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N.Yu. Emelyanova

GI «L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine», Kharkov

THE PERIODONTAL DISEASES INCIDENCE IN CASES OF THE VDR GENE POLYMORPHISM IN PATIENTS WITH BRONCHOCARDIAL PATHOLOGY

This paper presents the results of the study of the incidence and nature of periodontal diseases in cases of the VDR gene Taq1 polymorphism in patients with chronic obstructive pulmonary disease combined with coronary heart disease. It has been established that periodontal diseases are of multifactorial nature and have a genetic and phenotypic dependence. 144 patients were examined (115 people with chronic obstructive pulmonary disease combined with coronary heart disease and 29 patients with coronary heart disease). Complementary to clinical dental examination, there has been performed genotyping of T/C Taq1 T>t polymorphism (rs 731236) of the VDR gene using a polymerase chain reaction method. It has been noted that patients with coronary heart disease tend to have the TT genotype homozygotes more often if compared to the mutant C allele genotype. However, the primary group showed no differences between the TT and CC genotypes. It has been discovered that the patients of the primary group tend to have periodontal disease more often if compared to the group of patients with coronary heart disease. These results prove the need for future studies to develop methods for correction.

Keywords: *vitamin D receptor (VDR), VDR gene polymorphism, coronary heart disease, chronic obstructive pulmonary disease, periodontal disease.*

Introduction

Inflammatory periodontal diseases with further destruction are considered to be the main causes of the loss of tooth in adults. Periodontal disease is of multifactorial nature, it has a phenotypic dependence on environmental factors [1]. A combination of all etiological causes leading to periodontal pathology, complicating preliminary diagnosis and, consequently, effective timely treatment is poorly understood. While looking for all possible causes of pathological changes in the gum tissues it has been understood that the first place is taken by the factors that do not cause the disease as such, however, they can make the development of the pathological process even worse, making a person more responsive. These factors include the genetic status of the patient. Today there have been studied a great number of candidate genes involved in the process of development of gum pathology. However, the search for genetic markers of this pathology is kept up [2].

The vitamin D receptor gene (VDR) is one of the most frequently studied markers of the development of periodontal pathology. Vitamin D may be involved in the process of regulation of inflammatory reactions and immune response of the body. It also can affect the periodontal disease risk. The vitamin D receptors are encoded by the VDR gene [3].

A lot of studies have noted the relation between the VDR gene polymorphism and osteoporosis, diabetes mellitus, psoriasis and cardiovascular diseases. A close attention is focused on the relation of the VDR gene polymorphism in pulmonology, in particular, in cases of bronchial asthma (BA) and chronic obstructive pulmonary disease (COPD), since the

bone metabolism change is caused by both primary pathogenetic factors and glucocorticosteroids therapy (GC).

VDR is present in immune cells, such as antigen-presenting cells, N killers, T cells, and B cells. Moreover, VDR is present not only in classic target organs, such as the intestinal tract, kidneys and bones, but also in brain, heart, vascular endothelium, smooth muscle cells, pancreas, prostate, parathyroid glands, skin and other organs.

Still the intestinal tract is the main target tissue for vitamin D where it stimulates the expression of calcium-binding protein proportionately increasing the absorption of calcium. In the kidneys, it increases the reabsorption of calcium. In the bone tissue vitamin D has a double function, affecting the differentiation of osteoclasts and osteoblasts.

The VDR gene is located in the 12th chromosome (q13–14 segment) and made up of 60 thousand base pairs. Genetic polymorphism is typical for the VDR gene. In other words, there have been discovered the existence of different allelic variants of this gene in the population. There have been identified the most major VDR gene polymorphisms: TaqI, BsmI, EcoRV, ApaI and FokI. Lots of studies conducted around the world have found that the occurrence of the VDR gene polymorphism has racial and ethnic distinctions. It also includes contradictory information on the role of any given polymorphism of this gene.

In 1999, British authors published the results of the study on the identification of a correlation between early periodontal disease and the VDR gene TaqI polymorphism [4]. The analysis has found significant differences in the distribution of genotypes between the primary group of patients with periodontal disease and a group of healthy volunteers (p=0.001). The author concluded that the presence of a less frequent TaqI RFLP (t) allele in the VDR gene dramatically increases the risk of development of local forms of an early-onset periodontal disease.

Japanese authors studied the correlation of periodontal disease with TaqI polymorphism and proved that the TT genotype is related to periodontal disease in adults [5]. At the same time, the Chinese population is marked with the Tt genotype and t-allele.

A group of scientists studying the VDR gene polymorphism and its influence upon immune function and bone tissue resorption has discovered an interesting fact. The authors have found that the effects related to bone resorption are associated with the development of aggressive forms, whereas the influence of gene polymorphism upon immune function is related to the development of periodontal disease in adults.

The purpose of our study is the incidence of periodontal diseases in cases of the VDR gene Taq1 polymorphism in patients with chronic obstructive pulmonary disease combined with coronary heart disease.

Materials and methods

144 patients were examined, 115 of them entered the group with a verified chronic obstructive pulmonary disease combined with coronary heart disease and 29 patients with coronary heart disease.

The chronic obstructive pulmonary disease was established according to the provisions prescribed by the GOLD (Global Initiative for Chronic Obstructive Lung Disease) 2011–2015, considering anamnesis, general clinical check-up, chest X-ray and respiratory function (RF) [6]. According to the recommendations of the European Society of Cardiology (information about clinic, challenge tests, daily monitoring of ECG and coronary angiogram) verified the coronary heart disease diagnosis.

Main selection criteria of the patients for the study:

1. Age from 35 to 65 years;

2. The absence of comorbidity (type II diabetes, chronic pyelonephritis, chronic glomerulonephritis, malignant tumors, hemoblastosis, thyroid disorders, anemia);

3. The absence of previous courses of treatment by a periodontist within 6 months prior to the start of the examination.

While assessing the dental status there was examined the condition of the mucous membrane of the cheeks, lips and tongue was examined either; the condition of the gum margin, in particular the color, the size, the shape and the presence of fistulas, abscesses, supragingival and subgingival dental deposits. There were used the following methods during periodontal examination: the hygienic index determination (Green-Vermilion), inflammation severity according to the PMA index (Parma), gum bleeding determination (Muhlemann-Cowell), gingival pockets depth, loss of periodontal attachment level, complex periodontal index, teeth mobility degree and the presence of a gum regression.

Once the informed consent of all the patients received, the whole blood samples were taken, EDTA was used as an anticoagulant. DNA was

purified from the blood using 'DNA-Sorb-B' kits. The VDR gene T/C Taq1 T>t (rs 731236) polymorphism genotyping was performed using a PCR method with further analysis of the length of restriction fragments. The results were visualized by the electrophoretic method. The following primers were used during the amplification:

F: 5'-CAGAGCATGGACAGGGAGCAA-3,

R: 5'-GCAACTCCTCATGGCTGAGGTCTC-3'.

The restriction was performed using the Taq1 [7] restriction enzyme. Statistical processing of the obtained data was made using the "Excel" program. Since the data distribution law did not correspond to the normal one, the median and interquartile range were calculated, the Mann-Whitney criterion was used to compare the quantitative parameters.

Results

According to the result of genetic testing, the patients with chronic obstructive pulmonary disease combined with coronary heart disease were divided into groups depending on the genotypes of the Taq1 polymorphic marker: TT genotype carriers – 42 patients (36.5 %), TC genotype carriers – 44 patients (38.3 %) and CC genotype carriers – 29 patients (25.2 %). The frequency of distribution of the T and C alleles in this group was almost the same (T allele 1.3 times exceeded C allele).

In the group of patients with coronary heart disease, the frequency of the CC allele homozygotes associated with periodontal disease was significantly lower if compared to the TT allele homozygotes (14 % and 41 %, respectively).

If compare allele frequencies there were significant differences observed frequencies: the frequency of occurrence of C allele in the group of patients with coronary heart disease was not only 1.3 times lower than in the group of patients with chronic obstructive pulmonary disease combined with coronary heart disease, but had significantly low values if compared to the frequency of occurrence of T allele in their own group (*table*).

The most significant differences between groups of patients were observed in the incidence

Distribution of genotypes and frequencies of the VDR gene Taq1 alleles in patients with chronic obstructive pulmonary disease combined with coronary heart disease

Genotype	Group with coronary heart disease, n (%)	Group with chronic obstructive pulmonary disease combined with coronary heart disease, n (%)
TT	12 (41,0±9,1)	42 (36,5±4,5)
TC	13 (45,0±9,2)	44 (38,3±4,5)
CC	4 (14,0±6,4)	29 (25,2±4,0)
Alleles	n (%)	n (%)
T	30,5 (68,0±7,0)	106 (57,0±3,6)
C	14,5 (32,0±7,0)	80 (43,0±3,6)

of periodontal diseases of various types. It has been noted that inflammatory changes of periodontal tissues (generalized periodontal diseases of different severity levels) in the main group of patients occurred 1,5 times more often than atrophic one. It is characteristic that patients with bronchocardial pathology with the CC genotype tend to have four times higher incidence of periodontal diseases as to atrophic changes in the periodontium. In contrast, the group of patients suffering from coronary heart disease are more likely to have atrophic changes in periodontal tissues is compared to inflammatory ones.

Conclusions

Our paper has studied the incidence and the nature of pathological changes in the periodontium depending on the VDR gene Taq1 polymorphism.

The study has found that the control groups (with coronary heart disease) tend to have a lower frequency of homozygotes with the mutant C allele if compared to the TT genotype when the primary group (with bronchocardial pathology) has no significant differences between the TT and CC genotypes.

The primary group of patients tends to have inflammatory changes in the periodontal tissues more often if compared to the same index of the control group. It was peculiar that the patients with comorbid pathology with the CC genotype are significantly more likely to have inflammatory symptoms if compared to the TT genotype homozygotes.

Probably this VDR gene Taq1 polymorphism affects the nature of changes in the periodontium only if combined with phenotypic features (the

presence of bronchocardial pathology, basic therapy in cases of the chronic obstructive pulmonary disease, etc.).

The relation between the VDR gene polymorphism, the risk of occurrence and the nature of the development of pathologies in the periodontium in this category of patients shall be studied more deeply to develop the methods for complications prevention and adequate correction of the existing condition.

Conflict of interest. The author has no conflicts of interest or financial ties to disclose.

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Н.Ю. Ємельянова

ЗАХВОРЮВАННЯ ПАРОДОНТА ПРИ ПОЛІМОРФІЗМІ ГЕНА VDR У ХВОРИХ З БРОНХОКАРДІАЛЬНОЮ ПАТОЛОГІЄЮ

У даній статті представлені результати вивчення частоти та характеру захворювань пародонта у випадках поліморфізму Taq1 гена VDR у пацієнтів з хронічними обструктивними захворюваннями легень у поєднанні з ішемічною хворобою серця. Встановлено, що захворювання пародонта носять багатофакторний характер і мають генетичну й фенотипічну залежність. Обстежено 144 пацієнти (115 осіб з хронічними обструктивними захворюваннями легень у поєднанні з ішемічною хворобою серця і 29 пацієнтів з ішемічною хворобою серця). Окрім клінічного огляду порожнини рота було проведено генотипування T/C Taq1 T>t поліморфізму (rs 731236) гена VDR з використанням методу полімеразної ланцюгової реакції. Відмічено, що пацієнти з ішемічною хворобою серця частіше мають гомозиготний генотип TT у порівнянні з генотипом мутантного С-алеля. Виявлено, що пацієнти основної групи, як правило, частіше страждають на захворювання пародонта в порівнянні з групою пацієнтів з ішемічною хворобою серця. Ці результати доводять необхідність майбутніх досліджень для розробки методів корекції.

Ключові слова: *рецептор вітаміну D (VDR), поліморфізм гена VDR, ішемічна хвороба серця, хронічна обструктивна хвороба легень, пародонтоз.*

Н.Ю. Емельянова

ЗАБОЛЕВАНИЕ ПАРОДОНТА ПРИ ПОЛИМОРФИЗМЕ ГЕНА VDR У БОЛЬНЫХ С БРОНХОКАРДИАЛЬНОЙ ПАТОЛОГИЕЙ

В данной статье представлены результаты изучения частоты и характера заболеваний пародонта в случаях полиморфизма Taq1 гена VDR у пациентов с хронической обструктивной болезнью легких в сочетании с ишемической болезнью сердца. Установлено, что заболевания пародонта носят многофакторный характер и имеют генетическую и фенотипическую зависимость. Обследовано 144 пациента (115 человек с хронической обструктивной болезнью легких в сочетании с ишемической болезнью сердца и 29 пациентов с ишемической болезнью сердца). В дополнение к клиническому осмотру было проведено генотипирование T/C Taq1 T>t полиморфизма (rs 731236) гена VDR с использованием метода полимеразной цепной реакции. Отмечено, что пациенты с ишемической болезнью сердца чаще имеют гомозиготный генотип TT по сравнению с генотипом мутантного С-аллеля. Было обнаружено, что пациенты основной группы, как правило, чаще страдают заболева-

ниями пародонта по сравнению с группой пациентов с ишемической болезнью сердца. Эти результаты доказывают необходимость будущих исследований для разработки методов коррекции.

Ключевые слова: *рецептор витамина D (VDR), полиморфизм гена VDR, ишемическая болезнь сердца, хроническая обструктивная болезнь легких, пародонтоз.*

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Ємельянова Наталія Юріївна – лікар-стоматолог, кандидат медичних наук, старший науковий співробітник відділу комплексного зниження ризику ХНІЗ ДУ «Національний інститут терапії ім. Л.Т. Малої НАМН України».

Адреса: Україна, 61039, м. Харків, просп. Любові Малої, 2-а.

Тел.: +380978342429.

E-mail: natadenta@gmail.com.

ORCID: 0000-0001-6089-6206.