

신장이식에서 매트릭스 메탈로단백효소 유전자다형성과 이식후 신생당뇨병과의 연관관계

인제의대 부산백병원

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Association of Genetic Polymorphisms of Matrix Metalloproteinases with New-onset Diabetes after Transplantation in Renal Transplantation

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Background: New-Onset Diabetes After Transplantation (NODAT) is a serious metabolic complication that may follow renal transplantation. Excess fat deposition requires space, created by adipocyte (hypertrophy and hyperplasia) and extracellular matrix (ECM) remodelling. This process is regulated by several factors, including several adipocyte-derived Matrix metalloproteinases (MMPs) and the adipokine cathepsin, which degrades fibronectin, a key ECM protein. Excess fat, also deposited in visceral organs, generates chronic low-grade inflammation that eventually triggers insulin resistance and the associated diabetes mellitus. Therefore, we examined the association between NODAT and 11 single nucleotide polymorphisms (SNPs) located within the 3 genes of Matrix metalloproteinases (MMPs) which might be related with NODAT.

Methods: A total of 309 renal transplants recipients were included without a history of diabetes. We analyzed the association between NODAT development and a panel of 11 SNPs within 3 genes (MMP1, MMP2, MMP3) of MMPs.

Results: In terms of allele frequencies, rs243849*C (MMP2) was significantly higher in patients with NODAT. Two SNPs among 11 (18.1%) were significantly associated with NODAT development after adjusting for age, sex, and tacrolimus usage. They include MMP2 (rs1132896) and MMP2 (rs243849). In multiple logistic regression analysis, these 2 SNPs were significantly associated with the development of NODAT in the codominant and recessive or, codominant and dominant models, respectively.

Conclusions: The data suggest that excess fat deposition and ECM remodelling might play a role in the pathogenesis of NODAT in renal transplantation recipients. In particular, significant variations of MMP2 might confer susceptibility to NODAT in patients who receive renal transplants.

Key Words: 신장이식, 유전자다형성, 신생당뇨병

Kidney transplantation, Matrix metalloproteinase, Polymorphism