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Association of Polymorphism rs 1143634 IL-1β Gene with the Development of Chronic Paradontitis

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Abstract Associations of the IL-1β gene polymorphism (rs 1143634) with chronic periodontitis (CP) were studied and their contribution to the development of this pathology was assessed. For the study carried out the selection of patients with CP, as well as conditionally healthy individuals without periodontal pathology. The data obtained suggest that there is a possible association of the rs1143634 polymorphism of the IL-1β gene with the development of CP, which requires further research on a larger number of patients.

Keywords Associations, IL-1β gene polymorphism (rs 1143634), Chronic periodontitis (CP)

1. Introduction

Periodontal lesions, which are the main cause of tooth loss in middle and older age groups [5], lead to the development and progression of diseases of the gastrointestinal tract, reducing the quality the life of the population [5]. According to the World Health Organization (WHO), in various age groups the prevalence of periodontal diseases reaches 80-100% (The World Oral Health Report. WHO. Geneva, 2012) [5]. In the Republic of Uzbekistan, for people aged 12 to 44 years old, this prevalence of periodontal diseases is up to 83.3%, and at the age of 44 years and above, it reaches 91.7%. A person aged 40-65 years old loses an average of 15 to 20 teeth due to periodontitis.

It is known that periodontitis is currently regarded as a multifactorial disease, and therefore the manifestation and progression of signs of periodontitis depends on a variety of exogenous and endogenous predisposing factors and determinants [2], which include both the individual characteristics of the organism, social and genetic risk factors [1, 3, 7]. Given these facts, there are difficulties in determining any factor affecting the development and progression of periodontitis, the disease is initiated and progressed [5].

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Currently, there is information about the association of proinflammatory cytokine genes with the development of periodontitis in various populations [4, 6].

2. Main Body

2.1. The Purpose of Our Research

In this regard, we found it interesting to study the association of polymorphisms of the IL-1β genes (rs 1143634) with chronic periodontitis (CP) and the evaluation of their contribution to the development of this disease.

2.2. Material and Methods of Study

For the study carried out the selection of patients with CP in the amount of 138 people aged 15 to 70 years - the main group, as well as conditionally healthy people without periodontal pathology in the amount of 105 people - the control group of comparable age. The main group was divided into 3 subgroups: A - patients with mild CP (n = 61), B - patients with moderate severity of CP (n = 56) and C - patients with severe severity of CP (n = 21). All surveyed were persons of Uzbek nationality living in the city of Tashkent.

Detection of the IL-1β gene polymorphism (rs 1143634) was performed by SNP-PCR using an Applied Biosystems 2720 thermal cycler. The statistical analysis of the obtained results was performed using the "Open Epi 9.3" program.

2.3. Results of the Study

The results of the distribution of the allele C frequency - the rs 1143634 polymorphism of the IL-1β gene in the main

group were 77.2% ($\chi2$ = 1.2; P = 0.2; OR = 1.3; 95% CI 0.829-2.02), while in the control group this figure was 81.4%. The detection rate of the T allele of the studied gene in the main group averaged 22.8%, while in the control group this indicator was lower (22.8% versus 18.6%; $\chi2$ = 2.1; P = 0.1; OR = 1.7; 95% CI 0.820-3.52) (Table 1 and 2).

In the studied groups, homozygotes for the mutant T / T allele were detected, both in the main (5.1% vs. 2.8; $\chi2$ = 0.7; P = 0.4; OR = 1.9; 95% CI 0.458– 7.2), and in the control group, the frequency the distribution of C / T genotypes and exceeded that in the control group (35.5% vs. 31.4%; $\chi2$ = 0.4; P = 0.5; OR = 1.2; 95% CI 0.70– 2.06), the frequency of the C / C genotype in the main group was less than in the control group (59.4% vs. 65.7%; $\chi2$ = 1.0; P = 0.3; OR = 0.8; 95% CI 0.45-1.99). The T (OR = 1.3) allele and the C / T genotype (OR = 1.2) slightly increase the risk of developing chronic periodontitis (CP) by more than 1.3 and 1.2 times, respectively.

Table 1. Distribution frequency of alleles and genotypes of the rs 1143634 polymorphism of the IL-1β gene in patient groups and controls

Groups	Allele distribution frequency				Genotype distribution frequency					
	C		T		C/C		C/T		T/T	
	n	%	n	%	n	%	n	%	n	%
1, n=138	213	77.2	63	22.8	82	59.4	49	35.5	7	5.1
A, n=61	98	80.3	24	19.7	39	63.9	20	32.7	2	3.3
B, n=56	83	74.1	29	25.9	31	55.3	21	37.5	4	7.1
C, n=21	32	76.2	10	23.8	12	57.1	8	38.1	1	4.8
2, n=105	171	81.4	39	18.6	69	65.7	33	31.4	3	2.8

Table 2. Differences in the frequency of occurrence of alleles and genotypes of the rs 1143634 polymorphism of the IL-1β gene in the main and control groups

Alleles and genotypes	The number of examined alleles and genotypes		χ^2	P	RR	OR	95%CI
	Core group	Control					
C	213	171	1.2	0.2	1.2	1.3	0.829-2.02
T	63	39					
C/C	82	69	1.0	0.3	0.7	0.8	0.45-1.29
C/T	49	33	0.4	0.5	1.1	1.2	0.70-2.06
T/T	7	3	0.7	0.4	1.8	1.9	0.458-7.2

Further, the correspondence between the observed and expected frequencies of the distribution of genotypes in the Hardy-Weinberg equilibrium (PXB) with a chosen significance level of P> 0.05 was found, with $\chi2$ = 0.008 and P = 0.9. In particular, the observed frequency (0.59) of the C / C genotype in the group of patients coincides with the expected frequency (0.6); the observed frequency (0.36) of the C / T genotype in the group of patients completely coincides with the expected frequency (0.35); the values of the observed and expected frequency of T / T genotype in the group of patients were 0.05 and 0.052, respectively, and the difference between the observed and expected frequencies of heterozygotes is not statistically significant, which determines a statistically insignificant excess of heterozygotes in the group of patients. Statistical significant differences in the indices for homozygotes for this polymorphic variant were also not revealed.

The study of the relative deviation index between the expected and observed heterozygosity D * in the studied groups showed the presence of a moderate excess of heterozygotes (D * in both groups was +0.03).

In subgroup A of the main group (Table 3), the correspondence between the observed and expected frequencies of the distribution of genotypes in the Hardy-Weinberg equilibrium (RCS) was found with the chosen significance level P> 0.05, with $\chi2$ = 0.085 and P = 0.8. The frequency of C and T alleles was 0.77 and 0.23, the observed frequency of the G / G genotype in the group of patients completely coincides with the expected frequency (0.64 and 0.64, respectively); the observed frequency of the C / T genotype in the group of patients also practically coincides with the expected frequency (0.33 and 0.32, respectively); the values of the observed and expected frequency of T / T genotype in the group of patients were 0.03 and 0.04, respectively.

Table 3. The expected and observed frequencies of the distribution of genotypes in Hardy-Weinberg equilibrium (HWE) in subgroup "A" of patients with chronic chronic periodontitis (CP)

Alleles	Frequency of distribution of alleles				
C	0.77				
T	0.23				
Genotypes	Frequency of distribution of genotypes		χ^2	P	RR
	Core group	Control			
C/C	0.64	0.64	0.003	0.8	1
C/T	0.33	0.32	0.027		
T/T	0.03	0.04	0.055		
Total	1.00	1.00	0.085		

OR odds ratios (Table 4) in subgroup "A", the carriage of the functionally unfavorable T allele and the mutant T / T genotype of the rs1143634 polymorphism of the IL-1β gene ($\chi2$ = 0.06; P = 0.8; OR = 1.1; 95%, CI = 0.609-1.891 and $\chi2$ = 0.02; P = 0.9; OR = 1.1; 95% CI = 0.187-7.096, respectively), of the C / T heterozygous genotype ($\chi2$ = 0.03; P = 0.8; OR = 1.1; 95% CI = 0.54-2.09) a statistically insignificant increase in the risk of the formation and development of chronic periodontitis (CP) in this subgroup.

In the subgroup "B" of the main group (Table 5), the observed and expected genotype frequencies in the Hardy-Weinberg equilibrium (HWE) were found to have a chosen significance level of P> 0.05, with $\chi2$ = 0.029 and P = 0.9. The observed frequency of the C / C genotype in the group of patients completely coincides with the expected

frequency (0.55 and 0.55, respectively); the observed frequency and the expected frequency of the C / T genotype in the group of patients were 0.37 and 0.38, respectively; The values of such indicators of T / T genotype in the group of patients were 0.07 and 0.07, respectively.

Table 4. Differences in the frequency of occurrence of alleles and genotypes of the rs1143634 polymorphism of the IL-1β gene in subgroup "A" and the control group

Alleles and genotypes	The number of examined alleles and genotypes		χ^2	P	RR	OR	95%CI
	Subgroup "A"	Control					
C	98	171	0.06	0.8	1.0	1.1	0.609-1.891
T	24	39					
C/C	39	69	0.05	0.8	0.9	0.9	0.478-1.789
C/T	20	33	0.03	0.8	1.0	1.1	0.54-2.09
T/T	2	3	0.02	0.9	1.1	1.1	0.187-7.096

Table 5. The expected and observed frequencies of the distribution of genotypes in Hardy-Weinberg equilibrium (HWE) in subgroup "B" of patients with chronic chronic periodontitis (CP)

Alleles	Frequency of distribution of alleles				
C	0.77				
T	0.23				
Genotypes	Frequency of distribution of genotypes:		χ^2	P	df
	observed	expected			
C/C	0.55	0.55	0.002	0.9	1
C/T	0.37	0.38	0.011		
T/T	0.07	0.07	0.016		
Total	100.00	1.00	0.029		

According to the calculation of the OR odds ratio (Table 6) in subgroup "B", the carrier of the functional unfavorable T allele and the mutant T / T genotype of the rs1143634 polymorphism of the IL-1β gene ($\chi2 = 2.3$; P = 0.1; OR = 1.5; 95%, CI = 0.88-2.64 and $\chi2 = 1.7$; P = 0.2; OR = 2.6; 95% CI = 0.564-12.12, respectively), the heterozygous genotype C / T ($\chi2 = 0.6$; P = 0.4; OR = 1.3; 95% CI = 0.66-2.58) statistically insignificantly increases the risk of the formation and development of chronic periodontitis CP in this subgroup.

Table 6. Differences in the frequency of occurrence of alleles and genotypes of the rs1143634 polymorphism of the IL-1β gene in subgroup "B" and the control group

Alleles and genotypes	The number of examined alleles and genotypes		χ^2	P	RR	OR	95%CI
	Subgroup "B"	Control					
C	83	171	2.3	0.1	1.4	1.5	0.880-2.640
T	29	39					
C/C	31	69	1.7	0.2	0.8	0.6	0.330-1.250
C/T	21	33	0.6	0.4	1.2	1.3	0.660-2.580
T/T	4	3	1.6	0.2	2.5	2.6	0.564-12.120

In the subgroup "C" of the main group (Table 7), the correspondence between the observed and expected genotype frequencies in the Hardy-Weinberg equilibrium (RCS) was also found with the chosen significance level P> 0.05, with $\chi2 = 0.053$ and P = 0.8. The observed and expected frequencies in the group of patients with genotype C / C (0.57 and 0.58), C / T (0.38 and 0.36) and T / T (0.05 and 0.06) also coincided as in the previous groups.

Table 7. The expected and observed frequencies of the distribution of genotypes in Hardy-Weinberg equilibrium (HWE) in subgroup "C" of patients with chronic chronic periodontitis (CP)

Alleles	Frequency of distribution of alleles				
C	0.77				
T	0.23				
Genotypes	Frequency of distribution of genotypes:		χ^2	P	df
	observed	expected			
C/C	0.57	0.58	0.003	0.8	1
C/T	0.38	0.36	0.019		
T/T	0.05	0.06	0.030		
Total	1.00	1.00	0.053		

According to the calculation of the OR odds ratio (Table 8) in the "C" subgroup, there is a carrier of the functionally unfavorable T allele and the mutant T / T genotype of the rs1143634 polymorphism of the IL-1β gene ($\chi2 = 0.6$; P = 0.4; OR = 1.4; 95 %, CI = 0.621-3.02 and $\chi2 = 0.2$; P = 0.6; OR = 1.7; 95% CI = 0.168-17.1, respectively), of the C / T heterozygous genotype ($\chi2 = 0.3$; P = 0.5; OR = 1.3; 95 % CI = 0.50-3.5) insignificantly increases the risk of the formation and development of chronic periodontitis (CP) in this subgroup.

Table 8. Differences in the frequency of occurrence of alleles and genotypes of the rs1143634 polymorphism of the IL-1β gene in subgroup "C" and the control group

Alleles and genotypes	The number of examined alleles and genotypes		χ^2	P	RR	OR	95%CI
	Subgroup "C"	Control					
C	32	171	0.6	0.4	1.3	1.4	0.621-3.020
T	10	39					
C/C	12	69	0.2	0.6	0.9	0.7	0.260-1.800
C/T	8	33	0.3	0.5	1.2	1.3	0.050-3.500
T/T	1	3	0.2	0.6	1.7	1.7	0.168-17.100

3. Conclusions

Thus, the study of the frequency distribution of alleles and genotypes of the IL-1β gene (rs 1143634), allowed us to obtain data indicating a statistically insignificant difference in all the studied groups, in which the distribution of genotype frequencies corresponding to RCM was detected. These data suggest a possible association of the rs 1143634

polymorphism of the IL-1β gene with the development of CP, which requires further study in a larger number of patients.

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