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Abstract

Nitric oxide production is reduced in renal disease, partially due to decreased endothelial nitric oxide production. Evidence indicates that nitric oxide deficiency contributes to cardiovascular events and progression of kidney damage. A polymorphism in intron 4 of the endothelial constitutive nitric oxide synthase (ecNOS) gene is a candidate gene in cardiovascular and renal diseases. We investigated a potential involvement of this polymorphism in chronic renal failure. A case-control study involved 78 children with chronic kidney disease (CKD) and 30 healthy controls. All participants were genotyped for the ecNOS4 polymorphism by the polymerase chain reaction (PCR). Dialyzed (maintenance hemodialysis) and conservative treatment children had significantly higher frequency of the aa genotype and ecNOS4a allele (P<0.05) compared with controls. The combined genotype aa+ab vs. bb comparison validated that a allele is a high-risk allele for end-stage renal disease (ESRD) (P<0.05). Serum nitric oxide level was found to be lower in carriers of the ecNOS 4a allele than in noncarriers (100.29±27.32 vs. 152.73±60.39 μmol/l, P=0.04). Interestingly, 85.95% of the ecNOS 4a allele ESRD patients were found hypertensive in comparison to the 60.67% patients of noncarriers (bb genotype) (P=0.04). Also, 35.90% of the ecNOS 4a allele ESRD patients were found to have cardiovascular disease in comparison to the 5.13% patients of noncarriers (bb genotype) (P=0.01). On multiple linear regression analysis, a allele was independently associated with hypertension (P=0.03). There was a significantly higher frequency of the ecNOS4a allele carriers among CKD children, both on MHD and conservative treatment than in controls. This suggests that the ecNOS gene polymorphism may be associated with an increased risk of chronic renal failure.