## ■ S-533 ■

# Lipid profile & insulin sensitivity after conversion from standard immunosuppressant to once-daily

고신대학교 복음병원

*조대현, 신호식

**Background:** Tacrolimus (Tac) can cause impaired insulin release, dyslipidemia and may affect the development of post-transplant diabetes mellitus. These effects on insulin sensitivity and lipid profile have not been studied in renal transplant recipients receiving traditional twice-daily tacrolimus (TacBID) or cyclosporine compared to the new once-daily prolonged release formulation of tacrolimus (TacOD). **Methods:** We performed an observational prospective study of 15 stable non-diabetic renal transplant recipients to observe the changes in insulin sensitivity and lipid profiles for one year at a tertiary hospital. We evaluated the levels of hemoglobin A1c (HbA1c), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), apolipoprotein A1, apolipoprotein B, serum creatinine, fasting plasma glucose, fasting insulin, homeostatic model assessment (HOMA)-β and HOMA-IR (Insulin resistance index) at baseline and at two and four months. To analyze differences in parameters, we performed a Wilcoxon rank sum test and as well as general linear model (GLM)-repeated measures analysis of variance (ANOVA) in both groups (cyclosporine to TacOD conversion group/TacBID to TacOD conversion group). **Results:** At baseline, parameters were not different in the two groups. In GLM-repeated measures ANOVA, there was no change in insulin sensitivity or lipid profile after conversion at baseline or at two and four months. There were no complications after conversion from standard TacBID or cyclosporine to TacOD. **Conclusions:** There was no change in insulin sensitivity or lipid profile in renal transplant recipients. Any conversion from TacBID to TacOD should be performed in a controlled manner under close surveillance.

**Key Words:** cyclosporine, insulin sensitivity, renal transplantation, tacrolimus

**중심 단어:** 사이클로스포린, 인슐린 감수성, 신장이식, 타크로리무스

## ■ S-534 ■

# TGF-β1 Induces NADPH oxidase 4 Dependent Hypoxia Induced Apoptosis

[1]건양대학교 병원 신장내과, [2]건양대학교 약리학교실

*김동일[1], 황원민[1], 조성권[2], 강재구[2], 윤성로[1], 윤세희[1]

**Aims:** Ischemia/reperfusion injury, resulting from hypoxic damage within a graft, is the leading cause of cell death and graft rejection. In this study, we investigated whether Nox4 have a great role in ischemic injury in a cellular model in which experimental hypoxia was induced using CoCl2 **Main methods:** The ischemic injury induced in HK-2 cells by CoCl2 was validated by reduced cell viability at different times and doses. Reverse transcription polymerase chain reaction for Nox4 and TGF-β1 was performed. Western blotting for Nox4 and Smad pathway were done. ROS production was detected using a DHE stain and Amplex red assay. HK-2 cells were transfected with siNox4 and pretreated with GKT137831(most specific Nox1/4 inhibitor). ELISA has been used to measure TGF-β1 levels. The effect of treatment with TGF-β1 type 1 tyrosine kinase inhibitor SB431542 on Nox4 expression was observed. **Results:** Expression of Nox4 in HK-2 cells significantly increased by hypoxic stimulation. TGF-β1 was secreted endogenously by hypoxic HK-2 cells. SB4315432 significantly inhibited Nox4 expression in HK-2 cells via Smad2/3 dependent cell signaling pathway. Silencing of Nox4 recued production of reactive oxygen species (ROS), downregulation of proinflammatory markers and reduced caspase 3/7 activity in hypoxic HK-2 cells. Pretreatment of GKT137831 replicated theses results. **Conclusions:** Hypoxia induces HK-2 cell apoptosis through the signaling pathway involving Nox4 dependent ROS generation and TGF-β1 via Smad pathway. Therapies targeting Nox4 may be effective against ischemia induced kidney injury.