Letter

Lack of Association between *Interleukin-12* Gene Polymorphisms and Recurrent Aphthous Stomatitis

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Recurrent Aphthous Stomatitis (RAS) is the most common oral inflammatory disease, which is a painful, ulcerative condition of the oral cavity [1] and is characterized by episodic, small, round ulcers with erythematous halos [2]. Although several factors such as systemic diseases, nutritional factors, psychological stress, local trauma, allergies, smoking and hormonal alterations could be associated with RAS, genetic factors seem to have an important role in predisposition to this condition whereas the exact pathogenesis of the disease has not clearly been understood [3].

Interleukin (IL)-12 which is secreted by macrophages and dendritic cells has a key role in differentiation of Th0 cells into Th1 cells [4], and therefore it could theoretically have a role in RAS pathogenesis. Considering the fact that SNP could affect the cytokine secretion, an attempt was made to evaluate the alleles and genotypes frequencies of *IL12* gene in a group of patients with RAS.

In this investigation, 5 *ml* blood from sixty four Iranian patients with confirmed diagnosis of RAS [5] was collected in the EDTA tubes. DNA was extracted using a phenol-chloroform method. This project was approved by Ethics Committee of Tehran University of Medical Sciences. Written informed consent was obtained from all subjects before sampling. *IL12* gene typing was performed by Polymerase Chain Reaction with Sequence-Specific Primers (PCR-SSP) assay (PCR-SSP kit, Heidelberg University, Heidelberg, Germany), similar to what explained before [6]. The allele and genotype frequencies of *IL12* (A -1188 C) were investigated. Allele frequencies were estimated by direct gene counting. The results were compared to the number of alleles and genotypes in 140 healthy controls from the same region. Chi-square test was used to compare frequencies of alleles, genotypes and haplotypes between patients and control groups. The odds ratio (OR) and 95% Confidence Intervals (95%CI) were calculated. P-value (p) of less than 0.05 was considered significant.

The results showed that A allele was the most frequent allele among patients and controls. It was detected in 77.1% of patients and was detected in 72.9% of healthy controls. This has been reflected in AA genotype, which was the most common genotype among all enrolled individuals. AA genotype was detected in 57.9% of the patients, which was insignificantly higher than 51.4% in the controls. No significant difference was found on *IL12* alleles and genotype frequencies between the patients and the controls (Table 1).

In several studies, association of number of cytokine gene polymorphisms in pathogenesis of RAS has been investigated [7,8]. In this study, the possible role of *IL12* SNP with RAS was investigated and no association was found which is similar to previous studies [9]. It has been documented that an A to C exchange in the 3'-UTR of *IL12* gene at position -1188 correlates with low cytokine secretion [10]. In the present study, *IL12* SNP was evaluated at that position which is located in the promoter region of the gene. However, no significant difference on *IL12* (A -1188 C) alleles and genotypes between the patients and the controls was found.

Lack of association between *IL12* (A -1188 C) polymorphisms and RAS could indicate that IL-12 has no significant role in pathophysiology of RAS.

Keywords: Interleukin 12, Recurrent aphthous stomatitis, Single nucleotide polymorphisms

Table 1. Comparison of alleles, genotype frequencies of *IL12* between patients with RAS and the control group

Position	Alleles/ Genotypes/Haplotypes	RAS (n=60), n(%)	Controls (n=140), n(%)	p-value	Odds Ratio (95% Confidence Interval)
-1188					
	A	91(77.1)	204(72.9)	0.446	1.26(0.74-2.15)
	C	27(22.9)	76(27.1)	0.446	0.80(0.47-1.36)
	AA	34(57.6)	72(51.4)	0.519	1.28(0.67-2.48)
	CA	23(39)	60(42.9)	0.727	0.85(0.44-1.66)
	CC	2(3.4)	8(5.7)	0.387	0.58(0.08-3.08)

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