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aquaporin-2-667 A/G 유전자다형성과 만성신장병의 연관관계 연구

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Study of the Association of -667 Aquaporin-2 (AQP-2) A/G Promoter Polymorphism with the Incidence and Clinical Course of Chronic Kidney Disease in Korea

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Background : Impaired urinary concentration is uniformly present with advanced disease in chronic renal failure. Aquaporin-2 (AQP-2) is known to be expressed in the renal collecting duct cells and participates in urinary concentration in response to vasopressin. The urinary excretion of AQP-2 is decreased in accordance with the development of diabetic nephropathy. Recently, the study of AQP expression in various forms of chronic kidney disease (CKD) demonstrated a reduction in AQP-2 expression associated with a loss of nephrons and the presence of chronic interstitial fibrosis. No information on aquaporin genetic variations in CKD is available to date. The aim of our study was to evaluate the possible impact of aquaporin-2 genotype on development and clinical course of CKD.

Methods : Blood samples from 259 patients with CKD and 106 ethnically, age and sex-matched healthy controls were collected and genomic DNA was extracted. AQP-2 -667 genotype was assessed by PCR, followed by restriction fragment length polymorphism analysis. Differences in clinical parameters between different genotypes in the AQP-2 gene were tested with either a χ^2-test or with Fisher's exact test. Correlation analysis of continuous variables was carried out according to the Kruskal-Wallis test.

Results : 79 (30.5%) patients had the AQP-2-667 wild-type A/A, 123 (47.5%) were heterozygous for the G allele and 57 (22.0%) patients showed homozygosity. There were no significant differences in genotype and allele frequencies between the patients group and the group of healthy controls (p=0.3936, p=0.2941, respectively). After subclassification of CKD according to underlying disease, no significant differences were observed between any of the groups and the control group (p=0.72 for diabetic nephropathy, p=0.52 for hypertensive nephropathy, p=0.27 for chronic glomerulonephritis, and p=0.80 for unknown etiology). Genotype and allele frequencies of the AQP-2 gene polymorphism (rs3759126) of hypertensive patients in pre-ESRD did not show noticeable difference compared with normal blood pressure patients in pre-ESRD (p=0.50). No correlation was found to exist between the AQP-2 gene polymorphism (rs3759126) and serum electrolyte levels in pre-ESRD patients (p=0.38 for serum sodium level and p=0.44 for serum potassium level).

Conclusion : Our data indicate that no association exists between the -667 AQP-2 A/G polymorphism and susceptibility to CKD or its clinical course.