

**Pharmacogenetic studies for personalized patient therapy in rehabilitation treatment programs at different stages of rehabilitation**

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**Abstract.** The article presents the experience of introducing personalized medicine technologies into the clinical practice of a rehabilitation hospital. An innovative approach to the therapy of patients at various stages of medical rehabilitation using genotyping (to identify hereditarily determined

features that determine the pathogenesis of the development of pathology, restorative potential, kinetics of drugs) makes it possible to assess the prognosis of the effectiveness and safety of medical interventions (including when prescribing pharmaceuticals) individually, taking into account the polymorphism of the candidate genes of the examined patient.

**Keywords:** personalized approach; pharmacogenetics; genotyping; rehabilitation treatment, rehabilitation

## **Introduction**

Personalized medicine based on the determination of human genetic characteristics is a promising trend in the management of a medical process based on genotyping. This approach is used in modern algorithms for choosing diagnostic, treatment, rehabilitation and preventive programs. Technologies for detecting gene mutations, allelic variants of genes associated with a predisposition to common diseases, metabolic disorders, detoxification, to the characteristics of pharmacokinetics - make it possible to predict genetically determined risks of the implementation of multifactorial diseases in a patient, disruption of adaptation mechanisms when exposed to unfavorable environmental factors. The peculiarities of the patient's genotype enable the doctor to determine the choice of biomarkers for the prevention of the development of pathology and complications, with the choice of adequate treatment to reduce the risk of iatrogenism [1, 2, 3].

**Purpose of the study** – determination of the polymorphism of allelic variants of candidate genes (protein products of which are involved in the regulation of homeostasis, adaptation, restoration of the body, in the processes of metabolism of xenobiotics) to assess the risk of developing multifactorial pathology and unwanted drug reactions - for adequate therapy and prevention of complications in the patient.

## **Materials and methods**

The object of the study is patients examined at different stages of rehabilitation treatment; methods - analysis of clinical and laboratory data, functional studies; genealogical analysis of family history; genotyping - molecular genetic study of patients' biomaterial using polymerase chain reaction (isolation, amplification - building up of the studied target gene fragments, detection of the results obtained); biomaterial - venous blood. The diagnostic panels used are various sets of single nucleotide gene polymorphisms (products of which are involved in the regulation of blood pressure, endothelial function, thrombus formation and thrombolysis, angiogenesis and revascularization, tissue sensitivity to hypoxia and toxic effects of endogenous and exogenous origin, maintaining homeostasis, metabolic activity, reparative regeneration, direction and strength

of the immune response to allo- and autoantigens). Interpretation of identified gene polymorphisms (based on the use of published meta-analyses on proven associations of genotypes with clinical manifestations, pharmacokinetics [4, 5] with an assessment of the contribution of the studied polymorphic variants of genes to the development of adaptive and pathological processes and responses to non-drug effects, biotransformation of pharmaceuticals in the body patient) with individual recommendations.

### **Results and discussion**

At the Central Clinical Hospital for Rehabilitation of the Federal Medical and Biological Agency of Russia, genetic counseling is carried out in the department of personalized medicine for patients sent from outpatient appointments and from the hospital. Genotyping of patients is used to assess the rehabilitation potential, the choice of adequate pharmacotherapy, and preparation for surgical treatment [6, 7, 8]. This is a method for identifying individual biological characteristics of a patient (genetically determined molecular mechanisms of metabolic regulation, adaptive reactions, the risk of the formation of multifactorial diseases and comorbid conditions, complications, an unwanted response to anesthesia and medications). Cooperation with licensed laboratories that carry out the necessary molecular genetic studies of the biomaterial of patients allows obtaining genotyping data in order to prepare clinically meaningful interpretation of the results for patients and attending physicians. The choice of profiles for genotyping is carried out by a geneticist according to the history and clinical diagnoses of the patient, family history of multifactorial diseases (especially in cardiovascular pathology with a high risk of heart attacks and strokes: with arterial hypertension, with impaired hemostasis, lipid and carbohydrate metabolism). As part of the personalization of treatment, the pharmacogenetic characteristics of the patient are investigated (for drugs for long-term use - antihypertensive drugs, anticoagulants, antiplatelet agents, statins, non-steroidal anti-inflammatory drugs, etc.) - both for an adequate choice of the drug itself and for choosing its therapeutic dose [9, 10]. Also in demand are studies on the risk of developing cancer, endocrinopathies and osteoporosis, genetic testing for detoxification profiles, pro-inflammatory cytokines, metabolism for weight correction and the formation of individual programs of physical activity and nutrition, the choice and use of correctly dosed nutritional supplements, vitamins and micronutrients that optimize gene activity. The results of genotyping and subsequent genetic counseling, reflected in the conclusion of a geneticist, are important information for the patient and the attending physicians. The final genetic report presents the identified features of the patient's genotype. They can be regarded as individual predictors of insufficiency of adaptive-restorative processes, predisposition to pathology, risk of complications and adverse reactions to treatment. Therefore, in the conclusion of a geneticist, an interpretation of the clinical significance of the

results of genotyping is presented, on the basis of which the attending physician can reasonably choose: biomarkers for monitoring the clinical, laboratory and functional state of the patient; the most effective and least toxic drugs, calculate their dosage (based on the metabolic rate); use the information received to prevent complications and improve the effectiveness of rehabilitation treatment.

**Conclusion:** a personalized approach with the determination of the possibilities of individual rehabilitation in patients of various profiles (neurological, cardiological, orthopedic, therapeutic) allows doctors to carry out comprehensive rehabilitation treatment programs, taking into account the genetic determinism of pathological and restorative processes. To choose, taking into account the patient's genetic characteristics, the most effective and safe options for drug therapy and non-drug technologies: adequate nutrition; motor mode; physiotherapy exercises; treatment with physical factors (balneotherapy, peloid therapy; low-frequency laser and magnetic therapy, ultrasonotherapy, electro- and phonophoresis with various pharmaceuticals, etc.), as well as prescribe individual training programs, kinesitherapy, which reduces the risk of complications and increases the effectiveness of rehabilitation.

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