FMC 연구비

타르롤리무스와 1,25-비타민D3 병합치료를 이용한 Th17 면역반응의 효과적인 억제

가톨릭대학교 서울성모병원 내과학교실 신장내과[1], 가톨릭대학교 서울성모병원 면역질환융합연구사업단[2]

정병하[1], 김경운[2], 김보미[2], 도경찬[2], 조미라[2], 양철우[1]

Combined use of 1α,25 Vitamin D3 and Tacrolimus Effectively Suppressed Th17 Related Immune Responses

Byung Ha Chung[1], Kyoung Woon Kim[2], Bo-Mi Kim[2]
Kyoung Chan Doh[2], Mi-La Cho[2], Chul Woo Yang[1]

Division of Nephrology Department of Internal Medicine[1]
Seoul St. Mary's Hospital The Catholic University of Korea
Convergent Research Consortium for Immunologic Disease[2]
Seoul St. Mary's Hospital The Catholic University of Korea

Background: Accumulating evidence suggests that Th17 immune responses have an important role in the clinical outcome in kidney transplantation. However, currently used immune suppressant, tacrolimus (Tac) cannot effectively suppress this responses. The aim of this study is to investigate whether 1α,25-dihydroxyvitamin D3 (1,25(OH)2D3) could regulate Th17 allo-immune responses which is not suppressed by Tacrolimus.

Methods: First, T cell subset including Th1, Th2, Th17 and Treg cells were quantitatively determined upon T-cell-specific stimulation in peripheral blood mononuclear cells (PBMCs) from healthy individuals or kidney transplant recipients (KTRs) under clinically relevant concentrations of 1,25(OH)2D3 or Tac. Second, we investigated the suppressive effect of 1,25(OH)2D3 on interleukin-17 (IL-17) or TNF-α induced inflammatory cytokine secretion from human primary tubular epithelial cells. Third, we investigated the association between 25-hydroxyvitamin D (25(OH)D) level and Th17 associated cytokine level in those patients.

Results: Tac suppressed Treg cells in a concentration-dependent manner, but did not suppress Th17 cells even at high concentration. In contrast, addition of 1,25(OH)2D significantly suppressed Th17 related allo-responses which was not regulated by tacrolimus. In vitro study using HPRTEC, interleukin-17 (IL-17) and tumor necrosis factor-alpha (TNF-α) significantly induce the secretion of inflammatory cytokine, IL-6 and IL-8, however, addition of 1,25(OH)2D significantly reduces the secretion of those cytokines. In renal transplant recipients with stable allograft function, 1,25(OH)2D level was significantly inversely correlated with IL-17 level. In another group, 25(OH)D level at transplantation was significantly associated with the development of acute rejection within 3 months from KT.

Conclusion: This study suggests that addition of 1,25(OH)2D3 to Tac effectively regulate Th17 alloimmune responses, the high level of (25(OH)D is associated with low Th17 associated cytokine level in KTRs. The use of 1,25(OH)2D3 could be proposed as therapeutic strategy to improve allograft outcome.

Key Words: 신장이식, Th17세포, 비타민 D
Kidney transplantation, Th17, 1α,25-dihydroxyvitamin D3