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The effect of genetic polymorphisms of RARA gene on the adverse effects profile of isotretinoin-treated acne patients.

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Abstract: OBJECTIVE: Isotretinoin is a vitamin A-derived medication that is associated with significant adverse effects including arthralgia/ myalgia, nose bleeds, headache, dyslipidemia, liver dysfunction and depression. The mechanism for development of such adverse effects remains elusive, and it is not known why adverse effects develop only in some patients. In this study, we examined the association between rs9303285, rs2715554 and rs4890109 genetic polymorphisms in the retinoic acid receptor alpha (RARA), one of the main targets of isotretinoin, and the adverse effects of oral isotretinoin therapy. MATERIALS AND METHODS: Clinical adverse effects data were collected from patient file and by patient interview. Lipids and liver enzymes were measured in blood samples collected from acne patients (n = 300) at baseline and during oral isotretinoin treatment. RARA polymorphisms were genotyped using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). RESULTS: Three-locus haplotype (Rs2715554 C/T - Rs4890109 G/T - Rs9303285 T/C) analysis showed that frequencies of CTG and TTG haplotypes are significantly associated with occurrence of arthralgia, myalgia, nose bleeds and headache in patients treated with isotretinoin. In addition, TCG haplotype was associated with nose bleeds and headache, whereas TTT haplotype was associated with arthralgia and myalgia. Furthermore, levels of AST were increased, and AST% change was more, after 1 month of treatment in patients with the TC genotype of rs2715554 polymorphism. Finally, allele T of rs9303285 was found to be protective against developing depression in the patients treated with isotretinoin.