http://dx.doi.org/10.35630/2199-885X/2020/10/27

EFFECT OF THE INTERLEUKIN-1B -511 C/T GENE POLYMORPHISM ON THE COURSE OF DUODENAL ULCER AND EROSIVE GASTRODUODENITIS IN CHILDREN

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ABSTRACT — The effect of the interleukin-1β (IL1β, IL-1β)-511 c/t gene polymorphism on the characters of the pattern and the course of erosive gastroduodenitis (EG) and duodenal ulcer (DU) in children was studied. It was proved that the T\T genotype is predisposing to the development of duodenal ulcer and is associated with the onset of the disease at an early age. Associations of the C\T genotype with a typical phenotype of diseases were found while the C\C genotype is associated with a high significance of the genetic factor in the development of the disease.

KEYWORDS — duodenal ulcer (DU), erosive gastroduodenitis (EG), children, -511 c/t polymorphism, gene, IL-1β.

INTRODUCTION

Today the duodenal ulcer and the erosive gastroduodenitis are a multifactorial systemic disease with a polygenic inheritance. Currently, the study of the genetic basis of the immune response in duodenal disease in children, particularly the polymorphisms of IL-1β genes, allows expanding the etiopathogenetic ideas about the disease and identifying genetic risk factors for certain complications and course options which can promote a personalized approach to the treatment of diseases [1, 2]. The study was aimed to evaluate the effect of the interleukin-1β-511 c/t gene polymorphism on the course of duodenal ulcer and erosive gastroduodenitis in children.

MATERIALS AND METHODS

100 patients with gastroduodenal erosions and ulcers (the main group) were examined: 46 children with the duodenal disease (1st subgroup) and 56 children with the erosive gastroduodenitis (2nd subgroup). The mean age of diagnosing was 8.14 ± 0.25 years (3–17 years). The control group for genetic research included 100 healthy residents of Astrakhan. To perform molecular genetic analysis the total DNA was extracted from whole blood samples using the standard phenol-chloroform extraction method. Genotyping of polymorphic markers of the studied gene was carried out using polymerase chain reaction and analysis of restriction fragment length polymorphism. Statistical analysis was performed using the Statistica for Windows software package.

RESULTS AND DISCUSSION

When analyzing the frequencies of the T\T, C\T, C\C genotypes and the T and C alleles of IL1β (-511c/) there were no significant differences between the control and the main groups. Thus, there is no association between the T\T, C\T, C\C genotypes and the C and T alleles of the IL1β (-511c/t) gene polymorphism with erosive and ulcerative lesions of the gastrointestinal tract. There were no significant differences in the occurrence of C T alleles and T\T, C\T, C\C genotypes of IL1β (-511c/t) gene polymorphism in the control group and patients of the first subgroup, as well as in the control group and patients of the second subgroup ($\chi^2 = 0.846$, df2; $p = 0.655$ and $\chi^2 = 3.119$, df2; $p = 0.211$, respectively).

According to the data the T\T genotype is *predisposing* to the development of duodenal ulcer in children among the cohort of patients with gastroduodenal erosions and ulcers (Table 1). According to the data it was found that patients of the first subgroup with the C\C genotype had more often a genetic predisposition than those ones with the combination of the T\T + C\T genotypes ($\chi^2 = 4.221$; df1; $p = 0.040$; OR = 4.583 (CI 1.254–16.748)). No significant differences between the alleles in the study group were found ($\chi^2c = 0.915$; df1; $p = 0.339$).

It was found that the C\C genotype is *protective* for the development of erosive gastroduodenitis in children under 12 age (Table 2) while the T\T genotype is *predisposing* to the development of duodenal ulcer in young children (that is up to 12 years) in relation to patients of the older age group (Table 3).

We have analyzed the effect of genotypes and alleles of IL1β (-511c/t) gene polymorphism on the phenotypic manifestations of diseases in the patient group (Table 4) and in isolation in children of the first and second subgroups. It was found that the C\T genotype is *predisposing* to a typical disease pattern

Table 1. *Distribution of genotype and allele frequencies of IL1β (-511c/t) in children of the first and second subgroups*

Subgroup / genotype	DU n=46	EG n=54	χ^2 (df); p χ^2 = 5,553, df2; p = 0,063
T\T	8 (17,4%)	2 (3,7%)	χ^2 = 3,762; df1; p=0,053 Fisher test 0,04076; p < 0,05 OR=5,474 (CI 1,100–27,247)
C\T	20 (43,5%)	24 (44,4%)	χ^2 = 0,009; df1; p = 0,923
C\C	18 (39,1%)	28 (51,9%)	χ^2 = 1,618; df1; p = 0,204
alleles	n= 66	n=78	
T	28 (42,4%)	26 (33,3%)	χ^2 = 1,261; df 1; p=0,262
C	38 (57,6%)	52 (66,7%)	

Table 2. *Distribution of genotype and allele frequencies of IL1β (-511c/t) gene polymorphism in children with erosive gastroduodenitis depending on age*

age / genotype	children under 12 age n=24	children over 12 years old n=30	χ^2 (df1); p
T\T	2 (8,3%)	0 (0%)	----------
C\T	14 (58,4%)	10 (33,3%)	χ^2 = 3,375; df1; p =0,067
C\C	8 (33,3%)	20 (66,7%)	χ^2 = 4,674; df1; p =0,031 OR = 0,250 (CI 0,080–0,781)
alleles	n=38	n=40	
T	16 (42,1%)	10 (25,0%)	χ^2 = 2,566; df 1; p = 0,110
C	22 (57,9%)	30 (75,0%)	

Table 3. *Distribution of genotype and allele frequencies of IL1β (-511c/t) gene polymorphism in children of the first subgroup depending on age*

age / genotype	children under 12 years old n=6	children over 12 years old n=40	χ^2 (df); p χ^2 = 12,693; df 2; p = 0,002 (p<0,01)
T\T	4 (66,7%)	4 (10,0%)	χ^2 = 11,661 ; p < 0,001 OR = 18,000 (CI 2,468–131,290)
C\T	0 (0%)	20 (50,0%)	----------
C\C	2 (33,3%)	16 (40,0%)	χ^2 = 0,097; p =0,756 Fisher test 1,00000, p >0,05
alleles	n=6	n=60	
T	4 (66,7%)	24 (40,0%)	χ^2 = 1,588; df 1; p = 0,208 Fisher test 0,38874, p>0,05
C	2 (33,3%)	36 (60,0%)	

both in children of the main group (OR = 4.352 (CI 1.841–10.292) and in patients with duodenal ulcer (OR = 4.200 (CI 1.132–15.587)) and with erosive gastroduodenitis (OR = 4.583 (CI 1.442–14.571)) in isolation. At the same time, the C\C genotype appears as *protective* (OR = 0.314 (CI 0.133–0.744)) for the development of the classic pattern of the disease and is reliably associated with the erased symptoms of the disease in children of the main group. There were no significant phenotypic differences between the C and T alleles in the pattern between patients with duodenal ulcer (χ^2 = 0.512; p = 0.475) and erosive gastroduodenitis (χ^2 = 1.257; p = 0.263).

It was found statistical differences in the frequency of the T\T, C\T and T\T genotypes of IL1β (-511c/t) gene polymorphism in the frequency of Helicobacter pylori in the main group and in children with duodenal ulcer. The protective effect of the T\T genotype on the development of HP infection in children of the first subgroup was proved (χ^2 = 20 583; df2; p <0.001; OR = 3 182 (CI 0.721–14 047)) (Table 5).

CONCLUSION

During the study, it was examined the effect of the IL1β -511 c/t gene polymorphism on the characters of the pattern and the course of erosive gastroduo-

Table 4. *Phenotypic variant of the set of symptoms in patients with duodenal ulcer and erosive gastroduodenitis with different alleles and genotypes of IL1β (-511c/t) gene polymorphism*

Diagnosis / genotype	DU + EG (n=100)		χ^2 (df); p
	typical (n= 38)	atypical (n= 62)	χ^2 = 11,863; df 2; p = 0,003
T\T	2 (5,3%)	8 (12,9%)	χ^2 = 0,979; df1; p = 0,372
C\T	25 (65,8%)	19 (30,6%)	χ^2 = 11,810; df1; p < 0,001 OR = 4,352 (CI 1,841–10,292)
C\C	11 (28,9%)	35 (56,5%)	χ^2 = 7,175; df1 ;p = 0,008 OR = 0,314 (CI 0,133-0,744)
alleles	typical (n= 63)	atypical (n= 81)	
T	27 (42,9%)	27 (33,3%)	χ^2 = 1,371; df1; p = 0,242
C	36(57,1%)	54 (66,7%)	

Table 5. *Helicobacter pylori frequency in children with duodenal ulcer and erosive gastroduodenitis with different alleles and genotypes of IL1β (-511c/t) gene polymorphism*

genotype	DU + EG		DU		EG	
	identified n=25	not identified n=75	identified n=9	not identified n=37	identified n=16	not identified n=38
T\T	6 (24,0%)	4(5,3%)	6 (66,7%)	2 (5,4%)	0 (0%)	2 (5,3%)
C\T	8(32,0%)	36 (48,0%)	0 (0%)	20 (54,1%)	8 (50,0%)	16 (42,1%)
C\C	11(44,0%)	35 (50,7%)	3 (33,3%)	15 (40,5%)	8 (50,0%)	20 (52,6%)
χ^2 (df); p	χ^2 = 7,653; df 2; p = 0,022		χ^2 = 20,583; df 2; p <0,001 OR =3,182 (CI 0,721 – 14,047)		χ^2 = 1,015, df 2; p = 0,602	
alleles	identified n=33	not identified n=111	identified n=9	not identified n=57	identified n=24	not identified n=54
T	14 (42,4%)	40 (36,0%)	6 (66,7%)	22 (38,6%)	8 (33,3%)	18 (33,3%)
C	19 (57,6%)	71 (63,9%)	3 (33,3%)	35 (61,4%)	16(66,7%)	36 (66,7%)
χ^2 (df); p	χ^2 = 0,443; df 1; p= 0,506		χ^2 = 1,490; df 1; p =0,223		χ^2 = 0,068, df 1; p = 0,795	

denitis and duodenal ulcer in children. It is proved that the T\T genotype is predisposing for the development of the duodenal ulcer and is associated with the onset of the disease at an early age and HP infection. Associations of the C\T genotype with a typical phenotype of diseases were identified while the C\C genotype is associated with a high significance of the genetic factor in the development of the disease. Thus, the study of the genotypic basis of duodenal ulcer and erosive gastroduodenitis in children is an important task, the solution of which will promote the development of fundamental ideas about the pathogenesis of the disease and the formation of a personalized approach to treating patients.

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