ETHICAL AND LEGAL IMPLICATIONS OF GENETIC TESTING IN TRAUMATOLOGY AND ORTHOPEDICS

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The field of medicine has traditionally focused on such symptoms of a disease as pain, inflammation, and tissue deformity. However, according to the modern approach, it is necessary to identify the cause of the disease, which is often hidden deep inside the body. Examining genetic polymorphism as the basis for purulent complications after treatment of the lower limb injury was one of the method that could solve the problem. Epidemiological observations confirm that purulent complications after orthopedic surgery are associated with hereditary predisposition factors. This highlights the important role of genetic changes in development and course of this pathology. However, any medical intervention is associated with potential risks, including emotional pain of the patient, violation of personal data confidentiality and misuse of the obtained information. That is why it is important to think in advance about the possible consequences of genetic tests and to find ways how to resolve ethical issues.

Keywords: genetic research, polymorphism, ethics, lower limb injury

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ЭТИЧЕСКИЕ И ПРАВОВЫЕ АСПЕКТЫ ПРИ ПРОВЕДЕНИИ ГЕНЕТИЧЕСКОГО ИССЛЕДОВАНИЯ В ТРАВМАТОЛОГИИ И ОРТОПЕДИИ

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Традиционно медицина уделяла внимание лишь симптомам заболевания — боли, воспалению, деформации тканей. Но современный подход требует выявления причины болезни, часто скрытой глубоко внутри организма. Одним из методов решения этой проблемы стало изучение генетического полиморфизма как основы формирования гнойных осложнений после лечения травмы нижних конечностей. Эпидемиологические наблюдения подтверждают связь возникновения гнойных осложнений после проведенных хирургических вмешательств в ортопедической практике с факторами наследственной предрасположенности. Это подчеркивает важную роль генетических изменений в развитии и течении данной патологии. Однако любые медицинские вмешательства связаны с потенциальными рисками, включая эмоциональные переживания пациента, нарушение конфиденциальности личных данных и неправильное использование полученной информации. Именно поэтому важно заранее учитывать возможные последствия проведения генетических тестов и найти пути разрешения этических вопросов.

Ключевые слова: генетическое исследование, полиморфизм, этика, травма нижних конечностей

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Соблюдение этических стандартов: исследование выполнено в рамках выполнения утвержденной на ученом совете ЯГМУ докторской диссертации на тему «Лечение гнойных осложнений и прогнозирование их исходов у пациентов с травмой среднедистального отдела нижней конечности» (выписка из протокола № 11 заседания ученого совета ЯГМУ от 26.06.2024, номер госрегистрации: 124071000009-0). Работа одобрена этическим комитетом (выписка из протокола заседания этического комитета ЯГМУ от 14 июня 2024 г. № 68).

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BACKGROUND

To understand how genetic components can influence occurrence and course of purulent complications in trauma patients, scientists apply comprehensive research strategies, including family history, identification of differences in gene expression and a detailed study of the structural features of the genome [1].

Understanding the individual genetic characteristics of patients helps to create personalized treatment protocols that enhance effectiveness of therapeutic measures [2]. Though the mechanism of complications is still poorly understood, it obviously includes multiple factors and regulatory mechanisms [3]. Individual features of gene functioning have a little impact on the overall risk of disease development in the population. The significance of a specific genetic variation depends on its interaction with external conditions, influence of environmental factors and changes as a result of epigenetic processes characterized by unique physiological reactions in each patient [4].

The study of the impact produced by different genes on formation of a pathogenic cascade leading to purulent complications constitutes a promising trend. Taking into account the key role of immunity in the pathogenesis of purulent complications, genes involved in regulating the immune response are of particular interest. They include IL-17A, which is responsible for synthesis of protein interleukin 17A, and IL-6 that controls cytokine production. Both of these genes are essential in triggering and maintaining inflammation, and are also associated with a variety of diseases, including autoimmune disorders, infections, and cancer [5]. Thus, the significance of genetic research in trauma patients cannot be questioned. However, it is important to consider various ethical and legal implications. Both Russian, and foreign authors highlighted the complexity of resolving ethical issues while dealing with this type of research [6, 7].

ETHICS, MATERIALS AND METHODS OF GENETIC RESEARCH

At the first stage of selecting patients for genetic testing, each potential participant obtained the following information.

The study will be conducted at the laboratory of the Federal State Budgetary Educational Institution of Higher Education Yaroslavl State Medical University of the Ministry of Health of the Russian Federation (Rector, Professor, Academician of the Russian Academy of Sciences Khokhlov AL). A candidate genetic study will be performed. The study is about identification of IL17A and IL6 gene polymorphisms in the genome of patients treated for purulent complications after therapy of lower limb injury using allele-specific polymerase chain reaction (ASPCR) with SNP-EXPRESS-RV, a real-time fluorescent product detection system. This study is being carried out as part of a doctoral dissertation approved by the Academic Council of YSMU and entitled as ''Treatment of purulent complications and prediction of their outcomes in patients with medial lower extremity injuries" (the work was approved by the ethics committee (extract from the minutes of the meeting of the YSMU Ethics Committee dated June 14, 2024 No. 68)).

Inclusion criteria:

1) patients with a history of acute injuries of the musculoskeletal system at the level of the knee joint, shin, ankle and foot (fractures, dislocations, ligament tears);
2) patients who developed purulent and inflammatory complications (osteomyelitis, purulent arthritis, phlegmon, abscess) in the course of therapy and within a year after treatment;
3) the patients are 18–75 years old;
4) informed consent of the patient to participate in the study.

Exclusion criteria:

1) patients with chronic diseases that may influence the course of purulent complications (oncological diseases, HIV infection);
2) patients receiving immunosuppressive therapy;
3) patients with a recurrence rate of purulent and inflammatory complications for less than a year;
4) patients with a known history of genetic diseases associated with impaired immunity;
5) patients who refused to participate in the study.

The materials for the analysis were as follows.

Samples: 2000 µl sample of whole venous blood collected for testing into a disposable Lab-Vac vacuum tube with 200 µl of ethylenediaminetetraacetate anticoagulant solution.

Reagents: a set of reagents for testing single nucleotide polymorphism of the G-197A polymorphism of IL17A with ASPCR Mutation of IL-17A SNP-express-RV undiscovered-100 (Litekh, Russia); a set of reagents for testing single nucleotide polymorphism of the 174G in the IL6 gene with ASPCR Mutation of interleukin IL6 SNP-screen-RV undiscovered-100 (Syntol, Russia); SYBR Green is an asymmetric cyanine dye used in molecular biology for staining nucleic acids (SY for Synthetic, BR for Bromide, Green for the fluorescent properties of the dye, which emits green light when excited) (Thermo Fisher Scientific, USA).

Equipment: the amplification reaction will be carried out using the following devices: Dtlight detecting amplifier according to TU 9443-003-96301278-2010, 4S1 modification and DTprime according to TU 9443-004-96301278-2010, 5M3 modification from NPO DNA Technology LLC (Protvino). The devices used ensure implementation of qualitative and quantitative studies using the allele-specific polymerase chain reaction (ASPCR) method without the stage of electrophoresis of PCR products in agarose gel using reagent kits based on the principles of fluorescence detection.

Analysis methods: detection of PCR results using intercalating agents (SYBR Green I with an emission wavelength of 520 nm). The amount of accumulated PCR amplification product is estimated directly during the temperature reaction cycles (real-time PCR). The quantitative analysis is based on the standard PCR curve study with an analysis of the accumulated fluorescent signal through the FAM channel using an appropriate mathematical apparatus.

As mentioned above, detailed presentation of information to each subject will allow to get rid of unnecessary questions, on the one hand, and to identify misunderstandings and address the issue locally to avoid the loss of a specific potential participant in the study, on the other hand.

To ensure a special solution of ethical and legal issues, each of the implications should be considered in a more detailed way.

INFORMED CONSENT

First and foremost, every patient is entitled to receive complete information about the purposes, methods and possible consequences of genetic testing. It is important to explain to the patient the significance of the results obtained, the risks and benefits of the procedure, as well as the degree of diagnostic accuracy. A person can make an informed decision regarding their participation in the study only after complete information has been obtained.

Moreover, informed consent should include an explanation of how the data obtained will be used. The patient should clearly understand who will get access to the results of the DNA analysis, who else can see the information, and what goals the researchers have.

CONFIDENTIALITY OF PERSONAL DATA

Another important implication is protection of personal information from unauthorized access by third parties. Genetic information is a valuable resource for pharmaceutical companies, insurance companies, and even employers. If such information gets into the hands of unauthorized persons, discrimination of patients can be possible, medical care or employment can be denied.

To prevent the leakage of confidential information, the following precautions should be observed:

- separate storage of biosamples and databases;
- limited access of laboratory staff to patient data;
- transferring encrypted data between medical institutions;
- regular security audit of information systems of medical institutions.

RISKS OF FALSE POSITIVE AND FALSE NEGATIVE RESULTS

No test warrants that the result can be totally accurate. False positive and false negative conclusions can significantly damage the patient's health, cause unnecessary concerns, or lead to unreasonable treatment costs.

Thus, it is important to repeat tests if there are doubts about accuracy of the initial result. It is necessary to clearly understand what limitations the method have and inform patients about all known risk factors associated with the test.

LEGAL RULES AND QUALITY STANDARDS

Special attention is given to development of laboratory research quality standards, regulation of laboratory activities and protection of rights of patients. In most countries, the legislation provides for mandatory licensing of genetic laboratories, certification of equipment and specialists working with biosamples.

For example, Federal Law No. 323-FZ "On the Basics of Public Health protection in the Russian Federation", adopted in 2011, establishes rules for handling personal data of citizens, prohibits collection and processing of biometric data without the consent of the subject, regulates the storage, processing and transfer of such information [8].

There are also international normative acts, such as the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (ETS No. 164), aimed at protecting the dignity of the individual and the right of every citizen to privacy and health [9].

It is the legislation that creates conditions for safe and effective introduction of new technologies into medical practice, ensuring compliance with the basic principles of medicine such as respect for patient autonomy, fair allocation of health resources and concern for well-being for all as a whole [10].

MODERN APPROACHES TO SOLVING ETHICAL PROBLEMS

The use of genetic research in clinical practice is accompanied by a number of serious ethical issues. Thus, to overcome the difficulties, a solution of the issue and a solution of the ethical implication are proposed (see Table).

Thus, according to the table, the most problematic ethical implications in genetic research include confidentiality and discrimination, which, most probably, consist of the fear of information leakage into the Internet and building further negative stereotypes about a person. It is the demonstration of the database formation that will help overcome these implications, where the subject can see how the identifying information is specifically deciphered. Thus, the procedure of virtual depersonalization is shown. Every patient should be adequately informed about the goals, methods, and potential risks of genetic testing. The doctor must provide all the details about the clinical significance of the results obtained, potential dangers and benefits of the procedure. Meanwhile, existing modern technologies can minimize many of the risks that arise during genetic research. For example, modern sequencers decode the sequence of nucleic acids with a high accuracy, which helps avoid errors while interpreting the analysis results.

Automated information management systems make database secure, prevent the leakage of confidential information and reduce the likelihood of abuse by clinic staff.

New methods used by the physician council ensure a rapid exchange of experience between different regions of the country and the world, improving the quality of medical care provided to the population.

If necessary precautions are taken, genetic research brings significant benefits to patients, doctors, and society as a whole. Such tests help identify pathologies in a timely manner, select the optimal treatment strategy and prevent complications.

CONCLUSION

Genetic research opens up new perspectives for prevention, diagnosis and therapy of various diseases of the musculoskeletal system. It also raises a number of complex ethical issues related to protection of privacy, compliance with the principle of voluntariness and equal distribution of health resources.

Compliance with strict rules for genetic research will make this tool an effective means of improving public health, minimizing negative consequences and protecting the interests of all participants in the process. Successful implementation of the project depends on competence of health professionals, public awareness and willingness of the state to support the initiatives of scientists and doctors.

Table. Stages of solving ethical issues

Stage	Issue and solution	Solution	Overcoming success* %
Awareness	The duty of total patient awareness of purposes, methods and risks of a genetic testing	To provide as many details about the essence and purpose of the study as possible	85
Confidentiality	Reliable storage and processing of data exclusively by authorized persons	To tell and, if possible, to show in what form and where the received data will be stored	60
Legal liability	Liability for non-compliance with regulatory requirements	To concentrate on elements of informed consent, where liability in case of non-compliance with the regulatory requirements of the researcher is provided	90
The risk of erroneous conclusions	Possible incorrect conclusions due to incorrect tests	Explain the importance of a repeated examination in case of a negative result that will help eliminate errors	95
Discrimination	Possible influence of genetic testing results on availability of services and insurance	Medical secrecy is above all, data is depersonalized and not included into registers	65

* Note: the issue solving success rate was obtained based on the present study on genetic polymorphism in trauma patients, where out of the initial 269 people, 61 refused to participate after the selection procedure according to the ethical implication criteria.

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