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Analysis of Candidate Gene Polymorphism Associations With Vibration Syndrome

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ABSTRACT

BACKGROUND: Identifying molecular genetic markers associated with a high risk of occupational diseases facilitates the development of timely preventive strategies. The molecular genetic basis of vibration syndrome remains insufficiently understood.

AIM: To investigate the associations between polymorphisms in the *SOD2*, *TNF-α*, *IL-1β*, *MMP-1*, and *IL-6* genes and vibration syndrome.

METHODS: A case–control study was conducted involving 71 patients diagnosed with vibration syndrome. Patients diagnosed with vibration syndrome were consecutively recruited from those undergoing examination and treatment at the Ufa Research Institute of Occupational Medicine and Human Ecology between 2022 and 2023. The control group included 76 individuals with no occupational exposure to vibration. Genotyping of polymorphic variants was performed using real-time polymerase chain reaction with locus-specific fluorescent-labeled DNA probes and specific oligonucleotide primers.

RESULTS: A statistically significant association was found between the rs4880 polymorphism of the *SOD2* gene and the development of vibration syndrome: the *T* allele was identified as a risk factor, whereas the *C* allele appeared to have a protective effect. No statistically significant differences were found in the genotype and allele frequencies of the rs361525 (*TNF-α*), rs16944 (*IL-1β*), rs1799750 (*MMP-1*), and rs1800795 (*IL-6*) polymorphisms between patients with vibration syndrome and the control group.

CONCLUSION: The rs4880 polymorphism of the *SOD2* gene is associated with an increased risk of developing vibration syndrome. No significant associations were found for polymorphisms in the *TNF-α*, *IL-1β*, *MMP-1*, or *IL-6* genes and developing vibration syndrome. These findings may serve as a basis for developing screening programs aimed at identifying individuals with an increased risk of developing vibration syndrome.

Keywords: vibration-induced disease; occupational diseases; gene polymorphism; alleles; genotypes.

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Анализ ассоциаций полиморфизмов ряда генов-кандидатов с вибрационной болезнью

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АННОТАЦИЯ

Обоснование. Выявление молекулярно-генетических маркеров высокой вероятности возникновения профессиональных заболеваний способствует разработке мер своевременной профилактики. В настоящее время остаются малоизученными молекулярно-генетические аспекты вибрационной болезни.

Цель. Изучение ассоциаций полиморфизмов генов *SOD2*, *TNF-α*, *IL-1β*, *MMP-1* и *IL-6* с вибрационной болезнью.

Материалы и методы. В одномоментное исследование по типу «случай–контроль» был включён 71 пациент с вибрационной болезнью. Отбор в группу с диагностированной вибрационной болезнью производили сплошным образом из пациентов, проходивших обследование и лечение в клинике Уфимского научно-исследовательского института медицины труда и экологии человека в 2022–2023 гг. Группу контроля составили 76 человек, не подвергавшихся в профессиональной деятельности воздействию вибрации. Полиморфные варианты генов анализировали при помощи полимеразной цепной реакции с использованием специфических олигонуклеотидных праймеров и локус-специфичных меченых олигонуклеотидных ДНК-зондов в режиме реального времени.

Результаты. По результатам исследования выявлена ассоциация полиморфного варианта rs4880 гена *SOD2* с развитием вибрационной болезни: аллель Т является фактором риска развития заболевания. Аллель С данного полиморфного варианта имеет протективное значение при формировании вибрационной болезни. При изучении распределения частот генотипов и аллелей полиморфных вариантов rs361525 гена *TNF-α*, rs16944 гена *IL-1β*, rs1799750 гена *MMP-1* и rs1800795 гена *IL-6* не обнаружено статистически значимых различий у обследованных больных с вибрационной болезнью по сравнению с контрольной группой.

Заключение. Обнаружена ассоциация полиморфного варианта rs4880 гена *SOD2* с возникновением вибрационной болезни. При этом не найдено значимой связи между полиморфизмами генов *TNF-α*, *IL-1β*, *MMP-1*, *IL-6* и развитием вибрационной болезни. Полученные данные могут использоваться для разработки скрининговых программ, направленных на выявление лиц с повышенным риском развития вибрационной болезни.

Ключевые слова: вибрационная болезнь; профессиональные заболевания; полиморфизм генов; аллели; генотипы.

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候选基因多态性与振动病的关联性分析

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摘要

背景。鉴定与职业病发生密切相关的分子遗传标志物，有助于制定及时有效的预防措施。目前，振动病的分子遗传学机制尚未得到充分研究。

目的。探讨SOD2、TNF-α、IL-1β、MMP-1和IL-6基因多态性与振动病之间的关联。

材料与方法。本研究为一项“病例－对照”类型的单时点研究，共纳入71名经诊断为振动病的患者。所有病例组患者均为2022－2023年间在Ufa Research Institute of Occupational Medicine and Human Ecology附属诊所接受检查和治疗的对象，通过全纳方式纳入研究。对照组为76名在职业活动中未接触振动因素的个体。基因多态性检测采用实时荧光定量聚合酶链式反应（qPCR）方法，使用特异性寡核苷酸引物和位点特异性标记寡核苷酸探针进行。

结果。研究发现，SOD2基因rs4880多态位点与振动病的发生存在显著关联：T等位基因是发病的风险因素，而C等位基因具有保护作用。TNF-α基因rs361525、IL-1β基因rs16944、MMP-1基因rs1799750和IL-6基因rs1800795多态位点在病例组与对照组的基因型及等位基因频率分布中未发现统计学显著差异。

结论。SOD2基因rs4880多态性与振动病的发生具有显著相关性。而TNF-α、IL-1β、MMP-1和IL-6基因多态性与振动病之间未见明显关联。本研究结果可作为制定针对振动病高风险人群的筛查方案的依据。

关键词：振动病；职业病；基因多态性；等位基因；基因型。

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BACKGROUND

Vibration syndrome (VS) belongs to occupational diseases. Workers in construction, shipbuilding and aircraft manufacturing, mining, metallurgy, agriculture, and transportation industries are at the highest risk of developing VS. The main cause of VS is prolonged exposure to industrial vibration exceeding permissible levels. VS holds one of the leading positions in the structure of occupational pathology [1]. The disease is characterized by diverse clinical symptoms involving various homeostatic components, multiple organs and systems, with specific course features that often lead to disability. Typical manifestations include changes in the nervous and cardiovascular systems, musculoskeletal apparatus, and metabolic processes. These disorders may occur concomitantly or sequentially, affecting reflex, neurohumoral, and neuroendocrine mechanisms [2, 3].

Genetic predisposition plays a significant role in individual susceptibility to occupational factors, as well as in the development and progression of occupational diseases. Recent studies regularly publish new findings evaluating the contribution of genetic factors to the mechanisms underlying occupational diseases [4–6]. The *SOD2* gene, which encodes superoxide dismutase 2 (SOD2), a manganese-containing enzyme belonging to the core antioxidant defense system, is of particular interest. Impaired enzymatic activity of SOD2 leads to increased oxidative stress [7]. Tumor necrosis factor-alpha (TNF-α), a proinflammatory cytokine, plays a crucial role in vascular endothelial activation and immune response regulation. Additionally, it affects type 1 collagen synthesis by fibroblasts, demonstrating antifibrotic properties. Cytokines of the interleukin-1 (IL-1) family participate in inflammatory processes and immune regulation, serving as key mediators of both innate and adaptive immunity. Studies have identified direct effects of IL-1 on bone tissue homeostasis, with regulatory disruptions potentially linked to various bone pathologies [8]. The matrix metalloproteinase-1 (*MMP-1*) gene, expressed in various cells including chondrocytes, fibroblasts, and epithelial and endothelial cells, also warrants attention. *MMP-1* expression levels significantly increase under pathological conditions, leading to abnormal connective tissue degradation. Interleukin-6 (IL-6), a pleiotropic inflammatory cytokine, plays a substantial role in immune response modulation.

Modern methods for identifying markers of high occupational disease risk provide new opportunities for developing timely preventive measures. However, despite significant progress, molecular genetic aspects of many occupational diseases remain poorly studied.

AIM. The study aimed to investigate the associations between polymorphisms in the *SOD2*, *TNF-α*, *IL-1β*, *MMP-1*, and *IL-6* genes and vibration syndrome.

METHODS

A cross-sectional case-control study was conducted. The study included patients with VS caused by exposure to whole-body vibration, local vibration, and combined vibration. The patient sample consisted of 71 individuals (22.5% women and 77.5% men) aged 23 to 79 years (mean age 59.9±1.6 years). Patients diagnosed with vibration syndrome were consecutively recruited from those undergoing examination and treatment at the Neurology and Occupational Pathology Department of the clinic of the Ufa Research Institute of Occupational Medicine and Human Ecology between 2022 and 2023. The inclusion criteria for the group were confirmed VS diagnosis, at least three years of work experience at the enterprise, and residence in the Republic of Bashkortostan. All participants were exposed to occupational vibration. The majority in this group were employees of a mining and processing plant.

The control group comprised 76 individuals (17.1% women and 82.9% men) aged 23 to 79 years (mean age 53.0±1.0 years). The inclusion criteria for the control group were excluded VS diagnosis, absence of chronic rheumatoid, cardiovascular, or musculoskeletal diseases, no exposure to vibration, and residence in the Republic of Bashkortostan.

The study protocol was approved by the Biomedical Ethics Committee of the Ufa Research Institute of Occupational Medicine and Human Ecology (Protocol No. 01-01 dated January 22, 2024). All patients provided written informed consent to participate in the study.

DNA extraction was performed using the MAGNO-sorb reagent kit (Central Research Institute of Epidemiology of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing). The study included the following polymorphic variants: rs4880 of the *SOD2* gene, rs361525 of the *TNF-α* gene, rs16944 of the *IL-1β* gene, rs1799750 of the *MMP-1* gene, and rs1800795 of the *IL-6* gene. Polymorphisms were detected using real-time polymerase chain reaction with locus-specific fluorescently labeled oligonucleotide DNA probes and specific oligonucleotide primers synthesized by DNA-Sintez (Moscow, Russia). The Rotor-Gene Q cycler manufactured by Qiagen (Germany) was used for the analysis.

The statistical analysis was conducted using Microsoft Excel and IBM SPSS Statistics v.21 software packages. The chi-square (χ^2) test was used to assess the compliance of genotype frequency distributions with Hardy–Weinberg equilibrium. The comparative analysis of allele and genotype frequencies in the samples was performed using the χ^2 test, Yates correction χ^2 test, or Fisher exact test. The odds ratio (OR) with 95% confidence intervals (95% CI) were calculated to evaluate the influence of polymorphisms on disease risk. OR > 1 was interpreted as a positive correlation between the disease and the studied genotype or allele (risk factor). Conversely, OR < 1 indicated a negative correlation (protective

factor). The statistical significance of differences was set at $p < 0.05$.

RESULTS

No deviations from Hardy–Weinberg equilibrium were observed for the studied polymorphisms in the control group. In patients with VS, Hardy–Weinberg equilibrium was not maintained for the polymorphic variants rs361525 of the *TNF-α* gene, rs16944 of the *IL-1β* gene, and rs1800795 of the *IL-6* gene.

The results of the genotype and allele frequency distribution analysis for the studied polymorphic variants are presented in Table 1. When analyzing the genotype frequencies of the rs4880 polymorphic variant of the *SOD2* gene, no statistically significant differences were found between the patients with VS and the control group ($p > 0.05$). However, a trend toward increased frequency of the homozygous T/T genotype was observed compared with the controls. In the patients with VS, the TT genotype was identified in 43.3% of cases, whereas it occurred in 29.7% of the control group ($\chi^2 = 2.80$, $p = 0.135$). The analysis of allele frequency distribution for the rs4880 polymorphic variant of the *SOD2* gene revealed a statistically significant increase in the frequency of the T allele in the patients with VS (65.7% vs 52.7% in the controls; $\chi^2 = 4.88$, $p = 0.027$). The calculated OR indicated that the T allele was associated with a 1.72-fold increased risk of VS (OR = 1.72; 95% CI: 1.06–2.78). Conversely, the C allele showed a significant decrease in frequency in the VS group: 34.3% compared with 47.3% in the controls ($\chi^2 = 4.88$, $p = 0.027$). OR = 0.58 suggests a protective role of this allele against VS (OR = 0.58; 95% CI: 0.36–0.94). The analysis of

Table 1. Comparison of the frequencies of polymorphic variant alleles and genotypes in the examined groups

Polymorphisms	Genotypes and alleles	Group with vibration disease		Control group		χ^2 or Fisher *F*-test	*p*
		n	%	*n*	%		
rs4880 (*SOD2* gene)	T/T	29	43.3	22	29.7	2.80*	0.094
	T/C	30	44.8	34	46.0	0.02*	0.889
	C/C	8	11.9	18	24.3	2.81**	0.094
	T	88	65.7	78	52.7	4.88*	0.027
	C	46	34.3	70	47.3		
rs361525 (*TNF-α* gene)	G/G	61	85.9	63	84.0	0.82***	0.928
	G/A	8	11.3	12	16.0	0.48***	0.557
	A/A	2	2.8	0	0.0	0.24***	0.470
	G	130	91.6	138	92.0	1.00***	0.333
	A	12	8.4	12	8.0		
rs16944 (*IL-1β* gene)	A/A	15	25.9	12	16.4	1.75*	0.185
	A/G	20	34.5	32	43.9	1.18*	0.277
	G/G	23	39.6	29	39.7	0.00*	0.993
	A	50	43.1	56	38.4	0.60*	0.437
	G	66	56.9	90	61.6		
rs1799750 (*MMP-1* gene)	1G/1G	20	37.0	27	35.5	0.03*	0.860
	1G/2G	21	38.9	34	44.7	0.44*	0.506
	2G/2G	13	24.1	15	19.8	0.35*	0.553
	1G	61	56.5	88	57.9	0.05*	0.820
	2G	47	43.5	64	42.1		
rs1800795 (*IL-6* gene)	C/C	12	20.3	9	12.2	1.09**	0.297
	C/G	19	32.2	29	39.2	0.69*	0.405
	G/G	28	47.5	36	48.6	0.02*	0.891
	C	43	36.4	47	31.8	0.64*	0.422
	G	75	63.6	101	68.2		

χ^2 test; ** Yates correction χ^2 test; *** Fisher exact test.

the *TNF-α* gene rs361525 polymorphic variant revealed no statistically significant differences in the genotype frequency distribution between the patients with VS and the controls. The dominant G/G genotype was observed in 85.9% of patients and 84.0% of the controls (F = 0.82; p = 0.928). The A/A genotype was detected in 2.8% of the patients with VS, but was absent in the controls (F = 0.24; p = 0.470). Similarly, no significant differences in allele frequencies were found between the groups (F = 1.00; p = 0.333). The *IL-1β* gene rs16944 polymorphic variant showed no significant differences in genotype frequencies between the patients with VS and controls, though a slight increase in A/A homozygotous variant was observed in the patients (χ^2 = 1.75; p = 0.185). No statistically significant differences in allele frequencies were detected between the patients with VS and controls (χ^2 = 0.60; p = 0.437). The analysis of the *MMP-1* gene rs1799750 polymorphic variant revealed no significant differences in genotype or allele frequencies between the groups (p > 0.05). The 1G/1G, 1G/2G, and 2G/2G genotype frequencies in the patients with VS were 37.0%, 38.9%, and 24.1% respectively, compared with 35.5%, 44.7%, and 19.8% in the controls. The 1G allele frequency was 56.5% vs 43.5%, and 2G allele 57.9% vs 42.1% in the patients with VS and the controls, respectively. The *IL-6* gene rs1800795 polymorphic variant also showed no significant differences in the genotype or allele distribution between the groups (p > 0.05). Despite no statistical significance, a non-significant increase in C/C homozygotes was observed in the patients with VS (20.3% vs 12.2% in the controls; χ^2 = 1.09; p = 0.297), with both groups showing G allele predominance (63.6% vs 68.2%; χ^2 = 0.64; p = 0.422).

DISCUSSION

This study evaluated the association between polymorphisms in the *SOD2*, *TNF-α*, *IL-1β*, *MMP-1*, and *IL-6* genes and the risk of VS. An association was found between the rs4880 polymorphic variant of the *SOD2* gene and VS. However, no data were obtained indicating associations of the rs361525 (*TNF-α*), rs16944 (*IL-1β*), rs1799750 (*MMP-1*), and rs1800795 (*IL-6*) polymorphic variants with VS.

The rs4880 single nucleotide polymorphism of the *SOD2* gene, characterized by an alanine-to-valine substitution at position 16, plays a significant role in various diseases. It is believed that the T allele induces structural changes in the mitochondrial domain of *SOD2*, which, in turn, leads to less efficient post-transcriptional transport into mitochondria and reduced superoxide anion neutralization capacity. Our study demonstrated an association between the T allele of the rs4880 *SOD2* gene polymorphic variant and VS. This finding partially aligns with the published data indicating this allele's association with increased risks of ischemic heart disease, stroke, and cardiomyopathy (T allele frequencies in patient cohorts with these diagnoses were 0.577, 0.481, and 0.670, respectively) [7, 9, 10]. A higher frequency of the TT homozygous genotype of the rs4880 *SOD2* polymorphic variant was observed in the patients with VS and comorbid arterial hypertension [11]. T allele may reduce resistance to mitochondrial reactive oxygen species and promote oxidative protein damage due to inefficient mitochondrial transport [12].

The studies have shown that finger numbness and other symptoms in hand-arm vibration syndrome may be associated with elevated TNF-α levels [13, 14]. Increased TNF-α levels have been detected in the patients with VS [15, 16]. The *TNF-α* gene contains several polymorphic sites, including the extensively studied rs361525. Some studies have reported an association between the rs361525 polymorphic variant of the *TNF-α* gene and susceptibility to rheumatoid arthritis and psoriatic arthritis [17, 18]. The GG genotype and G allele were more frequent in the patients with rheumatoid arthritis compared with the controls (0.931 vs 0.839 and 0.965 vs 0.905, respectively). However, similar results were not observed in our study of the patients with VS.

Interleukin-1 beta (IL-1β) participates in various pathological disc degeneration processes, with its expression significantly increased in the cells and tissues of degenerative intervertebral discs [19]. Elevated IL-1β levels have also been identified in the patients with VS [15, 16]. Elevated proinflammatory cytokine levels in the patients with VS indicate activation of inflammatory processes, potentially initiated by altered immune reactivity during prolonged exposure to physical factors [20]. TNF-α and IL-1β are among the first responders to vibration exposure. Inflammatory mediators cross the blood-brain barrier into the bloodstream, inducing glucocorticoid production, which subsequently suppresses the immune system [21]. The IL-1β cytokine is encoded by the *IL-1β* gene, which is highly polymorphic. The polymorphic variant rs16944 of the *IL-1β* gene is known to influence susceptibility to intervertebral disc degeneration, with evidence also linking it to predisposition for rheumatoid arthritis [22, 23]. For this polymorphism, the frequency of the C/C genotype was 21.4% in the control group versus 34.7% in the patients with intervertebral disc degeneration; C/T genotype was 50.5% vs 44.4%; and T/T genotype was 28.1% vs 20.9%, respectively [23]. The comparative analysis of genotype frequencies in the patients with rheumatoid arthritis revealed statistically significant increases in T/T homozygotes (13.4%) and C/T heterozygotes (49.2%), along with a decrease in C/C homozygotes (40.4%) compared with the controls (6.6%, 34.6%, and 58.8%, respectively) [22]. However, we found no association between the rs16944 polymorphic variant of the *IL-1β* gene and VS.

The evaluation of systemic inflammation markers revealed a significant increase in MMP-1 levels in the group of comorbid VS and arterial hypertension model [24]. The key intronic variant of the *MMP-1* gene is the rs1799750 polymorphism, which may lead to increased transcriptional activity and *MMP-1* expression. The studies of the rs1799750 polymorphism have shown its association with various inflammatory diseases, including rheumatoid arthritis and knee

osteoarthritis [25, 26]. The frequency distribution of 1G1G, 1G2G, and 2G2G genotypes in the patients with knee osteoarthritis was 24.7%, 50.0%, and 24.7%, respectively, compared with 34.4%, 49.8%, and 15.1% in the control group [26]. However, we found no association between this polymorphic variant and VS.

The patients with VS combined with arterial hypertension showed elevated levels of pro-inflammatory cytokines, including IL-6 [27]. The authors suggest that alterations in the cytokine profile intensify as VS progresses. Evidence indicates that *IL-6* gene polymorphisms may influence blood IL-6 concentrations and functional characteristics. The rs1800795 polymorphic variant, located in the promoter region of this gene, is a factor determining individual susceptibility to inflammatory processes and oxidative stress levels. This polymorphic variant has been associated with susceptibility to intervertebral disc diseases, rheumatoid arthritis, and the onset or progression of knee osteoarthritis [28–31]. Higher frequencies of GC (46.5%), CC (9.1%) genotypes, and the C allele (32.3%) were observed in the patients with rheumatoid arthritis compared with the controls (23.2%, 1%, and 12.6%, respectively) [28]. The CC genotype frequency (15.0%) was also higher in the knee osteoarthritis group than in the controls (4.3%) [30]. Our study revealed no statistically significant association between the *IL-6 gene* rs1800795 polymorphic variant and VS. When analyzing the data, we compared our results with those from the studies by other authors focusing on VS and conditions significantly influencing VS manifestations.

Study limitations. The main limitations include the small sample size, which may have limited the ability to fully achieve the study aim.

CONCLUSION

The study revealed an association between the rs4880 polymorphic variant of the *SOD2* gene and VS. It can be hypothesized that the T allele serves as a risk factor for VS, while the C allele exerts a protective effect against disease onset. No significant associations were found for polymorphisms in the *TNF-α*, *IL-1β*, *MMP-1*, or *IL-6* genes and developing VS. These findings may serve as a basis for developing screening programs aimed at identifying individuals with an increased risk of VS.

ADDITIONAL INFORMATION

Authors' contribution. G.F. Mukhammadiyeva — data collection, analysis and interpretation of results, literature review, preparation and writing of the article; E.R. Shaikhlislamova — study conception and design, literature review, editing the article; D.D. Karimov — data collection, analysis and interpretation of results; D.O. Karimov — study conception and design, literature review, editing the article; T.G. Yakupova — data collection, analysis and interpretation of results; Ya.V. Valova — data collection, analysis and interpretation of results; A.A. Gizatullina — data collection, analysis and interpretation of results. All authors confirm that their authorship meets the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research and preparation of the article, read and approved the final version before publication).

Ethical expertise. The study protocol was approved by the Committee on Biomedical Ethics of the Ufa Research Institute of Occupational Medicine and Human Ecology (Protocol No. 01-01 dated 01/22/2024). All patients signed an informed consent to participate in the study.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Г.Ф. Мухаммадиева — сбор данных, анализ и интерпретация результатов, обзор литературы, подготовка и написание текста статьи; Э.Р. Шайхлисламова — концепция и дизайн исследования, обзор литературы, редактирование статьи; Д.Д. Каримов — сбор данных, анализ и интерпретация результатов; Д.О. Каримов — концепция и дизайн исследования, обзор литературы, редактирование статьи; Т.Г. Якупова — сбор данных, анализ и интерпретация результатов; Я.В. Валова — сбор данных, анализ и интерпретация результатов; А.А. Гизатуллина — сбор данных, анализ и интерпретация результатов. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

Этическая экспертиза. Протокол исследования одобрен комитетом по биомедицинской этике ФБУН «Уфимский НИИ медицины труда и экологии человека» (протокол № 01-01 от 22.01.2024). Все пациенты подписали информированное согласие на участие в исследовании.

Источники финансирования. Работа выполнена в рамках отраслевой научно-исследовательской программы Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека на 2021–2025 гг. «Научное обоснование национальной системы обеспечения санитарно-эпидемиологического благополучия, управления рисками здоровью и повышения качества жизни населения России», пункт 2.2.9.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, иллюстрации, данные).

Доступ к данным. Редакционная политика в отношении совместного использования данных к настоящей работе не применима, новые данные не собирали и не создавали.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали два внешних рецензента, член редакционной коллегии и научный редактор издания.

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