WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 3, Issue 5, May., 2022

SOME MOLECULAR GENETIC ASPECTS OF THE FORMATION OF PREDISPOSITION TO BRONCHIAL ASTHMA

Turdibekov Husan Ibragimovich
Assitant of the deportament of Ftiziopulmonologii, Samarkand State Medical University Samarkand, Republic of Uzbekistan.

Nizomov Bakhtiyor Urakovich
Assistant Deportment of Internal Medicine Pediatric fakulty, Samarkand State Medical University Samarkand, Republic of Uzbekistan.

Toshnazarov Shuxratillo Mizamovich
Assistant Deportment of Internal Medicine Pediatric fakulty, Samarkand State Medical University Samarkand, Republic of Uzbekistan.

Turkmanov Ma'mur Matmusaevich
Assistant Deportment of Internal Medicine Pediatric fakulty, Samarkand State Medical University Samarkand, Republic of Uzbekistan.

Abstract
It is known that activation of the β2-adrenergic receptor leads to a rapid relaxation of bronchial smooth muscle cells and an increase in the airway lumen; There fore, in BA, the attention of researchers is focused specifically on possible dysfunctions of the β2-adrenergic receptor, which may be important in the pathogenesis of the disease. The regulatory effect of β2-agonists on the production of cytokines by Th cells was studied [5,8], where β2-agonists have a stimulating effect on the production of IFN-γ, IL-2, and also block the production of IL-4, IL-13 by isolated T cells. . In this regard, the search for an association of the ADRB2 gene with a predisposition to BA has been the task of many studies [6,10,12]. According to genotyping data, a number of studies have established a link between the Gln27Glu polymorphism of the ADRB2 gene and bronchial hyperreactivity [7,9,13].

Keywords: bronchial asthma, cytokine, disease, β2-agonists, gene, polymorphism.

Relevance

According to modern ideas, bronchial asthma (BA) - is a multifactorial disease characterized by a plurality of clinical phenotypes that are caused by the interaction of different genes and the interaction of environmental factors that cause the

appearance of symptoms. With the development of the program "Human Genome" has become possible to conduct the study of the whole genome. As a result of these studies were verified candidate portions structural changes, which contribute to the formation of BA. Candidate genes in asthma include IL-4 genes, β2-adrenergic receptor (ADRB2), TNF-β, IFN-γ, T cell receptor, mast cells and other proteins [1-4,11]. Variability pharmacological response β2-agonists and contradictory literature data obtained in evaluating the effectiveness of therapy of the respiratory function in BA patients with different genotypes of polymorphic variants of a gene ADRB2, determine the relevance subsequent studies.

Purpose of the Study

Analysis of the association of the Gln27Glu polymorphic locus of the ADRB2 gene with various pathogenetic variants of BA, as well as with the main parameters of external respiration.

Material and Methods

A total of 130 people of Uzbek nationality in the 3 rd generation (the survey was conducted before the third degree of consanguinity), including 83 patients with asthma. Patients with asthma are divided into groups according to the international classification of WHO and by the diagnostic criteria of GINA in 2006 to carry out a comparative analysis of the clinical and pathogenetic variants of asthma based on differential-diagnostic criteria allocated 31 patients with allergic asthma (37%), 24 patients with non-allergic asthma (NBA) (29%) and 28 patients with mixed BA (MBA) (34%). The average age of the patients was 42,5 ± 1,41 years. The control group consisted of 47 healthy individuals. External respiration was studied alone for spirograph «SPIROSIFT SP-5000» (Fukuda DENSHI, Japan) with automatic processing parameters. The results were evaluated according to the boundaries of rules and gradation abnormalities performance curve "flow-volume": forced vital capacity (FVC), forced expiratory volume in one second (FEV1), maximum volumetric curve velocity at points corresponding to the volume of light of 75%, 50%, 25% (MOS75, MOS50, MOS25). Since the estimate of the patient at the beginning levels of respiratory function is fairly approximate and does not reflect the reversibility of bronchial obstruction (BO), it seemed appropriate to analyze the active component in patients with asthma, depending on the clinical disease pathogenic variant. After fixing the initial parameters of spirometry patient inhalation offered two doses 2-short-acting agonist (salbutamol). Then, after 10 and 30 minutes was repeatedly performed spirometry. Sample results were assessed by FEV1. The calculation was

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 3, Issue 5, May., 2022

performed by the formula reversibility ratio measuring absolute increase in FEV1 index, expressed as a percentage of the proper:

$$\Delta ОФВ_1 = \frac{ОФВ_{1дилат}\,(мл) - ОФВ_{1исх}\,(мл)}{ОФВ_{1\ долж}(мл)} \cdot 100\%$$

where ΔFEV1 is the increase in the indicator, FEV1 ref. - initial value, FEV1 dilat. - indicator after bronchodilatory test, FEV1 due - due value.

BO considered positive for growth in FEV1 of 15% or more.

Isolation of DNA from whole blood was carried out a set of reagents Diatom ™ DNA Prep 200 (production of "Laboratory isogene", Moscow, Russia). Isolation of DNA was carried out according to standard protocols for the isolation of DNA using a set of DNA Prep 200. supernatant DNA Diatom ™ reagents more directly subjected to genotyping by PCR amplification. DNA typing samples of ADRB2 gene was performed using two pairs of oligonucleotide primers specific portions ADRB2 gene - Forward 5'-CCGGACCACGACGTCACCCAG-3 '; Reverse 5'-CCAGTGAAGTGATGAAGTAGTT-3 '. PCR analysis was performed using a reagent kit for PCR amplification of DNA GenePak ™ PCR Core (production of "Laboratory isogene"). PCR amplification was performed according to standard protocol. Data obtained in the study were subjected to statistical analysis on Pentium-IV PC using Microsoft Office Excel-2003 software package, including the use of built-in statistical processing functions.

Results

Analysis of the frequency of occurrence of the alleles and genotypes Gln27Glu polymorphism ADRB2 gene among patients depending on the clinical pathological embodiments of the process showed that the Gln27 allele in patients ABA occurs significantly more frequently than in the group of healthy individuals (86% compared with 70.2%, respectively , χ2 = 4,2; R 0,05). Consideration polymorphism genotypes found that in this subgroup of patients the frequency of homozygous gene variants Gln27Gln significantly higher than in the control group of healthy individuals (73% vs. 44.6%, respectively, χ2 = 4,7; R 0,05). At the same time Gln27Glu heterozygote frequency in patients ABA was markedly lower level characteristic for healthy individuals part of the surveyed population (27% versus 51%, respectively, χ2 = 3,5). Options Glu27Glu homozygous genotype among patients with ABA were observed.In patients with non-allergic asthma (NBA) revealed the following values in frequency polimornyh markers: Gln27 allele – 73,5%, Glu27 – 26,5%; genotype Gln27Gln – 47%, Gln27Glu – 53% of patients with genotype Glu27Glu were noted. Patients with mixed bronchial asthma (MBA) these figures, respectively, accounted for 69%, 31%;

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 3, Issue 5, May., 2022

48%, 43% and 9%. Thus, the analysis of features of the genotype in groups of patients non-allergic asthma (NBA) and mixed bronchial asthma (MBA) showed no significant statistically significant differences in allele and genotype frequencies of the polymorphism Gln27Glu ADRB2 gene compared with the control group of healthy individuals.

Overall, these data suggest the existence of unions, c the one hand, the genotype Gln27Gln gene ADRB2, and on the other carrier Gln27 allele with allergic asthma form. Determination of FER as a valuable method for diagnosing AD, is the criterion for determining the severity of the pathological process. FEV1 values increase when analyzing severe asthma patients varied considerably as parameters the above group of patients with moderate asthma, and when a comparison between different groups of individuals with AD pathogenic variants (Table. 1).

Table 2 Increase in FEV1 during bronchodilation test in patients with BA depending on the form of the disease

Form of the disease	Severe asthma, n=51		
	ABA, n=17	NBA, n=14	MBA, n=20
ΔFEV1 %	23,5±1,47	18,6±1,5*	21,5±1,50

Note: * - differences are significant relative to the data of the AAA group P<0.05

The most pronounced reaction to the β2-agonist has been identified in patients with severe ABA (23,5 ± 1,47%) and the MBA (21,5 ± 1,50%). Salbutamol bronchodilation effect was less pronounced in patients NBA (18,6 ± 1,54%), when compared with other groups.

We evaluated the BO and the frequency of occurrence of alleles and genotypes ADRB2 gene in position 27 of the Uzbeks (Table. 3).

Table 3 Association of genotypes of the β2-adrenoreceptor gene in the 27th position of salbutamol efficiency

Genotype	Gln27Gln	Gln27Glu	Glu27Glu	*P*1– 3	*P*2–3	*P*1– 2
% increase in FEV1 at position 27	23,5±3,47	19,5±2,50	17,6±3,54	< 0,05	< 0,01	ND

As seen from Table 3, depending on embodiment of asthma ADRB2 gene polymorphisms in 27 position has been found that patients of asthma, Uzbeks having genotype Gln27Gln, on bronchodilation β2-agonist (salbutamol) respond significantly greater increase in FEV1 (increase of 23.5 ± 3,47%), than those with genotype Glu27Glu (increase of 17,6 ± 3,54%)

Conclusions

When studying Gln27Glu polymorphisms in the ADRB2 gene Uzbekistan population revealed the predominance frequency Gln27Gln genotypes among AD patients compared with healthy part of the population. The severity association studied genetic markers varies depending upon clinical disease pathogenic variant. An increased risk of allergic forms of asthma associated with Gln27 allele and genotype Gln27Gln polymorphic locus Gln27Glu gene ADRB2.

Thus, in the study according BO from clinical disease pathogenic variant was determined that patients with the most pronounced characteristic NBA reduction BO growth. In general, the analysis of indicators of respiratory function showed that in patients with asthma are severe violations of ventilating function of lungs of a mixed character with a predominance of obstruction of bronhiticheskomu type. Joining restrictive respiratory component failure can be attributed to the deterioration of the elastic properties of the lung, the addition of pulmonary fibrosis, emphysema, respiratory muscle exhaustion. Some decrease RF patients with severe asthma, probably has a connection with a partial desensitization β2-adrenoretseptsii observed against the background of intensive care β2- agonists. According to the results of our studies, gene polymorphism β2-adrenoceptor bronchi in patients with asthma Asthma affects Uzbeks bronchodilator effect of β2-agonists, in particular Glu27Glu polymorphism reduces and Gln27Gln Gln27Glu polymorphisms and improve the sensitivity of β2-adrenergic receptors to the β2-agonists.

References

1. Karunas AS, Izmailov, AR, Zagidullin Sh.Z., Khusnutdinova EK Study of molecular-genetic basis of susceptibility to asthma in Bashkortostan // Medical Genetics. - 2004. - №6. - S. 284-290.
2. Paponov VD, Paponov VV, Baidakova GV abnormal manifestations of the human genetic apparatus in pathology and prospects for improving the treatment of diseases of various etiology // Ter. archive. - 2004. - №1. - S. 82-87.
3. Turdibekov HI, Umarov AA Haitova NM Aripova TW, TA Petrova Study of serum levels of immunoregulatory mediators in different variants of bronchial asthma with severe // Immunology. - Moscow, 2008. - № 6. - S. 354-356.
4.Турдибеков Х., Агабабян И., Низомов Б. ИССЛЕДОВАНИЕ УРОВНЯ СЫВОРОТОЧНЫХ ЦИТОКИНОВ ПРИ РАЗЛИЧНЫХ ФОРМАХ БРОНХИАЛЬНОЙ АСТМЫ С ТЯЖЕЛЫМ ТЕЧЕНИЕМ //Журнал кардиореспираторных исследований. – 2020. – Т. 1. – №. 1. – С. 95-98.

6. Шодиева Г. Р., Улугбеков К. У. У. НЕИНВАЗИВНЫЙ МЕТОД ОЦЕНКИ СТЕПЕНИ ОБСТРУКЦИИ БРОНХОЛЕГОЧНОЙ СИСТЕМЫ У БОЛЬНЫХ БРОНХИАЛЬНОЙ АСТМОЙ //Современные инновации. – 2020. – №. 4 (38). – С. 15-17.
7. Шодиева Г. Р., Ибрагимова Э. Ф. КОМОРБИДНОСТЬ ПРИ БРОНХИАЛЬНОЙ АСТМЕ //БАРҚАРОРЛИК ВА ЕТАКЧИ ТАДҚИҚОТЛАР ОНЛАЙН ИЛМИЙ ЖУРНАЛИ. – 2022. – С. 264-266.
8. Тошназаров Ш. М. и др. Эффективность дигитализации-дигоксином у больных с хронической сердечной недостаточностью //Фундаментальные основы инновационного развития науки и образования. – 2019. – С. 175-177.
9. Matheson M. C., Ellis J. A., Raven J. Beta 2-adrenergic receptor polymorphisms are associated with asthma and COPD in adults // J. Hum. Genet. - 2006. - Vol.51, №11. - P. 943-951.
10. Тошназаров Ш. М. и др. Эффективность применения бета-блокаторов при лечении дилятационной кардиомиопатии, осложненной хронической сердечной недостаточностью II б стадии (по NYHA III ФК) //International scientific review. – 2019. – №. LXV. – С. 107-108.
11. Шодиева Г. Р. Роль Цитокинов у больных циррозом печени вирусной этиологии //Вестник науки и образования. – 2020. – №. 10-4 (88). – С. 104-106.
12. Turdibekov H.I., Ziyadullaev Sh. Kh., Kholliev R.Kh. Significance of β2-adrenoreeptor gene polymorphism molecular genetic mechanisms of formatiton of bronchial asthma // International Journal of Pharmaceutical Research. - Jan - Mar 2020. - Vol 12 / Issue 1. - P.1243-1249
13. Шодиева Г. Р., Низомов Б. У. Роль функциональной диагностики в оценке степени обструкции дыхательных путей при бронхиальной actme //Наука и образование сегодня. – 2020. – №. 5 (52). – С. 81-82.