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Osteoporosis in Combination with Osteoarthrosis: Of the rs731236 Polymorphism of the VDR Gene Research

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Abstract The relationship of the pathogenesis of osteoarthritis and osteoporosis continues to be the subject of research specialists. The purpose of this study was to establish the role of the rs731236 polymorphism of the VDR gene in the development of osteoporosis in combination with osteoarthritis. Comparative analysis of the frequency distribution of the genotypes of this polymorphism revealed a trend indicating the significance of the homozygous t/t genotype of the rs731236 polymorphism of the VDR gene in the development of osteoporosis in patients with osteoarthritis.

Keywords Osteoarthritis, Osteoporosis, rs731236 polymorphism, VDR gene, t/t genotype

1. Introduction

The relationship of the pathogenesis of osteoarthritis and osteoporosis continues to be the subject of research specialists. The study of the molecular basis of the onset of osteoporosis, for example, identification of associations with the identification of polymorphic loci of candidate genes is one of the topical directions in the study of this pathology [1,2]. Vitamin D homeostasis, the importance of its status and participation in bone formation is known to be indisputable, as is its genetic component, in particular, the distribution of vitamin D (VDR) gene polymorphisms in various populations and pathologies accompanied by a decrease in bone mass and structure [3-5].

Considering all the above, a comparative analysis of the distribution of the alleles and genotypes of the TaqI polymorphic locus (T/t, rs731236) of the VDR gene among patients with osteoarthritis and among patients with osteoporosis in combination with osteoporosis was carried out [2,7,8].

2. Main Body

2.1. Purpose of the Study

The purpose of this study was to establish the role of the rs731236 polymorphism of the VDR gene in the development of osteoporosis in combination with osteoarthritis.

2.2. Material and Methods of Investigation

The study included a total of 284 subjects, including the main group consisting of 147 people, of which 100 patients had osteoarthritis without osteoporosis (1a-subgroup) and 47 patients with osteoarthritis combined with osteoporosis (1b-subgroup). The control group consisted of 137 conditionally healthy persons of Uzbek nationality.

The diagnosis was established on the basis of clinical and anamnestic examination, laboratory tests, X-ray and densitometric studies. In patients with an established diagnosis, the distribution of the DR731236 polymorphic locus of the VDR gene was studied.

DNA was isolated from venous blood using a DNA sorb and "Ribo-sorb" kit (AmpliSens®, Russia). The concentration and purity of the isolated DNA was determined on a "NanoDrop 2000" Microvolume UV-Vis Spectrophotometer (ThermoFisher Scientific™, USA).

Genotyping of the rs731236 polymorphism of the VDR gene was performed by PCR-RFLP using an Applied Biosystems 2720 instrument.

Statistical processing of the research results was performed using the statistical software package "OpenEpi 2009, Version 2.3" and "DoctorStat 2013, Version 1.9". The following statistical criteria were used: chi-square (χ^2), p-criterion, odds ratio (OR) and confidence interval (95% CI).

2.3. Results and Discussion

Studies have shown that, in general, the distribution of

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genotypes of the T/t polymorphic locus of the VDR gene in the main and population groups corresponds to the Hardy-Weinberg equilibrium (HWE) ($\chi 2 < 0.11$, $p > 0.74$).

The data obtained indicate a higher level of detectability of the T allele and T/T genotype, relative to the t allele and other genotypes, both among patients with osteoarthritis and among healthy individuals.

In the main and control groups, the T and t alleles of the rs731236 polymorphism of the vitamin D gene (VDR) were distributed as 75.2 / 77.5 and 24.8 / 22.5, respectively.

The genotypes of this polymorphic locus were distributed among patients with osteoarthritis and among healthy individuals as follows: T/T: 57.1 / 59.5, T/t: 36.1 / 36.2 and t/t: 6.8 / 4.3.

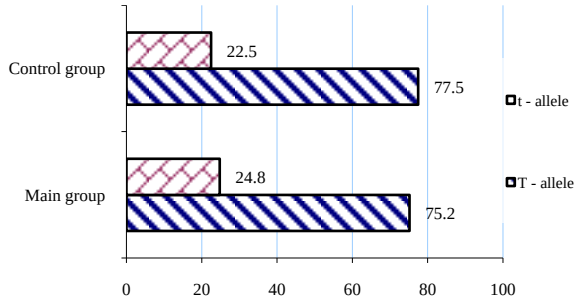

Figure 1. The distribution frequency of the T and t alleles of the rs731236 polymorphism of the VDR gene in patient groups and controls

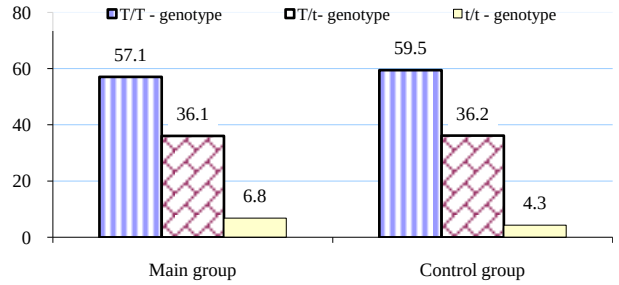

Figure 2. The frequency of distribution of genotypes T/T, T/t and t/t of the rs731236 polymorphism of the VDR gene in patient groups and controls (%)

Comparative analysis showed that differences in the distribution of the T allele are insignificant. The frequency of detection of the T allele in the control group statistically insignificantly exceeded the detection rate in the main group (OR = 0.88; 95% CI: 0.54 - 1.42). The frequency of detection of the allele t among patients with osteoarthritis in the main group was statistically insignificantly higher than among the relatively healthy individuals in the population group (OR = 1.14; 95% CI: 0.71 - 1.84).

A comparative analysis of the frequency distribution of the genotypes of the T/t polymorphism of the VDR gene in the main and control groups revealed certain differences that, however, were not statistically significant ($\chi 2 = 0.51$; $p = 0.77$) (Table 1).

The homozygous t/t genotype of the polymorphic locus of the VDR gene, unlike the two genotypes described above, was statistically insignificantly prevalent among patients with osteoarthritis of the main group (OR = 1.61; 95% CI: 0.43 - 6.03) (Table 1).

Studies of the distribution of alleles and genotypes of the rs731236 polymorphic locus of the VDR gene showed some differences between subgroups of patients with osteoarthritis without accompanying osteoporosis and among patients with osteoarthrosis in combination with osteoporosis (Table 1).

Studies have shown the predominance of the T allele both among patients in the 1a-subgroup and in the 1b-subgroup, and the distribution frequency values were slightly higher among patients in the 1a-subgroup (77.0% versus 71.3%, respectively; $\chi 2 = 1.12$; $p = 0.29$). The allele t, on the contrary, prevailed insignificantly among patients in whom osteoarthrosis was accompanied by osteoporosis (28.7% versus 23.0%, respectively; $\chi 2 = 1.12$; $p = 0.29$).

Table 1. General model of inheritance (chi-square test, df = 2)

Geno-types	Main group, n=147	Control group, n=67	χ^2	p	OR	
					Mean	95% CI
T/T	0.571	0.594	0.51	0.77	0.91	0.51 – 1.63
T/t	0.361	0.362			0.99	0.55 – 1.80
t/t	0.068	0.043			1.61	0.43 – 6.03

Studies have shown the predominance of the T allele both among patients in the 1a-subgroup and in the 1b-subgroup, and the distribution frequency values were slightly higher among patients in the 1a-subgroup (77.0% versus 71.3%, respectively; $\chi 2 = 1.12$; $p = 0.29$). Allele t, on the contrary, prevailed insignificantly among patients in whom osteoarthrosis was accompanied by osteoporosis (28.7% vs. 23.0%, respectively; $\chi 2 = 1.12$; $p = 0.29$).

The frequency of homozygous wild genotype T/T is statistically insignificant, predominant in the group of patients with osteoarthritis without osteoporosis, compared with patients in whom osteoarthrosis was detected against the background of osteoporosis (59.0% and 53.2%, respectively; $\chi 2 = 0.4$; $p = 0.5$; OR = 0.8, 95% CI: 0.393-1587).

The detection rates of the heterozygous T/t genotype were almost at the same level, with an extremely insignificant and statistically insignificant predominance among patients with osteoarthrosis and osteoporosis combined (36.0% and 36.2%, respectively).

It should be noted that in the subgroup of patients with osteoprosis there was a tendency to an increase in the proportion of persons with an unfavorable homozygous t/t variant compared with the subgroup of patients without osteoporosis (10.6% and 5.0%, respectively). According to the calculated odds ratio, the risk of osteoporosis in patients with osteoarthritis is 2.3 times less significant than in patients with osteoarthritis without osteoprosis ($\chi 2 = 1.6$; $p = 0.2$; OR = 2.3, 95% CI: 0.6216, 8.23). Based on the results obtained, it can be concluded that the rs731236 polymorphism of the VDR gene involved in the regulation of calcium metabolism enhances the development of osteoporosis in patients with osteoarthritis [9,10].

Apparently, due to the small number of the studied subgroup and the carriage of this genotype, the results did not reach statistical significance (P> 0.05).

In general, studies of the relationship between the rs731236 polymorphism of the VDR gene and the risk of developing osteoarthritis gave mixed, sometimes contradictory results [11,12].

There were no statistically significant differences in the frequency distribution of genotypic variants for this gene between a sample of conditionally healthy donors and a group of patients with osteoarthrosis. The contribution of this polymorphism to the formation of the risk of osteoarthritis is insignificant.

However, a comparative analysis of the frequency of distribution of genotypes of this polymorphism revealed a tendency to increase the proportion of homozygous t/t variant in comparison with the subgroup of patients without osteoporosis. These data may indicate the importance of the homozygous t/t genotype of the rs731236 polymorphism of the VDR gene in the development of osteoporosis in patients with osteoarthritis.

It should be borne in mind that the development of both osteoporosis and osteoarthritis is largely due to similar factors. This is largely the reason for the study of the relationship of these pathologies. According to researchers, the vitamin D (VDR) gene is one of the genes associated with the polymorphism of the VDR gene with a risk of osteoporosis, although there were other opinions on this subject [13]. However, modern studies indicate a stable relationship between changes in the vitamin D gene (VDR) and osteoporosis [3,14].

Also, researchers point to the connection of polymorphic loci of the VDR gene with the risk of susceptibility to the development of osteoarthritis of large joints, in particular the knee joint. However, there are directly opposite features, for example, characteristic of osteoarthritis, but not osteoporosis. These features include the presence of increased bone mineral density (BMD), characteristic of OA, with which they are associated with the relationship between this pathology and such a gene determining bone density as VDR. Researchers R.W. Keen et al. and A.G. Uitterlinden et al. the relationship between the VDR gene and osteoarthrosis of the knee was confirmed. The presence of relationships between osteoarthrosis and the VDR gene was also confirmed by Spector T. D., MacGregor A.J. and recent research data [3,15,16].

3. Conclusions

Thus, we can conclude that our results in general do not contradict the results of foreign researchers, while complementing and enriching the already existing knowledge about the relationship of the VDR gene with the risk of osteoarthritis and osteoporosis.

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