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Gut microbiota may affect a variability of tacrolimus trough levels in kidney transplant recipients

Ji Eun Kim[1], Hyunjung Cho[2], Ji In Park[3], Seung Hee Yang[4], Jung Pyo Lee[6], Jongwon Ha[5], Yon Su Kim[1], Hajeong Lee[1]
[1]Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Chungbuk National University Hospital, Korea, Republic of
[3]Department of Internal Medicine-Nephrology, Kangwon National University Hospital, Korea, Republic of
[4]Department of Kidney Research Institute, Seoul National University College of Medicine, Korea, Republic of
[5]Department of Surgery, Seoul National University Hospital, Korea, Republic of
[6]Department of Internal Medicine-Nephrology, SMG-SNU Boramae Medical Center, Korea, Republic of

Objectives: The gut microbiota alters expression of drug-metabolizing enzymes and transporters, and consequently affects therapeutic dose and response of medicines. We aimed to investigate the effect of the gut microbiome on the variation of blood tacrolimus concentration, one of the most important immunosuppressant in kidney transplant (KT) recipients.

Methods: We prospectively enrolled KT recipients at two centers. Pretransplant stool samples were collected and stored at -80℃ immediate after collection. From DNA extracted from the feces, the composition of the microbiota was analyzed using metagenomic sequencing with the Illumina MiSeq system. All of the tacrolimus trough levels from every recipients were obtained for 1 year after KT and their standard deviation (SD)s were calculated from each recipients, which used to determine intrapatient variability (IPV) of tacrolimus. We divided patients into high, middle, and low IPV groups according to their tacrolimus SD tertiles.

Results: We prospectively enrolled KT recipients at two centers. Pretransplant stool samples were collected and stored at -80℃ immediate after collection. From DNA extracted from the feces, the composition of the microbiota was analyzed using metagenomic sequencing with the Illumina MiSeq system. All of the tacrolimus trough levels from every recipients were obtained for 1 year after KT and their standard deviation (SD)s were calculated from each recipients, which used to determine intrapatient variability (IPV) of tacrolimus. We divided patients into high, middle, and low IPV groups according to their tacrolimus SD tertiles.

Conclusions: A decrease in the abundance of the genus *Eubacterium* among the gut microbiome in kidney recipients is associated with increased fluctuation of the tacrolimus level after transplantation. Further studies on the mechanism of the effect of genus *Eubacterium* on tacrolimus levels are needed.