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ASSOCIATION BETWEEN RS10735810 POLYMORPHISM OF THE VITAMIN D RECEPTOR (VDR) GENE AND THE DEVELOPMENT OF PHYSICAL QUALITIES IN UKRAINIAN ATHLETES FROM THE SUMY REGION

ABSTRACT

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Introduction. Modern scientists have identified more than 25 thousand polymorphisms of the VDR gene, some of which, in particular, rs10735810, are associated with the development of physical qualities: speed and strength. Regarding the Ukrainian population, the results of the influence of the rs10735810 polymorphism on the development of speed and power qualities in track and field athletes are contradictory and ambiguous. Data on the relationship with speed and power qualities in track and field athletes are absent. Therefore, we have begun our own research to study the role of the rs10735810 polymorphism of the VDR gene in the development of speed and power qualities of track and field athletes of the Sumy region of Ukraine.

Objective. The aim of the study was to study the distribution of rs10735810 polymorphic variant of the VDR gene in athletes of the Sumy region of Ukraine.

Materials and methods: The buccal epithelium of 228 individuals living in the Sumy region of Ukraine was used for the study (104 athletes, including: a group of athletes with sports categories and a group of athletes with sports titles; control group – 124 individuals). Anthropometric methods were used to calculate body mass index (BMI). Genotyping of athletes and individuals of the control group for the rs10735810 polymorphism of the VDR gene was performed using polymerase chain reaction with subsequent restriction fragment length polymorphism (PCR-RFLP). Statistical analysis of the results was performed using SPSS software (version 25.0).

Results. The distribution of genotypes by rs10735810-polymorphism of the VDR gene in the group of athletes was as follows: in athletes with a high rank, the ratio of homozygotes for the F-allele (F/F), heterozygotes (F/f) and homozygotes for the f-allele (f/f) is 64.28%, 14.29% and 21.43%; in the

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group of athletes with ranks – 47.8%, 25.5% and 26.7%; and in individuals from the control group – 27.4%, 48.4% and 24.2%, respectively. The differences in the distribution of different genotype variants in these groups are beyond statistical significance (P < 0.01). There are statistically significant differences between female and male athletes with *Fok*I polymorphism (χ^2 = 10.01; P < 0.05). The difference in the frequency of female and male individuals with the F/F genotype in the comparison groups is present (χ^2 = 9.69, P < 0.05), unlike the F/f genotype in (χ^2 = 6.051; P = 7.84) and f/f genotype (χ^2 = 1.263; P = 0.93). A significant effect of the *Fok*I polymorphism of the 2nd exon of the VDR gene on the presence of sports achievements was found. The ratio of allelic variants of the VDR gene according to the *Fok*I polymorphism (F/F, F/f, f/f) in women in the group of people with sports categories was 48.8%, 23.3% and 27.9%, while in men the corresponding indicators were 46.8%, 27.7% and 25.5%. These results indicate the presence of statistically significant differences between female and male athletes with sports categories (χ^2 = 10.01; P < 0.05). In women, there are no significant differences between height, weight and BMI. As for the data in the group of men with sports categories, the following can be determined. Height and BMI indicators in both men and women with high sports achievements did not show significant differences (P > 0.05), that is, it can be concluded that the *Fok*I VDR polymorphism does not affect height in this group of men. But if we analyze the data on body weight in the group of men, we can observe statistically significant differences (P < 0.05), which may indicate a possible influence of the *Fok*I genotype on weight, unlike women.

Conclusions. In the Sumy region of Ukraine, the F allele according to the rs10735810 polymorphism of the VDR gene in high-class athletes is dominated by individuals with the F/F genotype, and in untrained people, the heterozygous genotype – F/f – prevails. Thus, in the male group, as in the female group, a tendency can be observed that people with sports titles and ranks were more likely to have the dominant F/F genotype. When studying the ratio of individuals of different sexes with the F/F genotype in the control group, the group of individuals with sports ranks and the group of individuals with high sports ranks, statistically significant differences were found. The difference in the frequency of female and male individuals with the F/F genotype in the comparison groups is present (χ^2 = 9.69, P < 0.05). Thus, the analysis of associations of the *Fok*I polymorphism of the VDR gene indicates that these polymorphisms indeed have a potential role in modulating physiological processes that determine the functional state of the athletes' body, which confirms our study.

Keywords: gene polymorphism, vitamin D receptor (VDR), athletes.

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РЕЗЮМЕ

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АНАЛІЗ ЗВ'ЯЗКУ RS10735810 ПОЛІМОРФІЗМУ ГЕНА VDR ІЗ РОЗВИТКОМ ФІЗИЧНИХ ЯКОСТЕЙ УКРАЇНСЬКИХ ЛЕГКОАТЛЕТІВ СУМСЬКОГО РЕГІОНУ

Вступ. Сучасні науковці виділяють понад 25 тисяч поліморфізмів гена VDR, деякі з них, зокрема rs10735810, асоційовані з розвитком фізичних якостей: швидкості та сили. Щодо української популяції, то результати впливу rs10735810 поліморфізму на розвиток швидкісно-силових якостей легкоатлетів

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суперечливі та неоднозначні. Дані щодо зв'язку з швидкісно-силовими якостями легкоатлетів відсутні. Тому нами було розпочате власне дослідження щодо вивчення ролі rs10735810 поліморфізму гена VDR у розвитку швидкісно-силових якостей легкоатлетів Сумського регіону України.

Мета роботи: вивчення розподілу rs10735810 поліморфного варіанту гена VDR у легкоатлетів Сумського регіону України.

Матеріали та методи: Для дослідження було використано буккальний епітелій 228 осіб, що мешкають у Сумському регіоні України (104 легкоатлети, серед яких: група спортсменів, що мають спортивні розряди та група спортсменів, що мають спортивні звання; група контролю – 124 особи). Були використані антропометричні метод, розрахунок показників індексу маси тіла (ІМТ). Генотипування спортсменів та осіб групи контролю за rs10735810-поліморфізмом гена VDR проводили за допомогою полімеразної ланцюгової реакції з наступним аналізом довжини рестрикційних фрагментів (PCR-RFLP). Статистичне опрацювання отриманих результатів проведено з використанням програмного забезпечення SPSS (версія 25.0).

Результати дослідження. Розподіл генотипів за rs10735810-поліморфізмом гена VDR у групі спортсменів був наступним: у спортсменів з високим званням співвідношення гомозигот за F-алелем (F/F), гетерозигот (F/f) і гомозигот за f-алелем (f/f) складає 64,28%, 14,29% і 21,43%; у групі спортсменів з розрядами – 47,8%, 25,5% і 26,7%; а у осіб з контрольної групи – 27,4%, 48,4% та 24,2% відповідно. Відмінності у розподілі різних варіантів генотипу у даних групах виходить за межі статистичної значимості (P < 0,01). Наявні статистично значимі відмінності між особами жіночої і чоловічої статі серед спортсменів, що мають спортивні розряди за поліморфізмом *Fok*I (χ^2 = 10,01; P < 0,05). Відмінність у частоті осіб жіночої і чоловічої статі з генотипом F/F у групах порівняння присутня (χ^2 = 9,69, P < 0,05), на відміну від генотипу F/f у (χ^2 = 6,051; P = 7,84) та f/f генотипу (χ^2 = 1,263 P = 0,93). Було виявлено значний вплив поліморфізму *Fok*I 2-го екзону гена VDR на наявність спортивних досягнень. Співвідношення алельних варіантів гена VDR за поліморфізмом *Fok*I (F/F, F/f, f/f) у жінок у групі осіб, що мають спортивні розряди, становило 48,8%, 23,3 % і 27,9 %, тим часом як у чоловіків відповідні показники дорівнювали 46,8%, 27,7% і 25,5%. Дані результати свідчать про наявність статистично значимих відмінностей між особами жіночої і чоловічої статі серед спортсменів, що мають спортивні розряди (χ^2 = 10,01; P < 0,05). У жінок немає значущих відмінностей між показниками зросту, маси та ІМТ. Що стосується даних у групі чоловіків, що мають спортивні розряди, то можна визначити наступне. Показники зросту та ІМТ як у чоловіків так і жінок, що мають високі спортивні досягнення, не показали значущих відмінностей (P > 0.05), тобто можна зробити висновок, що поліморфізм *Fok*I VDR не впливає на зріст у даній групі чоловіків. Але якщо аналізувати у групі чоловіків дані про масу тіла, то можна спостерігати статистично значущі відмінності (P < 0.05), що може говорити про можливий вплив генотипу *Fok*I на вагу, на відміну від жінок.

Висновки. В Сумському регіоні України алель F за rs10735810-поліморфізмом гена VDR у спортсменів високого класу переважають особи з генотипом F/F, а у нетренованих людей переважає гетерозиготний генотип – F/f. Так, у чоловічій групі, що і у жіночій можна спостерігати тенденцію, що люди, які мають спортивні звання та звання з більшою вірогідністю мали домінантний генотип F/F. Під час вивчення співвідношення у осіб різної статі з генотипом F/F у контрольні групі, групі осіб, що мають спортивні розряди та групі осіб, що мають високі звання у спорті, було виявлено статистично значимі відмінності. Відмінність у частоті осіб жіночої і чоловічої статі з генотипом F/F у групах порівняння присутня (χ^2=9,69, P < 0,05). Отже, аналіз асоціацій поліморфізму *Fok*I гена VDR свідчить про те, що дійсно дані поліморфізми мають потенційну роль у модулюванні фізіологічних процесів, що визначають функціональний стан організму спортсменів, що підтверджує наше дослідження

Ключові слова: поліморфізм генів, рецептор вітаміну D (VDR), спортсмени.

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INTRODUCTION

Genetic factors play a key role in shaping the physical qualities of athletes, in particular speed and strength characteristics that determine success in sports such as sprinting, weightlifting and martial arts [1; 2]. As is already known, the vitamin D receptor (VDR) is a key factor mediating the biological effects of vitamin D through the regulation of the expression of numerous genes related to calcium homeostasis, the immune response and the development of the musculoskeletal system [3, 4]. The vitamin D receptor (VDR) gene, a member of the nuclear receptor superfamily of transcription regulators, is crucial for calcitriol signaling [5, 6]. Vitamin D is an important nutrient in many aspects related to sports performance and recovery after training [7], as well as muscle mass and function [8]. The most studied function of this vitamin is related to bone metabolism and the maintenance of stable calcium levels in the body [9]. However, vitamin D plays a key role in modulating the function of many other cell types and tissues that play an important role in the sporting context, including immune cells and skeletal muscle fibers [10, 11]. Due to this immunoregulatory role, vitamin D is of considerable interest as a candidate factor for reducing muscle damage after exercise [12]. Vitamin D regulates muscle cell differentiation, as well as the transport of calcium and phosphate into intracellular compartments [13]. All these factors are crucial for elite athletes, as they can affect athletic performance, health, and training capacity [14, 15]. It has been studied that polymorphisms of the VDR gene, in particular *Fok*I, can modulate the functional activity of the receptor, which affects the sensitivity of tissues to vitamin D and is associated with various physiological and pathological conditions [16]. Modern scientists have identified more than 25 thousand polymorphisms of the VDR gene, some of which, in particular, rs10735810, are associated with the development of physical qualities: speed and strength. [17, 18].

There is a connection between vitamin D deficiency and myopathy, which reduces the physical activity of athletes [19]. Myopathy is associated with the degeneration of muscle fibers and their atrophy, which is clinically characterized by weakness, decreased endurance, persistent inflammation and infiltration of damaged cells into skeletal muscles [20, 21]. It has been shown that sufficient vitamin D levels allow maintaining and developing athletic performance; therefore, low vitamin levels prevent muscle relaxation required after exercise and increase muscle pain [22, 23]. This leads to a significant risk of injuries and stress fractures [24], causing loss of muscle strength and a decrease in bone mineral density [25, 26].

Regarding the Ukrainian population, the results of the influence of the rs10735810 polymorphism on the development of speed and power qualities in track and field athletes are contradictory and ambiguous. Data on the relationship with speed and power qualities in track and field athletes are absent. In addition, the clinical significance of VDR polymorphisms should be considered in a broader biomedical context, since disorders of vitamin D signaling are often associated with immune dysfunction and infectious diseases [27]. Therefore, we have begun our own research to study the role of the rs10735810 polymorphism of the VDR gene in the development of speed and power qualities of track and field athletes of the Sumy region of Ukraine [28, 29]. It should be noted that understanding the role of VDR polymorphisms will allow us to identify speed and power qualities at an early stage of human development and will contribute to sports selection.

MATERIALS AND METHODS

The experimental tasks were solved at Sumy State University. 228 people living in the Sumy region of Ukraine participated in the study. The main group was 104 track and field athletes, including: a group of athletes with sports categories and a group of athletes with sports titles; the control group was 124 students. The age of the athletes ranged from 18 to 26 years and was on average 22 years. The control group was from 18 to 24 years old, on average 21 years old. The comparison groups were comparable in age (P = 0.052, according to the Mann-Whitney U-criterion) [30]. Before the study, all people were informed about the objectives and hypothesis of the study, and consent was obtained to participate in the study and conduct genetic analysis.

The buccal epithelium sample was taken using a non-invasive non-traumatic method using special brushes. Before the procedure, the subjects performed the following actions: one hour before the sample collection, they refrained from smoking, eating, and drinking any beverages; before the sample collection itself, they rinsed their mouths several times with clean water. The subject placed the brush in their mouths and passed it at least 10 times along the inside of their cheeks, rotating it around its axis for approximately 10 seconds, trying to cover the entire inner surface of the right and left cheeks.

Molecular genetic studies were conducted in the scientific laboratory of molecular genetic studies of Sumy State University. DNA was isolated using the Isogen kits. The method is based on the use of a lysis reagent with guanidine isocyanate, which is designed for cell lysis, solubilization of cellular debris, and denaturation of cellular nucleases. In the presence of the lysis reagent, DNA is actively adsorbed onto the NucleoS™ sorbent, then easily washed away from proteins and salts with an alcohol solution. Subsequently, DNA is extracted from the sorbent and transferred into sterile DNA- and RNA-free microtubes. The obtained DNA can be directly used for polymerase chain reaction. The kit allows for the isolation of high-molecular-weight DNA (40–50 thousand nucleotide pairs) of high purity (OD260/280 nm 1.6–2.0) from fresh biological material [31].

Determination of *Fok*I polymorphism of the VDR gene was performed using the polymerase chain reaction method with subsequent analysis of the length of restriction fragments when they were detected by agarose gel electrophoresis. Amplification of the gene region containing the *Fok*I polymorphism site was performed using a pair of specific primers: forward (sense) – 5`-AGCTGGCCCTGGCACTGACTCTG- 3`, reverse (antisense) – 5`-ATGGAAACACCTTGCTTCTTCTCCCCTC-3`. For amplification, 50–100 ng of DNA were taken and added to a mixture containing 5 µl of 5-fold PCR buffer, 1.5 mM magnesium sulfate, 250 µM of a mixture of four nucleotide triphosphates, 15 pM of each of the primers and 0.75 U of Taq polymerase («Fermentas»), the volume was adjusted to 25 µl with deionized water. PCR was performed in a GeneAmp PCR System 2700 thermocycler (Applied Biosystems, USA) [32].

Amplification of the fragment containing the starting site consisted of 33 cycles: denaturation – 94°C (50 s), primer annealing – 64.5°C (45 s) and elongation – 72°C (1 min). For restriction analysis, 6 µl of the amplification product was incubated at 55°C for 20 hours with 3 U of *Fok*I restriction enzyme in Tango buffer with the following composition: 33 mM Tris-acetate (pH 7.9), 10 mM magnesium acetate, 66 mM potassium acetate, 0.1 mg/ml albumin. The presence of cytosine at position 25920 of the VDR gene prevents restriction, and when cytosine is replaced by thymine, *Fok*I restriction enzyme cleaves the amplified region with a length of 267 base pairs into two fragments: 204 and 63 base pairs. The amplicons of the studied VDR gene fragment after restriction were separated in a 2.5% agarose gel containing ethidium bromide. Horizontal electrophoresis (0.1A; 140V) was performed for 40 min. DNA visualization after electrophoresis was performed using a transilluminator («Biocom») [32].

Statistical data processing was performed on a personal computer using the standard programs Statgraphics and STATISTICA. For the initial preparation of tables and intermediate calculations, the Excel package was used. The compliance of the genotype distribution with Hardy–Weinberg equilibrium was checked using the online resource (http://www.oege.org/software/hwe-mrcalc.shtml). To compare the distribution of genotypes in the experimental and control groups, the Pearson χ^2 test was used.

RESULTS

The analysis showed that the distribution of genotypes and alleles according to the rs10735810 polymorphism of the VDR gene in the control group and in the group of athletes does not have statistically significant deviations from those expected according to the Hardy-Weinberg law (P > 0.05). The frequency of three possible genotype variants according to this polymorphism, as well as the verification of the compliance of the distribution of the F-allele and f-allele with the Hardy-Weinberg equilibrium are presented in Table 1.

Table 1 – Frequency of allelic variants and alleles according to the FokI polymorphism of the VDR gene in the control group, the group of athletes with sports categories and the group of athletes with sports titles

	Control group	Athletes who have sports categories	Athletes who have sports titles
F/F, n (%)	34 (27.4)	43 (47.8)	9 (64.28)
F/f, n (%)	60 (48.4)	23 (25.5)	2 (14.29)
f/f, n (%)	30 (24.2)	24 (26.7)	3 (21.43)
F-allele	0.52	0.494	0.464
f-allele	0.48	5.54	5.27
χ 2	9.619	0.134	2.12
P	> 0.01	> 0.05	> 0.05

Note: n is the number of patients, χ 2 and P reflect the deviations in each group from Hardy-Weinberg equilibrium

According to the results of the analysis of the frequencies of individual genotypes by *Fok*I polymorphism in individuals of the control group, the group of athletes with sports categories and the group of individuals with sports titles in sports, it was found that in athletes with a high rank, the ratio of homozygotes for the F-allele (F/F), heterozygotes (F/f) and homozygotes for the f-allele (f/f) is: 64.28%, 14.29% and 21.43%; in the group of athletes with categories – 47.8%, 25.5% and 26.7%; and in individuals from the control group – 27.4%, 48.4% and 24.2%, respectively. This indicates that among high-class athletes, individuals with the F/F genotype prevail, and among untrained people, the heterozygous genotype F/f prevails. Differences in the distribution of different genotype variants in these groups are beyond statistical significance (P < 0.01).

According to Table 2, we can analyze the data obtained and say that the distribution of F- and f-alleles in individuals from these groups does not have statistically significant deviations from the expected values according to the genetic-population law (P > 0.05). It was found that in the control group, the ratio of homozygotes for the F-allele (F/F), heterozygotes (F/f) and homozygotes for the f-allele (f/f) is 27.5%, 52.5% and 20%; in the group of individuals with sports degrees – 24.14%, 41.38% and 34.48%; and in individuals with high ranks in sports, respectively, 27.4%, 64.3% and 21.4%. It is also worth noting that the differences in the distribution of different genotype variants in the two groups did not exceed the limits of statistical significance (P = 0.11) (Table 2).

Table 2 – Frequency of allelic variants and alleles by FokI polymorphism of the VDR gene in athletes

	Athletes I-III classes	Candidates for Master of Sports	Master of Sports
F/F, n (%)	11 (27.5)	7 (24.14)	2 (14.3)
F/f, n (%)	21 (52.5)	12 (41.38)	9 (64.3)
f/f, n (%)	8 (20)	10 (34.48)	3 (21.4)
F-allele	0.5375	0.448	0.464
f-allele	0.4625	0.552	0.536
χ 2	0.666	2.049	1.16
P	> 0.05	> 0.05	> 0.05

When comparing data on the frequency of *Fok*I polymorphism variants in women and men, separately in the control group, in the group of individuals with sports categories and in the group of athletes with high ranks, the following results were obtained (Table 3). In the control group, women with the genotype F/F –20%, F/f –48.9%, f/f –31.1% were found, and in men, respectively, 31.6%, 48.1% and 20.3%. Comparison of the obtained data indicates the absence of statistically significant differences in the distribution of allelic variants of the *Fok*I polymorphism between women and men in the control group (χ^2 = 5.06; P_2 = 0.67). The ratio of allelic variants of the VDR gene according to the *Fok*I polymorphism (F/F, F/f, f/f) in women in the group of individuals with sports categories was 48.8%, 23.3% and 27.9%, while in men the corresponding indicators were 46.8%, 27.7% and 25.5%. These results indicate the presence of statistically significant differences between female and male individuals among athletes with sports categories (χ^2=10.01; P_3 < 0.05).

Table 3 – Distribution of individuals of different genotypes according to the FokI polymorphism of the VDR gene in women and men in the control group and in high-class athletes

Genotypes	Control group of women (n)	Women who have sports degrees (n)	Women who hold sports titles (n)	Control Group of Male (n)	Men who have sports ranks (n)	Men with sports titles (n)
F/F	9	21	3	25	22	6
F/f	22	10	0	38	13	2
f/f	14	12	0	16	12	3
P1 < 0.05; P2 = 0.9317; P3 < 0.05 ; P4 = 0.81; P5 < 0.05; P6 = 0.784; P7 = 0.93						

Note: n – number of individuals, P 1 – significance of differences in genotype distribution between the control and the group of individuals with sports degrees and the group that achieved high ranks in sports, P 2 – significance of differences in genotype distribution between women and men in the control, P 3 – significance of differences in genotype distribution between women and men in the group of individuals with sports degrees, P 4 – significance of differences in genotype distribution between women and men in the group of individuals with high ranks in sports, P 5 – significance of differences in the frequency of individuals of different sexes with the F/F genotype in the control group, in the group that has sports degrees and the group of individuals with high ranks in sports, P 6 – significance of differences in the frequency of individuals of different sexes with the F/f genotype in the control group, in the group of individuals with sports degrees and the group of persons with high ranks in sports, P 7 – significance of differences in the frequency of persons of different sexes with the genotype f/f in the control group, in the group of persons with a rank and in the group of persons with high ranks in sports

Analyzing the data in the groups of men and women with high sports achievements, we can observe the following situation. The ratio of women with different genotypes in this group was 100%, 0% and 0%, and in the male group with high indicators, respectively, 54.5%, 18.2% and 27.3%. Although the analysis suggests that these groups have significant statistical differences, based on the calculations it is impossible to say for sure that there is a significant difference (χ^2 =6.18; P_4 = 0.81). There is an assumption that the difference in the percentage ratio is associated with a small sample.

When studying the ratio of individuals of different sexes with the F/F genotype in the control group, the group of individuals with sports categories and the group of individuals with high ranks in sports, statistically significant differences were found. Thus, among the carriers of the F/F genotype in the control group, 20% of women and 31.6% of men were found, in the group with persons with a sports degree, 48.8% and 46.8%, respectively, and in the group of athletes with high ranks – 100% and 18.2%, respectively. The difference in the frequency of female and male individuals with the F/F genotype in the comparison groups is present (χ^2 =9.69, P_5 < 0.05). Among individuals with the F/f genotype in the control group, there were 48.9% women and 48.1% men, and in the group of persons with a degree in sports – 23.3% and 27.7%, and in the group of persons with high ranks in sports, their number was 0% and 54.5%, respectively. Differences in the frequency of individuals of different sexes according to the F/f genotype in the comparison groups do not exceed the norm (χ^2 = 6.051; P_6 = 7.84). The following ratio was found for carriers of the f/f genotype: in the control group, 53.8% of women and 51.6% of men were found, and among athletes with ranks – 46.2% and 38.7%, and among those with ranks, 0% and 9.7%, respectively. The frequency of individuals carrying the f/f genotype among representatives of different sexes in these groups also does not exceed the limits of statistical significance (χ^2 = 1.263 P_7 = 0.93).

Table 4 presents the height, weight and body mass index (BMI) in women and men of both comparison groups depending on the genotype of patients according to the *Fok*I polymorphism of the 2nd exon of the VDR gene. It can be observed that in women of both groups there are no significant differences between the height, weight and BMI indicators. Although, unfortunately, due to the small sample, we were unable to fully analyze all the criteria. As for the data in the group of men with sports categories, the following can be determined. Height and BMI indicators did not show significant differences (P_1 > 0.05), that is, it can be concluded that the *Fok*I VDR polymorphism does not affect height in this group of men. But if we analyze the body weight data in this group, we can observe statistically significant differences (P_1 < 0.05), which may indicate a possible influence of the *Fok*I genotype on weight.

Table 4 – Height, weight and body mass index (BMI) in female and male athletes. Comparison depending on genotype variants by *Fok*I polymorphism of the VDR gene (M±m)

Indicators		F/F	F/f	f/f	F	P_1
Women						
Height, cm	*Athletes with sports categories*	167.9±4.61 (10)	167.6±4.84 (21)	169±4.37 (12)	2.45	**0.099**
	Athletes with sports titles	0±0 (0)	165.6±5.13 (3)	0±0 (0)	-	**-**
	P_2	-	0.712	-		
Body weight, kg	*Athletes with sports categories*	54.2±5.52	56.95±4.64	55.6±6.81	5.61	**0.007**
	Athletes with sports titles	0±0	55±4.36	0±0	-	**-**
	P_2	-	0.697	-		
BMI, kg/m2	*Athletes with sports categories*	19.25±2.04	20.25±1.63	19.44±1.69	1.46	**0.243**
	Athletes with sports titles	0±0	20±0.46	0±0	-	**-**
	P_2	-	0.415	-	-	**-**
Men						
Height, cm	*Athletes with sports categories*	180.23±6.94 (13)	181.32±5.97 (22)	182.9±4.89 (12)	1.905	**0.161**
	Athletes with sports titles	183±0 (2)	182.3±5.72 (6)	183.67±5.69 (3)	0.564	**0.590**
	P_2	0.412	0.575	0.673		
Body weight, kg	*Athletes with sports categories*	70.38± 7.83	74.81±6.84	72.33±8.39	3.816	**0.030**
	Athletes with sports titles	79±5.66	76.33±5.16	75.6±4.51	1.505	**0.279**
	P_2	0.178	0.421	0.389		
BMI, kg/m2	*Athletes with sports categories*	21.62±1.28	22.74±1.18	21.63±2.38	3.128	**0.054**
	Athletes with sports titles	23.6±1.9	22.95±1.03	22.43±1.17	0.337	**0.723**
	P_2	0.095	0.634	0.512	-	**-**

Note: F – Fisher's exact test, P1 and P2 – significance of differences between genotypes according to one-way analysis of variance (P1) and between the control and the group of athletes with high achievements (with titles) according to Student's t-test (P2). In parentheses – number of athletes

In the group of male athletes with high ranks, data analysis indicates the absence of statistically significant differences between genotype groups. As for the comparison between groups, here too no significant differences in anthropometric data were found. Thus, a significant influence of the *Fok*I polymorphism of the 2nd exon of the VDR gene on the presence of sports achievements was found. Thus, in the male group, as in the female group, a tendency can be observed that people with sports titles and ranks with a greater probability had the dominant F/F genotype.

The lack of association of *Fok*I polymorphism with sports achievements in most comparison groups is revealed when factors such as gender and BMI are taken into account. Although among individuals with sports titles, statistically significant differences (P_1 < 0.05) can be observed in the male group, which may indicate a possible influence of the *Fok*I genotype on mass. In men with the f/f genotype in both groups of athletes, they have higher height than in individuals with the F/F and F/f genotypes.

DISCUSSION

The *Fok*I polymorphism is located in the exonic region of the VDR gene and affects the start of protein translation. It is represented by two alleles: Allele F is a short form of the protein (424 amino acids). At the same time, allele f is a longer form of the protein (427 amino acids). In the presence of the F allele, protein translation begins with the usual start codon (ATG in the 2nd exon), which leads to the formation of a shorter VDR isoform (424 amino acids). If a person has the f allele, an alternative start codon is created in the first exon, which adds three additional amino acids to the N-terminus of the protein, forming a longer version (427 amino acids) [33].

The *Fok*I polymorphism of the VDR gene is characterized by the fact that its variations change the start codon of translation, which affects the length of the resulting protein [34]. Studies have shown that the shorter form (F-allele) has higher biological activity and binds more efficiently to the corresponding promoters of target genes [35]. It has also been found that individuals with the F/F genotype have higher indicators of muscle strength and performance, especially in power sports, such as weightlifting and sprinting [36]. Similar methodological approaches to the analysis of SNPs have been successfully applied to other genes, such as TERT, confirming the universality and informativeness of PCR-RFLP genotyping in biomedical research [37]. There are also studies demonstrating the effect of genotypes on bone density [38]. Thus, the F/f or f/f genotype is more often associated with lower bone mineral density, which may increase the risk of osteoporosis in older people [39].

Let us consider in more detail the influence of the *Fok*l polymorphism on the development of the musculoskeletal system and speed-strength qualities of elite track and field athletes [40]. The *Fok*I polymorphism in the VDR gene affects the activity of the corresponding vitamin D receptor [41], which, in turn, regulates the expression of genes associated with muscle adaptation and bone structure [42, 43]. Studies by foreign scientists show that carriers of the F/F genotype have more effective activation of the vitamin D receptor, which contributes to better development of speed/strength qualities, in particular an increase in muscle strength and power [41]. Also, the study of the *Fok*I gene polymorphism showed that athletes with the F/F genotype have better muscle tissue regeneration, they have better strength and speed indicators [44]. An athlete with the F/f genotype has a slightly lower strength and speed of muscle fiber contraction, as well as muscle regeneration. On the other hand, carriers of the f/f genotype may have a lower level of muscle adaptation and, accordingly, a lower level of strength, speed and regeneration indicators [35]. For example, a study by scientists found that the F/F genotype is much more common among sprinters and weightlifters, which confirms its role in the development of speed and strength qualities [45, 46].

As noted, there is no data on the association of polymorphic variants of the VDR gene with the physical qualities of track and field athletes in the Ukrainian population. Therefore, our study was devoted to studying the role of the rs10735810 polymorphism of the VDR gene in the development of physical qualities of track and field athletes living in the Sumy region of Ukraine. We have shown that athletes who are dominant homozygotes F/F have higher performance in sports compared to recessive homozygotes f/f. It was found that such a relationship exists in the group of female and male individuals in groups of athletes with a normal body mass index. This fact indicates that in these groups it is the genetic factor under study that is associated with the development of physical qualities. This result may suggest that the analysis of the FokI polymorphism can help select young athletes who have the most favorable genetic potential for achieving success in athletics.

Thus, the analysis of associations of the *Fok*I polymorphism of the VDR gene indicates that indeed these polymorphisms have a potential role in modulating physiological processes that determine the functional state of the athletes' body, which confirms our study [47]. Variations in these loci can affect the expression and functionality of the vitamin D receptor, which, in turn, affects the regulation of calcium metabolism, and accordingly, the state of the skeletal system, muscle strength and other indicators [48, 49]. The FokI polymorphism, which is able to change the structural and functional characteristics of the VDR protein, contributes to the differentiation of athletes in terms of muscle strength and endurance. These mechanisms emphasize the biological significance of the polymorphism in the context of the body's adaptation to sports loads, and at the same time, they indicate the complexity of the interaction between genetic factors and other external factors [50, 51]. Therefore, the rs10735810 polymorphism of the VDR gene is an important marker in the development of physical qualities in Ukrainian track and field athletes.

It should be noted that not only the genetic component influences the results of physical qualities, but also the focus on the individual is of great importance, since only a few athletes reach the highest levels of performance, and their path to elite status is unique and peculiar. It is also necessary to include a wide range of determinants of elite performance from different scientific fields to characterize an individual athlete [52]. Some scientists note that genetic information is not able to accurately distinguish between elite athletes and a non-athletic control group, which indicates that the use of such information as a talent identification tool is unfounded and ineffective [53]. Thus, it can be concluded that the experience in sports is very individual and heterogeneous.

CONCLUSIONS

1. In our work, the association of the *Fok*I polymorphism of the VDR gene with the physical qualities of track and field athletes was analyzed for the first time. There is a significant difference in the distribution of allelic variants between athletes and

control group individuals for the *Fok*I polymorphism of the VDR gene (P < 0.01).

2. There are statistically significant differences between female and male individuals among athletes with sports categories for the *Fok*I polymorphism (χ^2 = 10.01; P < 0.05). The difference in the frequency of female and male individuals with the F/F genotype in the comparison groups is present (χ^2 = 9.69; P < 0.05), unlike the F/f genotype in (χ^2 = 6.051; P = 7.84) and f/f genotype (χ^2 = 1.263; P = 0.93).

3. A significant influence of the *Fok*I polymorphism of the 2nd exon of the VDR gene on the presence of sports achievements was revealed. Thus, in the male group, as in the female group, one can observe a tendency that people with sports titles and ranks were more likely to have the dominant F/F genotype. When studying the ratio of individuals of different sexes with the F/F genotype in the control group, the group of individuals with sports ranks and the group of individuals with high ranks in sports, statistically significant differences were found. The difference in the frequency of female and male individuals with the F/F genotype in the comparison groups is present (χ^2 = 9.69; P < 0.05).

4. In women of both groups, there are no significant differences between the indicators of height, weight and BMI. As for the data in the group of men with sports ranks, the following can be determined. Height and BMI indicators in both men and women with high sports achievements did not show significant differences (P > 0.05), i.e. it can be concluded that the *Fok*I VDR polymorphism does not affect height in this group of men. However, if we analyze the body weight data in the male group, we can observe statistically significant differences (P < 0.05), which may indicate a possible effect of the *Fok*I genotype on weight, unlike in women.

PROSPECTS FOR FUTURE RESEARCH

Perspectives for future research: to investigate the association of other single nucleotide polymorphisms of the VDR gene (BsmI, ApaI, and TaqI) in the development of physical qualities in track and field athletes for the purpose of sports prediction.

AUTHOR CONTRIBUTIONS

Biesiedina A.A.: work concept and design, data collection and analysis, responsibility for statistical analysis, writing (not revising) sections of the manuscript, final approval of the article.

HarbuzovaV. Yu.: critical review, final approval of the article.

Obukhova O. A.: laboratory research, analysis of the data obtained.

Oleshko T. M.: data collection and analysis.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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The authors confirm that no artificial intelligence-based technologies were utilized in the writing or editing of the manuscript.

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