has become a serious problem which threatens the prognosis of liver transplant recipients. This study was aimed to find out the relationship between serum cytokines, chemokines and chronic tacrolimus (Tac) induced nephrotoxicity. We detected the posttransplant serum inflammatory cytokines and chemokines levels in liver transplant recipients to illuminate the correlations of inflammatory cytokines or chemokines with the chronic renal injury.

Methods

A total of 136 living donor liver transplant recipients (107 males and 29 females) and 150 healthy controls (120 males and 30 females) were enrolled in this study. All the recipients had normal Cystatin C (Cys-C) and normal urine microalbumin before transplantation and received Tac-based immunosuppressive regime (Tac+MMF+ prednisone) afterwards. A human 10-plex antibody bead kit (BioSource, Camarillo,CA) was used to measure the levels of 10 cytokines and chemokines in 50 ml of serum from each transplant patient and controls. After transplantation, serum Cys-C and urine microproteins including α1 microalbumin (α1M), microalbumin (MA), transferring (TRU) and IgG (IgU) were measured among 136 allo-liver recipients to evaluate whether they had early renal injury and the probable location of the renal lesion.

Results

The levels of IL-6,IL-10, IFN-γ,IP-10 and MCP-1 in the recipients' group were significantly higher than those in the control group (P<0.05), while the levels of IL-8 was on the contrary (P<0.05). In early renal damage group (Cys-C>1mg/L), the concentration of IP-10 was much higher compared to the group with normal renal function (Cys-C≤1mg/L) (Figure 1), whereas the concentration of MCP-1 in early renal damage group was lower than the group with normal renal function.

The concentration of IP-10 in the group with tubulointerstitial injury (α1M >12.5 mg/L) was much higher compared with the group without such injury (α1M≤12.5 mg/L) (Figure 2).

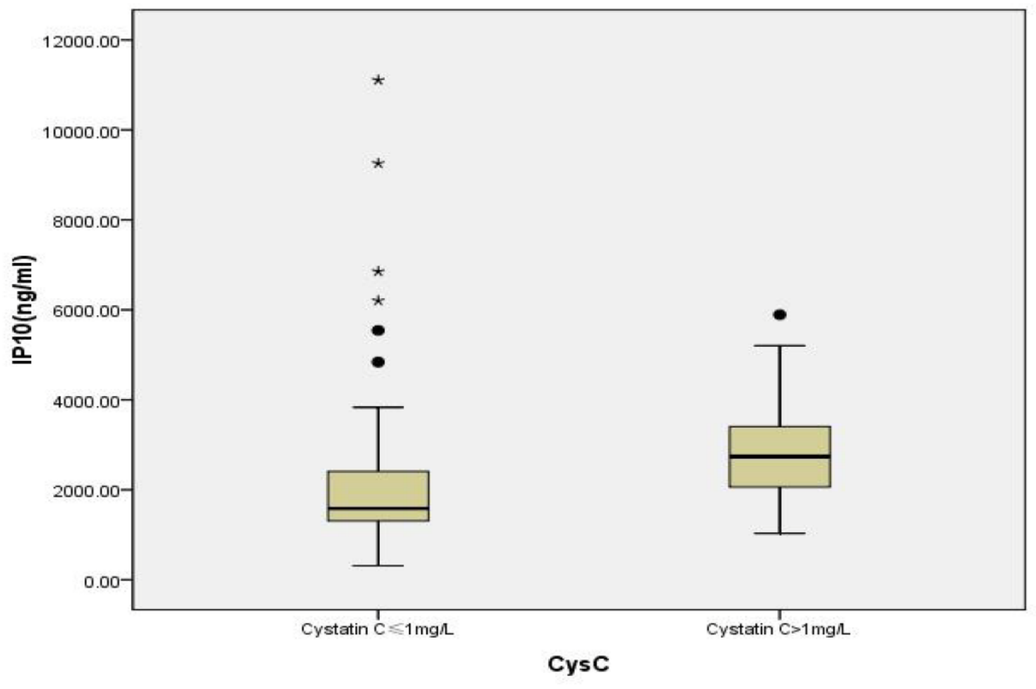

Figure 1 The levels of IP10 in distinct groups with diverse Cystatin C concentrations

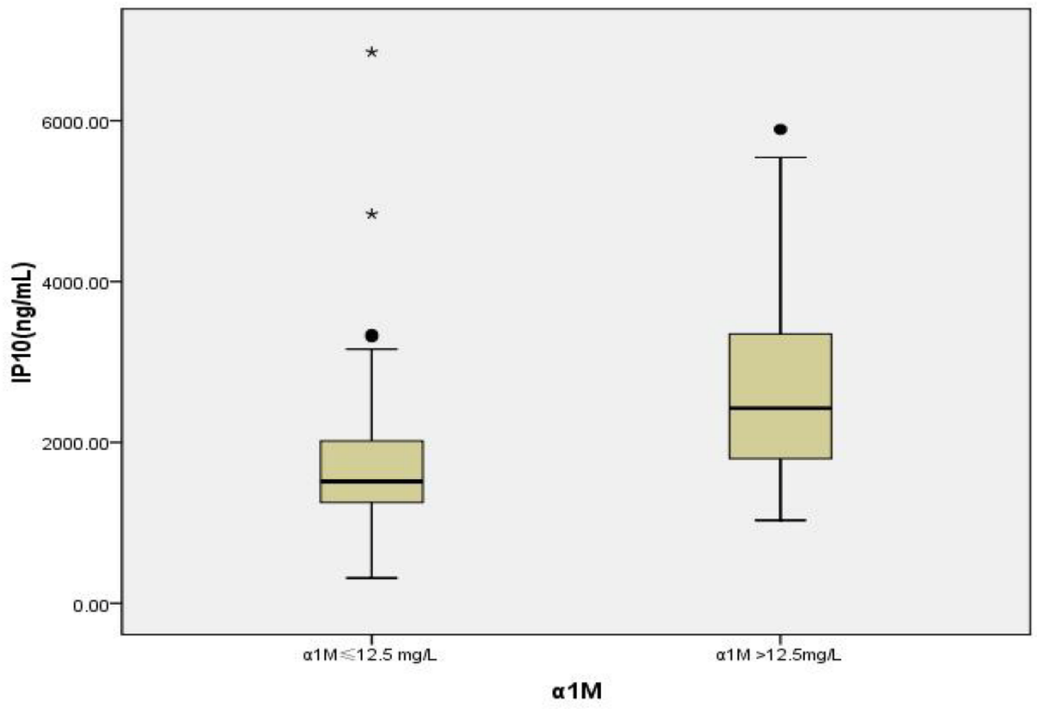

Figure 2 The levels of IP10 in distinct groups with diverse α1M concentrations

Conclusions

IP10 may be the important cytokine leading to chronic CNI-induced nephrotoxicity, especially the tubulointerstitial injury. Allo-liver recipients with high serum IP10 posttransplant levels might develop severe chronic CNI-induced nephrotoxicity due to increased immune activation.

West China Hospital of Sichuan University, P.R.C