Medication Overuse Headache – A Complex Neurologic Disorder: Genetic Susceptibility Deserves to be Studied

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Patients with primary headaches, especially migraine, often need symptomatic medications. Prolonged and frequent use of abortive medication for acute headache can lead to deterioration of the primary headache. This clinical phenomenon is well known as "medication overuse headache". Medication overuse headache is generally regarded as a consequence of the overuse of acute or symptomatic therapeutic agents in a susceptible patient. The pathogenesis remains unclear. Neurophysiological, functional imaging, genetic and neurochemical studies have provided information regarding the mechanism of headache chronification.

Patients without primary headaches usually do not develop medication overuse headache even regularly use analgesics. Furthermore, migraineurs are most susceptible to develop medication overuse headache. Genetic variation has been considered to play a role in the pathogenesis of such susceptibility. Previous studies have attempted to evaluate if genetic polymorphism is involved in the pathogenesis of medication overuse headache. One study found brain-derived neurotrophic factor Val66Met polymorphism is related to the clinical features of medication overuse headache [(1)]. Another study found methylenetetrahydrofolate reductase (MTHFR) C677T (rs1801133) and dopamine D2 receptor (DRD2) C939T (rs6275) polymorphisms are factors that independently contribute to the onset of medication overuse headache in patients with migraine [(2)].

It was proposed that neurochemical changes including alteration of serotonin (5-HT) function might be involved in the development of medication overuse headache [(3)]. Therefore, genetic polymorphisms of the 5-HT are reasonably the potential research targets for further elucidating this complex disorder.

Ishii et al. now report in the journal on the association between the tryptophan hydroxylase 2 (THP-2) gene polymorphisms and medication overuse headache in Japanese patients [(4)]. The enzyme TPH-2 is primary expressed in the serotonergic neurons of human brain. It is a rate-limiting enzyme in the synthesis of serotonin. The authors studied 47 patients with migraine and 22 patients with migraine and also having medication overuse headache. Three single-nucleotide polymorphisms (SNPs, rs4565946, rs4570625, and rs4341581) were analyzed. The results demonstrated the genotype distributions of these 3 SNPs were not significantly different between migraine patients without medication overuse headache and migraine patients with medication overuse headache.

Although this study did not demonstrate the positive finding, further researches are needed. The polymorphisms of other genes or other 5-HT related gene deserve future study, especially in combination with other research tools such as functional imaging and neurophysiologic tests.

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