Correlation between single nucleotide polymorphisms in hypoxia-related genes and susceptibility to acute high-altitude pulmonary edema

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ABSTRACT. This study aimed to explore the relationship between genetic changes and high-altitude pulmonary edema (HAPE) susceptibility, and to screen for the key single nucleotide polymorphism (SNP) loci in the HAPE-susceptibility gene, by investigating the SNPs occurring in hypoxia-related genes in HAPE-susceptible and control (non-susceptible) populations. This research was conducted on Han recruits, who travelled to the Lhasa plateau (altitude, 3658 m). Ten loci located on ten genes extracted from the HAPE and healthy populations were amplified by polymerase chain reaction, and subsequently sequenced. The investigated genes included those coding for aldosterone synthase 2 (CYP11B2), angiotensin-converting enzyme (ACE), heat-shock protein 70 (HSP70), nuclear factor kappa B (NF-κB), surfactant protein A2 (SP-A2), plasminogen activator inhibitor-1 (PAI-1), nitric oxide synthetase (NOS), vascular endothelial growth factor (VEGF), prolyl hydroxylase (EGLN1), and zinc finger protein A20. The gene distribution of each SNP loci and its correlation with...
HAPE was analyzed. Statistical analyses of the genotype frequencies of the SNPs revealed significant differences in the *ACE* (rs4309), *EGLN1* (rs480902), *SP-A2* (rs1965708), *HSP70* (rs1008438), *PAI-1* (rs1799889), and *NOS* (rs199983) expressions between the HAPE and healthy control groups (*P* < 0.05); therefore, these SNP loci were believed to indicate HAPE susceptibility. HAPE is correlated with multiple-SNP loci. A correlation analysis between genetic polymorphism and HAPE susceptibility revealed that 6 hypoxia-related genes were key sites accounting for HAPE. These findings could help assess the risk of HAPE in populations expressing different genotypes, in order to reduce the occurrence of HAPE.

**Key words:** HAPE; Heat-shock protein 70; Prolyl hydroxylase; Angiotensin-converting enzyme; Surfactant protein A2; Plasminogen activator inhibitor