ABSTRACT

Neuropeptide cholecystokinin (CCK) and its receptors (CCK-AR, CCK-BR) affect the dopaminergic function, which may in turn constitute a predisposition in schizophrenia. The present study have investigated genetic variations in the promoter region and the coding region of the CCK-AR, CCK-BR and CCK genes. An association analysis was conducted between 83 unrelated schizophrenic patients and 100 healthy controls. Novel polymorphisms (201A→G, 246G→A, 1260T→A , 1266T→C, Leu306Leu in the CCK-AR gene, -215C→A , Leu37Phe, Arg319Glu in the CCK-BR gene, and -196G→A in the CCK gene, respectively) were found in addition to the variants reported previously. Significant differences were found in the allele frequencies of the 201A→G nucleotide substitution in the promoter region of the CCK-AR gene between patients and controls (P=0.0181, Odds ratio: 1.972, Bonferroni correction: P=0.0905). These differences were also found between the patients with paranoid type and controls (P=0.0274, Odds ratio=3.667, Bonferroni correction: P=0.137). On the other hand, the genotype frequency of the -215C→A nucleotide substitution in the promoter region of CCK-BR gene was significantly higher in the schizophrenic patients than in the controls (P = 0.037, Odds ratio=5.600). However, the difference was not significant after Bonferroni correction (P=0.25). Moreover, there were no significant difference of the polymorphism of the CCK gene between patients and controls. These results suggested that the 201A allele frequency in the promoter region of the CCK-AR gene was higher in the schizophrenic group, especially in paranoid type, than the control group at a rate that was not quite significant after Bonferroni correction.

Key Words; Genetic variants, Linkge disequiribrium, Cholecystokinin-dopamine interactions, Paranoid type, Clinical heterogeneity