

KSN 2016 Abstract Submission

Volume, Acid-Base & Electrolyte

KSN2016ABS-1417

Expression of AQPs in Fabry disease mice

Ji-Eun Kim¹, Su-Youn Lee¹, Sae-Jin Lee¹, Sung-Chul Jung², Ki-Hwan Han*¹

¹Department of Anatomy, ²Department of Biochemistry, Ewha Womans University, Seoul, Korea, Republic Of

Background: Fabry disease is a lysosomal storage disorder caused by deficiency of the enzyme α -galactosidase A (α -Gal A). Misfolded enzymes are retained in the endoplasmic reticulum (ER) and degraded before sorting into lysosomes resulting in lysosomal accumulation of globotriaosylceramide (Gb3). The purpose of this study was to investigate the mechanism of the decreased urinary concentration, one of the earliest renal manifestation of Fabry disease, in α -Gal A deficient mice.

Methods: Kidney tissues were processed for α -Gal A enzyme activity assay, Gb3 level quantification, immunocytochemistry, and immunoblot analysis.

Results: α -Gal A deficiency caused significant polyuria that was associated with increased renal Gb3 level. Fabry kidneys showed a significantly increased expression of ER stress proteins, Bip and CHOP.

Immunocytochemistry revealed that the expression of Bip and CHOP was induced mainly in glomeruli, outer medullary vascular bundles, and medullary collecting ducts. AQPs are key transport proteins involved in urine concentration in the kidney. Expression of AQP2, 3, and 4 proteins significantly decreased in Fabry kidneys, but the abundance of AQP1 protein remained unchanged. Confocal microscopy demonstrated that AQP2 was abnormally localized in the cytoplasm in CHOP-expressing medullary collecting ducts. Electron microscopy confirmed the presence of typical lamellar inclusion bodies within collecting duct cells.

Conclusion: These findings suggest that collecting duct injury and altered expression of AQPs may play an important role in urinary concentration defect in Fabry disease.

This work was supported by funds from the National Research Foundation of Korea (NRF-2013R1A1A2058028).

Keywords: AQPs, collecting duct, Fabry disease