Th1, Th2, Th17 cell subsets in two different immunosuppressive protocols in renal allograft recipients (Sirolimus vs mycophenolate mofetil): A cohort study

Atefeh Eteghadi a, Fatemeh Pak b, Pedram Ahmadpoor b, Saeideh Jamali c, Mozdeh Karimi c, Mir Saeed Yekaninejad d, Parviz Kokhaei e, Mohsen Nafar b, Ali Akbar Amirzargar e,a,*

a Department of Immunology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
b Chronic Kidney Disease Research Center, Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
c Molecular Immunology Research Center, Tehran University of Medical Sciences, Tehran, Iran
d Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
e Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Long-term use of calcineurin inhibitors (CNI) is associated with nephrotoxicity, which is an important cause of renal dysfunction. Therefore, CNI-minimization strategies which decrease the CNI nephrotoxicity under the protection of additional immunosuppressant drugs have been developed. The aim of current cohort study was to compare the effect of two immunosuppressive protocols (Tacrolimus (TAC) in combination with mycophenolate mofetil (MMF) and prednisolone (PRED) versus TAC in combination with sirolimus (SRL) and prednisolone) on the frequency of T helper cell subsets (Th1, Th2 and Th17 cells) and their associated cytokine (IFN-γ, IL-4 and IL-17A) levels in renal allograft recipients. In this study, renal transplant recipients who received induction therapy (Antithymocyte globulin) and were also on triple immunosuppressive therapy were included and divided in to two groups: Group A was comprised of patients who received TAC, MMF and PRED whereas group B was comprised of 10 patients who received TAC, SRL and PRED. The frequency of Th1, Th2 and Th17 cells in the peripheral blood mononuclear cells (PBMCs) of the patients was analyzed by flow cytometry before and 4 months after transplantation. In addition, IFN-γ, IL-4 and IL-17A concentrations in PBMC culture supernatants of patients before and 4 months after transplantation were quantified by ELISA.

The results of our study showed that TAC, MMF and PRED protocol did not diminish the frequency of Th17 cells at 4 months post-transplantation (5% ± 2.5) compared with pre-transplantation (2.3% ± 1; P < 0.05). However, Th17 (3.6% ± 1.5 pre-transplantation vs 2.2% ± 0.9 at 4 months post-transplantation; P < 0.05), Th2 (1.4% ± 0.3 pre-transplantation vs 0.8% ± 0.4 at 4 months post-transplantation; P < 0.05) cell subsets and II-4 concentration (71.5 pg/ml ± 12 pre-transplantation vs 62.5 pg/ml ± 4.4 at 4 months post-transplantation; P < 0.05) were significantly decreased after transplantation in patients who had received SRL, TAC and PRED.

In conclusion, the data of the current study suggest that using reduced dose of TAC in SRL, TAC and PRED protocol is in favor of allograft survival; however a cohort study with larger sample size is needed for confirming our results.

1. Introduction

Recent improvement in immunosuppressive medications and therapy, make kidney transplantation as a standard treatment for end-stage renal disease (ESRD). However, these drugs cannot prevent the chronic rejection of the transplantation, and also prolonged use of these drugs has been associated with emergence of various types of malignancies and infections. Therefore avoiding long-term immunosuppression with the goal of achieving immunological tolerance can be considered as a final solution for long-term survival of allograft. One of the

---

Keywords: Kidney transplantation
Th1
Th2
Th17 cells
Tacrolimus
Mycophenolate mofetil
Prednisolone
Sirolimus

Abbreviations: SRL, sirolimus; mTOR, mammalian target of rapamycin; CNIs, calcineurin inhibitors; TAC, tacrolimus; PRED, prednisolone
* Corresponding author at: Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
E-mail address: amirzargar@sums.ac.ir (A.A. Amirzargar).

https://doi.org/10.1016/j.intimp.2018.12.033
Received 26 August 2018; Received in revised form 12 December 2018; Accepted 13 December 2018
1567-5769/ © 2018 Published by Elsevier B.V.