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PHARMACOGENETICS AS A TOOL IN PERSONALIZED MEDICINE: FROM GENOTYPE TO THERAPY SELECTION

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Abstract

Pharmacogenetics is an important component of personalized medicine that enables the individualization of pharmacotherapy based on patients' genetic characteristics. Genetic polymorphisms in genes encoding drug-metabolizing enzymes, transport proteins, and receptor structures can significantly affect the pharmacokinetics, pharmacodynamics, therapeutic efficacy, and safety of medications. This study presents an analytical review of contemporary scientific literature examining the clinical significance of pharmacogenetic variability and its application in individualized drug selection and dosage optimization. Particular attention is given to clinically relevant polymorphisms in the CYP2C19, CYP2D6, and VKORC1 genes and their association with variability in response to clopidogrel, codeine, and warfarin therapy.

The analysis demonstrates that pharmacogenetic testing can contribute to the identification of patients at increased risk of treatment failure or adverse drug

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reactions and can support the selection of appropriate therapeutic strategies and drug dosages. Clinical examples involving antiplatelet, analgesic, and anticoagulant therapy illustrate the practical value of integrating genetic information into clinical decision-making. The implementation of pharmacogenetic approaches may improve the effectiveness and safety of pharmacotherapy and facilitate the transition from standardized treatment strategies toward more individualized and scientifically grounded medical care. Further integration of pharmacogenetics into clinical practice represents an important step toward the development of precision and personalized medicine.

Keywords: Pharmacogenetics; personalized medicine; pharmacogenomics; genetic polymorphisms; CYP2C19; CYP2D6; VKORC1; drug metabolism; pharmacotherapy; precision medicine; adverse drug reactions; individualized therapy; pharmacogenetic testing; drug response.

Introduction

In recent years, the concept of a personalized approach to treatment, based on the consideration of individual biological characteristics of patients, has been actively developing in medicine. One of the key areas of this approach is pharmacogenetics, which studies the influence of genetic variations on the pharmacokinetics and pharmacodynamics of drugs. Individual differences in genotype determine the rate of drug metabolism, their bioavailability, and the sensitivity of receptor systems, which directly affects the effectiveness and safety of the therapy being conducted. As a result, traditional standardized treatment regimens are gradually giving way to more precise and justified methods of drug selection.

The relevance of pharmacogenetics is due to the high variability of patient responses to drug therapy, which is particularly significant in the treatment of chronic and life-threatening diseases. Differences in the activity of enzymes

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involved in drug metabolism can lead to both reduced therapeutic effects and the development of adverse side effects. The use of pharmacogenetic testing allows for the prediction of individual responses to medications, optimization of their dosages, and minimization of the risk of complications, thereby increasing the effectiveness and safety of treatment. Thus, the integration of genetic data into clinical practice represents an important stage in the development of modern medicine and forms the basis for the transition to personalized therapy [1].

The goal of the research:

The objective of this study is to conduct a comprehensive analysis of the role of pharmacogenetics as a key direction in personalized medicine aimed at enhancing the effectiveness and safety of drug therapy. The work examines the impact of genetic polymorphisms on individual characteristics of drug metabolism, distribution, and action, as well as their clinical significance in various therapeutic areas.

A separate task of the research is to study the relationship between the genetic characteristics of patients and the variability of their responses to medications. In particular, the mechanisms related to the activity of biotransformation system enzymes, transport proteins, and receptor structures that determine individual sensitivity to pharmacotherapy and the risk of adverse reactions are analyzed.

The aim of the work is also to assess the prospects of implementing pharmacogenetic testing in clinical practice as a tool for optimizing the selection of medications and their dosages. The significance of this approach for transitioning from standard treatment regimens to personalized therapy strategies aimed at improving the quality and safety of medical care is considered.

Materials and Methods:

This study employed an analytical review of contemporary scientific publications dedicated to the issues of pharmacogenetics and its role in personalized medicine.

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Scientific articles, reviews, and materials from international organizations reflecting current data on the influence of genetic polymorphisms on the pharmacokinetics and pharmacodynamics of drugs were selected as information sources [1].

The analysis was conducted using methods of comparative assessment and summarization of scientific data. The results of studies examining genetic variations that affect the activity of drug metabolism enzymes, transport proteins, and receptor systems were considered. Special attention was given to data on the clinical application of pharmacogenetic testing in therapy selection and the individualization of drug dosages.

Throughout the work, systematic selection and interpretation of information were carried out to identify key patterns determining the relationship between a patient's genotype and the effectiveness of drug treatment. The obtained data were structured and analyzed for subsequent use in evaluating the prospects for integrating pharmacogenetics into clinical practice.

Results and Discussion:

Analysis of current scientific data shows that pharmacogenetics plays a key role in shaping an individual's response to drug therapy. One of the most studied areas is the impact of polymorphisms in the cytochrome P450 (CYP450) gene system, which is responsible for the metabolism of a significant number of medications. In particular, variations in the CYP2C19 gene significantly alter the effectiveness of clopidogrel antiplatelet therapy, directly affecting the risk of thrombotic complications in patients with cardiovascular diseases [1].

Clinical Example 1: Patients with the "poor metabolizer" form of the CYP2C19 gene exhibit reduced conversion of clopidogrel into its active metabolite. This leads to insufficient antiplatelet effect and an increased risk of myocardial infarction or stent thrombosis. In such cases, switching to alternative antiplatelet agents that do not rely on this metabolic pathway is recommended. This example

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demonstrates the direct clinical significance of genetic testing before initiating therapy [2].

Another important example is the CYP2D6 gene, which is involved in the metabolism of opioid analgesics such as codeine. Codeine is a prodrug that must be converted into morphine to exhibit its analgesic effect. In patients with low CYP2D6 activity, insufficient analgesic effect is observed, whereas “ultra-rapid metabolizers” may experience toxic accumulation of morphine, leading to respiratory depression and other serious complications [3].

Clinical Example 2: A patient following surgery receives a standard dose of codeine but does not experience adequate pain relief. Genetic analysis reveals low CYP2D6 activity, explaining the therapy's ineffectiveness. As a result, a switch is made to an alternative analgesic that does not depend on this enzyme. This illustrates the importance of a pharmacogenetic approach in individualizing pain management therapy [3].

The VKORC1 gene, associated with sensitivity to the anticoagulant warfarin, is also of particular significance. Polymorphisms in this gene determine the level of sensitivity to the drug and the risk of bleeding. Patients with certain VKORC1 variants require significantly lower doses of warfarin to achieve therapeutic effect, making standard dosing regimens potentially dangerous [4].

Clinical Example 3: A patient with thrombosis is prescribed warfarin at a standard dosage, but significant bleeding occurs. Subsequent pharmacogenetic analysis reveals high sensitivity due to a VKORC1 variant. After dose adjustment, a stable anticoagulant effect is achieved without complications. This confirms the necessity of genetically informed dosage selection [4]. Summarizing the obtained data shows that pharmacogenetic characteristics not only influence the effectiveness of therapy but also the safety of treatment. Individual differences in enzyme activity, transport systems, and receptors create a unique profile of response to medications for each patient. This makes a one-size-fits-all approach

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to dosing impossible in several clinical situations and necessitates the implementation of personalized treatment algorithms [5].

Thus, pharmacogenetics represents one of the most promising directions in modern medicine, allowing a shift from universal treatment schemes to a scientifically grounded individualized approach to patient therapy. Considering genetic features that determine metabolic enzyme activity, transport systems, and receptor structures enables more accurate predictions of the effectiveness and safety of medications while minimizing the risk of adverse drug reactions. The application of pharmacogenetic technologies in clinical practice enhances the quality of medical care, optimizes drug dosages, and reduces the frequency of complications associated with drug therapy. This approach becomes particularly significant in the treatment of chronic, cardiovascular, and oncological diseases, where the precision of therapy selection directly affects patient prognosis. The development of pharmacogenetics and its integration into the healthcare system open up prospects for creating fully personalized medicine of the future, where treatment will be based not on average standards but on the individual genetic profile of each patient, significantly improving the effectiveness and safety of medical interventions [5].

Conclusions:

The analysis of literary data and clinical examples allows us to conclude that pharmacogenetics is a key area in the development of modern personalized medicine. It has been established that genetic polymorphisms, particularly in the genes of the cytochrome P450 system (CYP2C19, CYP2D6), as well as in the genes regulating the blood coagulation system (VKORC1), significantly influence the pharmacokinetics and pharmacodynamics of drugs. This determines individual differences in therapy effectiveness and the risk of adverse reactions, highlighting the necessity of considering genetic factors when prescribing treatment.

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The research results demonstrate that the implementation of pharmacogenetic testing in clinical practice can significantly increase the accuracy of drug selection and dosages. Utilizing genetic information helps reduce the frequency of ineffective therapy and severe adverse drug reactions, thereby enhancing the safety of patient treatment. The clinical examples discussed in this work vividly confirm the importance of an individualized approach in medical fields such as cardiology, oncology, and analgesic therapy. Thus, pharmacogenetics serves as a fundamental basis for the transition from empirical medicine to scientifically justified personalized therapy. Its further development and integration into the healthcare system open up prospects for improving the effectiveness of medical care, enhancing disease prognosis, and forming a new model of medicine focused on the individual genetic characteristics of each patient.

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