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RESEARCH ARTICLE

Characteristics of Tlr6 Receptor Expression in Patients with Bronchial Asthma

Shamsiev F.M.
Republican Specialized Scientific and Practical Medical Center of Pediatrics, Tashkent, Uzbekistan

Azizova N.D.
Republican Specialized Scientific and Practical Medical Center of Pediatrics, Tashkent, Uzbekistan

Musajanova R.A.
Republican Specialized Scientific and Practical Medical Center of Pediatrics, Tashkent, Uzbekistan

Abdullaeva M.K.
Republican Specialized Scientific and Practical Medical Center of Pediatrics, Tashkent, Uzbekistan

Karimova M.Kh.
Republican Specialized Scientific and Practical Medical Center of Pediatrics, Tashkent, Uzbekistan

Uzakova Sh.B.
Republican Specialized Scientific and Practical Medical Center of Pediatrics, Tashkent, Uzbekistan

Abstract: The aim of this study was to investigate the features of innate immunity receptor (TLR6) expression in patients with bronchial asthma (BA). The study examined 45 pediatric patients with BA aged 5 to 15 years. The comparison group consisted of 31 children with recurrent obstructive bronchitis (ROB). Genetic research methods were used during the comprehensive clinical and laboratory examination of the children. The results demonstrated a significant role of the TLR6 gene in forming predisposition to BA. The obtained data will contribute to a better understanding of the subsequent development of BA involving TLR6.

Key words: Children, bronchial asthma, Toll-like receptor gene.

INTRODUCTION

Bronchial asthma (BA) is a global problem affecting children and adults of all ages. The disease requires constant monitoring due to its chronic course [9]. Bronchial asthma is a chronic inflammatory disease, among the most common allergic diseases, associated with variable airway obstruction and bronchial hyperreactivity, manifested as recurrent episodes of wheezing, coughing, feelings of shortness of breath, and chest tightness [3,8]. It is a multifactorial disease: it develops under the influence of environmental factors in the presence of human genetic predisposition [1,2].

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In recent years, the problem of genetic predisposition to the development of BA has been actively discussed. According to several authors, a genetic component is observed in 60-80% of asthma cases. Numerous studies have proven that genetic factors repeatedly amplify environmental effects in BA patients [7]. The number of studied genetic predictors is constantly increasing [11], which supports the concept of genetic polymorphism in BA.

Promising targets for study in BA are innate immunity receptors (TLRs), which exert their effects at the initial stages of the immune response and largely determine the intensity of immune reactions to microbial and non-microbial allergens [10]. It is known that innate immunity represents the body's first line of defense against pathogens. The key recognition receptors of innate immunity are Toll-like receptors (TLRs), expressed predominantly on cells of the immune system, mucous membranes, and skin [4]. It has been established that TLRs participate in recognizing allergens in the respiratory tract, regulate the activity and polarization of the adaptive Th1, Th2, Th17 immune response, playing an important pathogenetic role in the development of BA [5]. Polymorphic variants of TLR genes can alter their normal reactivity and, consequently, affect immune system formation, contributing to the spread of allergic diseases [6]. Studying the role of Toll-like receptors in allergic inflammation is important for improving prevention and treatment programs for bronchial asthma.

Aim of the study

To investigate the features of innate immunity receptor (TLR6) expression in patients with bronchial asthma.

METHODS

The study included 45 pediatric patients with bronchial asthma aged 5 to 15 years, observed and treated in the allergology and pulmonology departments of the Republican Specialized Scientific and Practical Medical Center of Pediatrics, Ministry of Health of the Republic of Uzbekistan. The comparison group consisted of 31 children with recurrent obstructive bronchitis (ROB). The BA diagnosis was based on the classification adopted by the National Program "Bronchial Asthma in Children. Treatment and Prevention Strategy" in Russia (2006), updated in 2018 in accordance with GINA criteria. Genetic research methods were used during the comprehensive clinical and laboratory examination of the children.

Genetic methods: The study of TLR6 C745T gene polymorphism expression was performed using polymerase chain reaction (PCR). The research was conducted at the "Genotechnology" laboratory.

Statistical analysis of the obtained results was performed using a program developed in Microsoft Office Excel-2010. Variation statistics methods were used, calculating arithmetic means (M), their standard errors (m), and significant differences using the Fisher-Student criterion.

RESULTS AND DISCUSSION

It has been previously reported that the immune response induced upon interaction with TLR6 plays an important role in the development of Th2-associated diseases and may participate in the development of bronchial asthma. The study of polymorphic markers of the TLR6 C745T gene in patients with bronchial asthma differed from control group indicators and is presented in Table 1.

Table 1. Frequency distribution of alleles and genotypes of the C745T polymorphism of the TLR6 gene in examined children

No.	Groups	Allele frequency	Genotype distribution frequency			
		T,%	C,%	C/C,%	C/T,%	T/T,%

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1.	Control group (n=20)	2 (5.0)	38 (95.0)	18 (90.0)	2 (10.0)	-
2.	ROB (n=31)	16 (38.0)	26 (62.0)	9 (42.9*)	8 (38.1**)	4 (19.0)
3.	BA (n=24)	24 (50.0)	24 (50.0)	7 (29.2**)	7 (41.7**)	7 (29.2)

Note: * - significance relative to control group (* - P<0.05; ** - P<0.01); ^ - significance relative to ROB children (^ - P<0.05); a - significance relative to BA children (a - P<0.05).

The study results in children from the control group showed a predominance of the C allele of the TLR6 C745T polymorphism, which occurred in 95% of children, compared to the T allele at 5% (Table 1).

In children with BA, a predominance of the T allele was observed, 14 times higher than control group indicators (P <0.001). In the control group, the C/C genotype of the TLR6 C745T polymorphism was observed in 90.0% of cases, while the heterozygous C/T genotype occurred in 10% of cases. During the development of BA in children, a predominance of heterozygous genotypes of the TLR6 C745T polymorphism was established, accompanied by a reduced occurrence of the homozygous C/C variant.

It is also worth noting that the homozygous TT genotype of the TLR6 C745T polymorphism occurs only in sick children; this genotype is absent in practically healthy children. The homozygous C/C genotype of the TLR6 C745T polymorphism is associated with a reduced risk of developing ROB and BA. An association of the T/T genotype with the development of BA and ROB in children has been proven (χ^2 with Yates' correction = 3.859, p=0.038, df=1, OR=2.985 (CI 1.085–6.989)); this polymorphism is predisposing to the development of BA and ROB. The relative risk of developing bronchial asthma in patients with the major T allele is 1.99 (95% CI: 1.19–3.31).

Thus, it can be assumed that carriage of the polymorphic marker TLR6 745T is a genetic risk factor for the development of BA and ROB, while the presence of the homozygous genotype for the minor 745C allele reduces the risk of developing BA and exhibits protective properties.

CONCLUSION

Carriage of the polymorphic marker TLR6 745T is a genetic risk factor for the development of BA and ROB, while the presence of the homozygous genotype for the minor 745C allele reduces the risk of developing BA and exhibits protective properties.

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