ROLE OF T-31C POLYMORPHISM OF IL-1β GENE IN RECURRENT BRONCHITIS IN CHILDREN

Sharipova O.A.[1], Bahranov Sh.S.[2], Khamidov F.O.[3] (Republic of Uzbekistan)
Email: Sharipova579@scientifictext.ru

[1]Sharipova Oliya Askarovna – Doctor of Medical Sciences, Professor;
[2]Bahranov Sherzod Samievich – Assistant,
DEPARTMENT 3 PEDIATRICS AND MEDICAL GENETICS;
[3]Khamidov Fozilbek Olimovich – Student,
PEDIATRIC FACULTY,
SAMARKAND MEDICAL INSTITUTE,
SAMARKAND, REPUBLIC OF UZBEKISTAN

Abstract: *the analysis of the associative relationship of the gene polymorphism in the IL-1β promoter region in positions (T-31C) with the risk of developing RB in 93 children with recurrent bronchitis aged 2 to 7 years and in 110 apparently healthy children of the same age in the Uzbek population.*
The results of the study showed statistically significant differences in the frequency distribution of alleles and genotypes of the -31 T> C polymorphic locus of the IL-1β gene in patients with RB. The frequency of the unfavorable C and C / C allele of the genotype was significantly more often determined in RB patients against the background of LGD, which indicates a predisposing role of the rs 1143627 polymorphism of the IL-1β gene to the development of recurrent bronchitis in children of the Uzbek population.
Keywords: *recurrent bronchitis, lymphatic-hypoplastic diathesis, gene polymorphisms, cytokines.*

РОЛЬ ПОЛИМОРФИЗМА Т-31С ГЕНА ИЛ 1b ПРИ РЕЦИДИВИРУЮЩИХ БРОНХИТАХ У ДЕТЕЙ

Шарипова О.А.[1], Бахранов Ш.С.[2], Хамидов Ф.О.[3] (Республика Узбекистан)

[1]Шарипова Олия Аскаровна - доктор медицинских наук, доцент;
[2]Бахранов Шерзод Самиевич - ассистент,
кафедра 3 - педиатрии и медицинской генетики;
[3]Хамидов Фозилбек Олимович - студент,
педиатрический факультет,
Самаркандский медицинский институт,
г. Самарканд, Республика Узбекистан

Аннотация: *проведен анализ ассоциативной связи полиморфизма гена промоторной области IL-1β в позициях (Т-31С) с риском развития РБ у 93 детей в возрасте от 2 до 7 лет и у 110 условно-здоровых детей того же возраста в Узбекской популяции.*
Результаты исследования показали статистически значимые различия в распределение частот аллелей и генотипов полиморфного локуса -31 T>C гена IL-1β у больных РБ. Частота неблагоприятного аллеля С и С/С генотипа достоверно чаще определялся у больных РБ на фоне ЛГД, что свидетельствуют о предрасполагающей роли полиморфизма rs 1143627 гена IL-1β к развитию рецидивирующих бронхитов у детей узбекской популяции.
Ключевые слова: *рецидивирующий бронхит, лимфотико-гипопластический диатез, полиморфизм генов, цитокины.*

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The pathology of the respiratory tract in children is an urgent problem in pediatrics and has medical and social significance [1; 2; 8]. One of the most common nosological forms of respiratory tract damage in children is bronchitis [5,6]. In the Republic of Uzbekistan, according to statistical data, in the structure of the general morbidity, respiratory diseases make 24 persons per 100,000 population [9].

The proportion of recurrent bronchitis (RB) is increasing. Thus, the prevalence of RB in children is currently 2.5 per 1000 children [1, 7].

RB is common in young and preschool children [8]. Despite the fact that the problem of treatment and prevention of bronchitis in children is well covered in the literature, the genetic basis remains poorly studied. In this regard, it is relevant to identify and study genetic markers in children with RB [3,4]. Based on the current data on the pathogenesis of respiratory tract damage in children, the genes of pro- and anti-inflammatory cytokines are candidate genes and are closely associated the development and clinical course of these diseases [5,6].

Purpose of the study: To study the clinical significance and frequency of distribution of alleles and genotypes of the T-31C polymorphism of the IL-1β gene in children with recurrent bronchitis (RB) against the background of lymphatic-hypoplastic diathesis (LGD).

Materials and research methods: The study included 62 sick children aged 2 to 7 years with RB, who made up the main group. The control group consisted of 65 conditionally healthy children of the same age. Patients of the

main group were divided into 2 subgroups: subgroup I of 32 children with recurrent bronchitis, subgroup II consisted of 30 patients with RB on the background of LGD.

Objective, loboratorial and instrumental examinations of children were carried out according to the generally accepted clinical method.

In all patients with RB, with LGD, as well as conditionally healthy children of Uzbek nationality, who made up the control group, PCR genotyping of the T-31C polymorphism of the IL-1 β gene was performed in the laboratory of molecular genetics of the Research Institute of Hematology and Blood Transfusion. Blood sampling was carried out on an empty stomach from the cubital vein of the examined children under sterile conditions. DNA isolation from peripheral blood was performed using a standard Ribo-sorb kit (AmpliSens®, Russia). PCR genotyping of the T-31C polymorphism of the IL-1β gene was carried out using an Applied Biosystems 2720 thermal cycler (USA), using a test kit from OOO Litekh (Moscow) according to the manufacturer's instructions.

The estimation of the deviation of the frequencies of the observed and expected genotypes from the canonical Hardy-Weinberg distribution was carried out using the computer program "Gene Pop". The coefficient of deviation was calculated using the formula: D = (Hobs-Hexp) / Hexp, where: hobs and hexp-observed and expected heterozygosity, respectively.

The software package "R - programming language for statistical data processing" was used as a tool for statistical calculations.

Results. To assess the associative relationship of the rs1143627 polymorphism of the IL-1β gene with the risk of developing RB, a comparative analysis of the distribution of allele and genotype frequencies in the studied groups of patients and controls was carried out.

It was revealed that the frequency of distribution of genotypes and alleles of T-31C polymorphism of the IL-1β gene in both groups corresponded to the expected Hardy-Weinberg equilibrium law ($p < 0.05$).

The frequency of distribution of the T and C alleles of the IL-1β gene in the main group was: 68.5% and 31.5% (71.8% and 28.2% in the subgroup C RB and 59.7% and 40.3% - in the subgroup with RB on the background of LGD, respectively) and in the control group - 77.3% and 22.7%, respectively.

Statistical processing revealed a significant increase in the frequency of the unfavorable C allele, which showed a significant association with the disease (RR = 1.4; 95% CI: 1.031-2.375, $\chi 2 = 4.4$; $p < 0.03$).

The analysis of the distribution of T/ T genotypes in the main group of patients was 49.6% (53.2% - in the subgroup with RB and 38.7% - in the subgroup with RB on the background of LGD), in the control group 61.8% were recorded. Indicators of the homozygous T/T genotype tended to decrease compared to the control group. The frequency of heterozygous carriage of the T/C genotype in the main group of patients was 37.8% (37.1% in the subgroup with RB and 41.9% in the subgroup with RB against the background of LGD) in the control group there were 30.9%. Indicators of heterozygous carriage of the T/C genotype in the main group of patients tended to increase.

Analysis of the frequency of distribution of the mutant C/C genotype of the T-31C polymorphism of the IL-1β gene was 1.7 times increased in the main group of patients - 12.6% (1.32 times 37.1% - in subgroup I and 2.65 times 41, 9% - in the II subgroup). In the control group, 7.3% were recorded (RR = 1.7; 95% CI: 0.747-4.525, $\chi 2 = 1.8$; $p < 0.2$).

The results obtained on the T-31C polymorphism of the IL- 1β gene showed a high frequency of occurrence of the mutant C allele among RB patients against the background of LGD compared with the control group. This fact allows us to make an assumption about the functional significance of the 31C allele carriage in the development of RB in children with LGD.

Conclusion: Thus, as a result of the study of the T-31C polymorphic locus of the IL-1β gene in patients with recurrent bronchitis and RB against the background of LGD, marked differences in the distribution of allele and genotype frequencies between the group of patients and healthy individuals in the Uzbek population were found. In the presence of an unfavorable allele C, the risk of developing RB increases by more than 1.7 times in patients with RB on the background of LGD 2.65 times ($\chi^2 = 3.9$; P = 0.05; OR = 3.1; 95% CI 0.973, 9.619), which indicates a fairly independent and separate effect of the T-31C polymorphism of the IL-1β gene on the risk of developing recurrent bronchitis against the background of lymphatic-hypoplastic diathesis one.

References / Список литературы

1. *Bobomurotov T.A., Sharipova O.A., Yusupova U.U., Bakhronov Sh.S., Abdurakhmanov Zh.N.* The influence of ecological environment on the homeostatic system and the level of interleukins at acute bronchitis in early age children // Central Asian Journal of Medicine. V 0l, 2020. № 1. Pp. 84-91.
2. *Fishwick D., Sen D., Barber C. et al.* Occupational chronic obstructive pulmonary disease: a standard of care. Occup. Med. (Lond.), 2015; 65 (4): 270-282. DOI: 10.1093/occmed / kqv019.
3. *Henao M.I., Montes C., Paris S.C., Garcia L.F.* Cytokine gene polymorphisms in Colombian patients with different clinical presentations of tuberculosis. Tuberculosis, 2006. Vol. 86. Pp. 11-19.
4. Polymorphisms in the transforming growth factor-beta 1 gene and risk of asthma: a meta-analysis/ Y. Zhang, J. Zhang, J. Huang [et al.] // Respirology, 2010. Vol. 15.P. 643-650.
5. *Nesterenko Z.V.* Recurrent bronchitis as a phenotypic variant of acute bronchitis in children. Ukrainskij medichnij visnik, 2012; 15: 6: P. 121-123.

6. *Polyakov V.V., Senatorova A.S.* The clinical significance of endothelial dysfunction in children with recurrent obstructive bronchitis and bronchial asthma. Mezdunarodnij meditsinskij zhurnal, 2012; 2:32-36. (Ukr).
7. Polymorphisms in the transforming growth factor-beta 1 gene and risk of asthma: a meta-analysis / Y. Zhang, J. Zhang, J. Huang [et al.] // Respirology, 2010. Vol. 15. P. 643-650.
8. *Sharipova O.A., Bobomuratov T.A., Bahranov Sh.S.* Features of physical development and bone mineral density in children with chronic bronchitis. European science review. Austria. Vienna, 2016. № 11-12. P. 96-100.
9. Statistical materials on the activities of healthcare institutions of the Republic of Uzbekistan in 2015. Tashkent, 2016.