616.2-022.7-053.2:575.113

THE SINGLE POLYMORPHISM OF IL-1B(C-511T) GENE IN CHILDREN WITH RECURRENT RESPIRATORY INFECTIONS

Levytska S.A., Gozhenko A.I., Shustik R.P. Gashinskiy I.V.
Bukovinian State Medical University (Chernivtsi)
Ukrainian Scientific Research Institute of Transport Medicine

An analysis of single nucleotide polymorphism of the interleukin 1в gene was carried out in 80 children with frequent recurrence of respiratory infection and 35 healthy children. A predomination o the «wild» C-allele among the examinees has been established (63,04 %). A decrease of the shore of the heterozygotic CT variant and an increase of the frequency of the occurrence of homozygotes turned out to be typical for children with frequent recurrence of respiratory infection. The absence of «minor» T-allele of C-511T polymorphism of IL-1в gene in child is the risk factor of the development of frequent recurrence of respiratory infection (OR-3,55).

Key words: genetic polymorphism, interleukin 1в, recurrence of respiratory infection.

The general practitioners and pediatricians 4,5-5 million of cases of acute respiratory viral infections (ARVI) in children and the proportion of children with recurrent respiratory infections (RRI) is from 30% to 70% [3].

The topicality of the study of mechanisms of development of RRI in children is associated not only with their prevalence but high probability of complications [4].

Since the immune component has represented in the development of any inflammation, the immunological features of the response against pathogen invasion can be decisive in the resolution on respiratory tract infection [1].

The strength and direction of immune response of the body is largely genetically determined and connected with inherited levels of cytokines production [2]. The mutation of genes encoding components of the immune response may be the basis of genetically determined susceptibility to RRI in children.

Studying of influence of single mutations of gene of IL-1в (C-511T) on the prognosis of development of RRI in children was **a research objective**.

Materials and Methods

An analysis of single nucleotide polymorphism of the IL- 1в (C-511T) gene was carried out in 115 children divided into two groups. The first group consisted of 80 children with five or more episodes of ARVI during last year with the duration of the episode at least 7 days. The control group consisted of 35 children with less then five short-term episodes f ARVI. The both groups were comparable by age and sex criteria (c^2=0,97; p=1,00).

The concentration of IL-1в was determined using a diagnostic test system (ООО "Cytokine", St. Petersburg, Russia) by ELISA.

DNA allocated from lymphocytes was material for molecular and genetic research. PTsR-reaction was carried out with use of a Taq-DNA-polymerase and specific primers [4]. The result of amplification process was 305-bp-DNA-fragment from the 562th to the 756th nucleotide pairs of promoter zone of IL-1в gene. Discrimination of alleles was carried out by using of specific endonuclease of restriction AVA I («Fermentas®», Lithuania). We identified a "mutant" AVA resistant T-allele and a "wild" C-allele.

Statistical analysis of the results was performed using the program «Statistica 6" with the calculation of Student (t) and non-

parametric ^{2} criteria. Odds ratio (OR) was calculated to evaluate the studied parameters as a risk marker.

Results and discussion

The dominance of a "wild" C-allele among groups was revealed as result of our research: 63,04% (n=145) of 230 alleles had C (tsitizin) in 511 position of promoter of a gene IL-1в as well as "mutant" T-allele was revealed in 36,96 % (n=90) of cases (tab.).

In control group there were the higher frequency of the T-allele (45,71% in comparison with 33,12% in group with RRI, tab. 1) but with no statistically significant difference (p>0,05).

We found equally often the homozygotes by C-dominant allele (42.61%) and heterozygotes (40.87%; tab.) among children of both groups. The frequency of homozygotes by "mutant" T-allele was the lowest and amounted to 16.52%.

Table 1

The results of research of C-511T polymorphism of IL-1β gene

	Groups		Odds ratio (95 % CI)
	RRI (n = 80)	Control (n = 35)	
C-allele	107 (66,88 %)	38 (54,29 %)	
T-allele	107 (66,88 %)	38 (54,29 %)	0,28 (95 %CI — 0,11-0,70)
CC-genotype	41 (51,25 %)	8 (22,86 %)	3,55 (95 %CI — 1,42-8,94)
CT-genotype	25 (31,25 %)	22 (62,86 %)	0,31 (95 %CI — 0,14-0,70
TT-genotype	14 (17,5 %)	5 (14,29 %)	

Dominance of CC-homozygotes in group with RRI chidren was revealed (51,25%). The percentages of heterozygotes and T-"mutant"- homozygotes were lower and were 31,25% and 17,50% respectively (tab.).

There was the highest amount of the owners of heterozygotes (62,86%, n=22, tab.) in control group. The percentage of heterozygotes was twice as the corresponding parameter in RRI children.

There were less carriers of a CC-genotype (22,86%) and a TT-genotype (14,29%) in control group in compare with RRI children.

It is established that the CC-genotype of the C-511T polymorphism of the IL-1в gene was associated with high risk of development of RRI in children (OR-3,55, tab.), while the presence of "mutant" T-allele of this polymorphism was a protective factor (OR-0,28).

Conclusions

1. The determining of the distribution of single polymorphism of IL-1в gene (C-511T) showed a prevalence of cytosine at position 511 of promoter zone among children with recurrent respiratory infections and among their healthy peers. There were equally frequencies of heterozygotes and CC-genotype of C-511T polymorphism among children.
2. The lower percentage of heterozygotes and the higher percentage of homozygotes were found among children with recurrent respiratory infections.
3. The high risk of the development of recurrent respiratory infections is associated with the absence of the T-allele of the C-511T polymorphism of IL-1в gene.

References

1. Mfuna Endam L. Association of IL1A, IL1B, and TNF gene polymorphisms with chronic rhinosinusitis with and without nasal polyposis: A replication study / L.Mfuna Endam, C.Cormier, Y.Bossй, A.Filali-Mouhim, M.Desrosiers // Arch Otolaryngol Head Neck Surg. – 2010. – Vol.136(2). – P.187-192.
2. RSV respiratory infection in children under 5 y.o.—dynamics of the immune response Th1/Th2 and IgE / W.Gut, K.Pancer, E.Abramczuk [et al.] // Przegl. Epidemiol. – 2013. – Vol.67(1). – P.17-22
3. Salah M. Recurrent acute otitis media in infants: Analysis of risk factors / M.Salah, M.Abdel-Aziz, A.Al-Farok, A.Jebrini // Int. J, Pediatr. Otorhinolaryngol. – 2013. – Vol.77(10). – P.1665-1669.
4. Tewfik M.A. Genetics of chronic rhinosinusitis: a primer / M.A.Tewfik, Y.Bossй, H.Al-

Shemari, M.Desrosiers // J.Otolaryngol.Head.Neck.Surg. - 2010. – Vol.39, №1. – P.62-68.

Резюме

ОДИНОЧНЫЙ ПОЛИМОРФИЗМ ГЕНА IL-1 (C-511T) У ДЕТЕЙ С РЕЦИДИВИРУЮЩИМИ РЕСПИРАТОРНЫМИ ИНФЕКЦИЯМИ

Левицкая С.А., Гоженко А.И., Шустик Р.П., Гашинский И.В.

Буковинский государственный медицинский университет (Черновцы)

Украинский научно-исследовательский институт медицины транспорта

Анализ однонуклеотидного полиморфизма 1в гена интерлейкина IL-1 проводили у 80 детей с частыми рецидивами респираторной инфекции и 35 здоровых детей. Среди обследуемых было установлено преобладание «дикого» (wild type allele - аллель, кодирующий фенотипическую характеристику, свойственную дикому штамму (виду) организма, наиболее широко представленному в данной природной популяции.) С-аллеля (63,04 %). Уменьшение гетерозиготного варианта СТ и увеличение частоты встречаемости гомозигот оказалось типичным для детей с частыми рецидивами респираторной инфекции. Отсутствие «минорного» Т-аллеля С-511Т полиморфизма гена IL-1 у ребенка является фактором риска развития частых рецидивов респираторной инфекции (OR-3,55).

Ключевые слова: *генетический полиморфизм, интерлейкин 1в, рецидив инфекции дыхательных путей.*

Резюме

ОДИНОЧНИЙ ПОЛІМОРФІЗМ ГЕНА IL-1 (C-511T) У ДІТЕЙ З РЕЦИДИВНИМИ РЕСПІРАТОРНИМИ ІНФЕКЦІЯМИ

Левицька С.А., Гоженко А.І., Шустик Р.П., Гашинський І.В.

Буковинський державний медичний університет (Чернівці)

Український науково-дослідний інститут медицини транспорту

Аналіз однонуклеотидний поліморфізму 1в гена інтерлейкіну IL-1 проводили у 80 дітей з частими рецидивами респіраторної інфекції і 35 здорових дітей. Серед обстежуваних було встановлено переважання «дикого» С-алеля (63,04 %) (wild type allele - алель, який кодує фенотипічну характеристику, властиву дикому штаму (виду) організму, найбільш широко представленому у даній природній популяції.). Зменшення гетерозиготного варіанти СТ і збільшення частоти народження гомозигот виявилося типовим для дітей з частими рецидивами респіраторної інфекції. Відсутність «мінорного» Т-алеля С-511Т поліморфізму гена IL-1 у дитини є фактором ризику розвитку частих рецидивів респіраторної інфекції (OR-3,55).

Ключові слова: *генетичний поліморфізм, інтерлейкін 1в, рецидив інфекції дихальних шляхів.*

Впервые поступила в редакцию 10.02.2016 г. Рекомендована к печати на заседании редакционной коллегии после рецензирования