복막투석환자에서 fetuin-A 유전자 다형성과 혈청 fetuin-A 농도 동맥경직도 사이의 연관성

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Association Among Fetuin-A Gene Polymorphisms, its Serum Concentration and Arterial Stiffness in Peritoneal Dialysis Patients

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Background : Vascular calcification (VC) is associated with arterial stiffness and is a major risk factor of cardiovascular (CV) morbidity and mortality in ESRD patients. Fetuin-A, also known as α2-Heremans-Schmid glycoprotein (AHSG), is an important circulating plasma protein with inhibitory effects on VC. Our aim is to elucidate an association among fetuin-A single nucleotide polymorphisms (SNPs), its serum concentration and arterial stiffness in peritoneal dialysis (PD) patients.

Methods : A total of 209 stable patients on chronic PD were genotyped for six SNPs (rs2248690, rs2277119, rs4831, rs2593813, rs4917 and rs2518136). Variables such as age, mean arterial pressure (MAP), diabetes, serum albumin, Ca, P, intact parathyroid hormone (iPTH), uric acid, total bilirubin, high-sensitivity C-reactive protein (hsCRP) were evaluated. Pulse wave velocity (PWV) and serum fetuin-A concentration were measured. Vascular calcification score (VCS) were assessed based on plain radiograph of the pelvis and both hands.

Results : Five SNPs (rs2248690, rs2277119, rs2593813, rs4917 and rs2518136) in fetuin-A gene were associated with its serum concentration ($p<0.01$). When two sets of haplotype blocks (H1 and H2) were built, two haplotypes in each block were associated with serum fetuin-A concentration ($p<0.01$). Univariate analysis revealed that serum fetuin-A concentration was inversely correlated with VCS ($r=-0.442$, $p=0.004$) and PWV ($r=-0.338$, $p<0.001$). VCS was positively correlated with PWV ($r= 0.312$, $p=0.042$). In addition, PWV was positively correlated with age, male gender, diabetes, duration of PD, MAP, whereas serum albumin and total bilirubin level were inversely correlated with PWV. In a multiple regression model, age ($\beta=0.359$, $p<0.001$), diabetes ($\beta=0.335$, $p<0.001$), MAP ($\beta=0.325$, $p<0.001$), albumin ($\beta=-0.133$, $p=0.014$) and serum fetuin-A level ($\beta= -0.112$, $p=0.034$) were independent determinants of PWV in PD patients.

Conclusion : The fetuin-A gene polymorphisms affected its serum concentration, which, subsequently, was one of determinants for both the vascular calcification and aortic stiffness in PD patients. These results suggest a role of fetuin-A in the development of VC in PD patients. Future research will follow in order to investigate whether the genetic variants with decreased circulating fetuin-A levels are associated with the risk of VC and CV morbidity and mortality.

Key Words : Fetuin-A, 유전자 다형성, 동맥 경직도, 복막투석
Fetuin-A, Gene polymorphism, Aortic stiffness, PD