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Calcineurin inhibitor toxicity in renal transplantation: The good, bad and ugly

Calcineurin inhibitors (CNI) cyclosporine (CsA) and Tacrolimus have significantly improved the early outcome of renal transplantation (RT) by reducing the incidence of acute rejections. Toxicity in the form of diabetogenicity, tremors, gastrointestinal disturbances, hyperlipidemia, and hirsutism are known. Acute CNI nephrotoxicity in the form of acute arteriolopathy, tubulopathy with isometric vacuolization and glomerulopathy in the severest form of thrombotic microangiopathy has been recorded at normal blood levels and chronicity in the form of irreversible stripped interstitial fibrosis, tubular atrophy, and associated glomerular loss are known. Our experience with about 5000 RTs in Indian and African patients shows that these races require lower doses of CNI and yet graft function can be maintained. In a 9 year study of 2392 renal allograft biopsies, we have found CNI toxicity in 11.3% biopsies. In a subset of 157 RT patients, we found that with doses of 0.02-0.03 mg/KgBW Tacrolimus, trough levels were 3.6±3 ng /ml in age group <30 years and 6.3±3.9 ng /ml in patients >30 years. With doses of 0.04-0.05 mg/KgBW, trough levels were 4.3±2.1 ng /ml for patients <30 years and 8.4±5.5 ng /ml in patients > 30 years. Tissue toxicity was noted in the majority of the patients with normal trough levels. To conclude, CNI is essential to game winners in early RT however they prove to be losers when used for > 5 years.

Biography

Aruna Vanikar a Professor and Head, Dept. of Pathology, Lab Medicine, Transfusion Services and Immunohematology, Stem Cell Therapy and Regenerative Medicine, IKDRC-ITS, Ahmedabad. Awards: 1st recognized teacher of Post-Doctorate Renal And Transplant Pathology Course by Indian Academy of Pathologists, pioneer lady scientist of India, etc; 2 patents: adipose-derived mesenchymal stem cells, and insulin-making SC (given away to IKDRC-ITS), >200 publications. Research: immune tolerance, history, and evolution of Indian renal diseases; generation of MSC, Insulin-secreting SC, Neuronal SC, Cardiomyocytes, Hepatocyte-like cells, regulatory cells etc. On editorial board+reviewer for several journals and TTS abstracts. Currently, President of ISRTP.

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