KSN 2018
Seoul, Korea · May 17 - 20

Abstract Type : Oral
Presentation No. : OR 08 CK-04

Urinary myo-inositol as a potential marker for focal segmental glomerulosclerosis: NMR-based metabolomics study

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Objectives: Minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) have similar histological findings initially, however, response to steroid treatment and long-term prognosis are quite distinct from each other. Therefore, it is of great importance to discriminate FSGS from MCD in the early phase of disease and predict clinical prognosis.

Methods: Discovery set consisted of 185 urine samples (62 healthy controls, 81 MCD, and 42 FSGS) collected at the time of kidney biopsy from 2010 to 2017 at Seoul National University Hospital and Seoul National University Boramae Medical Center. As validation set, we used 61 urine samples (12 healthy controls, 26 MCD, and 23 FSGS) from Gangdong Kyung Hee University Hospital and Gyeongbuk National University Hospital. Characteristic differences of urine metabolites depending on MCD and FSGS were examined using 800 MHz nuclear magnetic resonance (NMR) spectroscopy. After normalization by urine creatinine, the values were transformed to log values.

Results: Of 73 urine metabolites, log-transformed myo-inositol was significantly higher in FSGS patients compared with control patients (2.63-fold; $P < 0.001$) and with MCD patients (2.79-fold; $P < 0.001$). Log-transformed myo-inositol showed an inverse relationship between the initial chronic kidney disease stages ($P < 0.001$) or estimated glomerular filtration rate at baseline ($R^2 = 0.465$, $P < 0.001$). In addition, it was significantly associated with plasma level of soluble urokinase-type plasminogen activator receptor in FSGS patients ($R^2 = 0.228$, $P < 0.001$). Validation set revealed that log-transformed myo-inositol in urine samples of FSGS patients increased by 2.6-fold ($P < 0.001$) and 1.8-fold ($P < 0.05$) than control patients and MCD patients, respectively.

Conclusions: Myo-inositol, as urine metabolite, discriminated FSGS patients from MCD or control patients at the time of early diagnosis and significantly associated with initial renal function. Further studies including the correlation with clinical prognosis and the possible mechanism will be performed.