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Research Article

Review on: Pharmacogenomics from Genetic Code to Personalized Drug Therapy.

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ABSTRACT

Pharmacogenomics (PGx) is one of the main branches of personalized medicine and concerns genetic variations between people that affect their susceptibility to medications. In spite of equal drug and dosing prescriptions to different patients, some discrepancies in therapeutic effects can be observed. Some of them get a good effect from the prescribed drug, while other patients will not feel any effect or even have an adverse reaction. It is due to genetic variability that impacts drug absorption, distribution, metabolism, elimination, transport, and targets. Pharmacogenomics implies using genetic data to increase the accuracy of drug therapy. At the moment, pharmacogenomics is especially actual for cardiovascular diseases, oncology, neurology, psychiatry and pharmacovigilance. Many significant gene-drug interactions exist with CYP2C19, CYP2D6, CYP2C9, DPYD, TPMT, NUDT15, HLA genes and SLCO1B1. India has enormous opportunities for pharmacogenomics development because of its huge population and genetic diversity. However, there are some obstacles caused by lack of population-based data, high costs of testing, interpreting genetic information and implementing pharmacogenomic data into clinic practice. Innovative approaches in such fields as artificial intelligence, real-world data, databases and decision support systems can help to promote pharmacogenomics.

INTRODUCTION

Individuals react differently to a particular drug. Something that might give good results to one person as far as drug response is concerned may not work for another individual. Some individuals may also develop adverse reactions to drugs despite receiving them at the

recommended doses. There exist several factors behind individual variations such as age, sex, diseases conditions, foods, drug interaction, organ function, adherence and genetics. Pharmacogenomics can be defined as the field of science studying the influence of genetic composition on drug response. It is a combination of pharmacology – a study of medicines and effects – and

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genomics – a study of genes and their functions. The main purpose of pharmacogenomics is to understand the connection between the two in order to improve treatment methods. In general, medicine practice uses a population-oriented approach in which the standardized dose of a drug is used in treating particular diseases. This approach works well but does not address individual variations fully. Pharmacogenomics is a way to achieve a personalized treatment strategy. Genetic variations affect proteins that influence drug absorption, distribution, metabolism and action. Metabolism variations may imply that somebody absorbs and metabolizes a particular drug faster or slower than others. People can be grouped into five categories based on the speed of drug metabolism: poor, intermediate, normal, rapid and ultrarapid. Development of pharmacogenomic database and genomic testing has led to an increasing interest in the use of genetic information in medicine practice. Nevertheless, pharmacogenomics is not fully developed yet and not all genetic associations have enough evidence to justify their use in a clinical setting. Thus, pharmacogenomic data should be analyzed in light of scientific data and clinical guidelines.

Objectives

The following are some of the objectives that have been set for the current review:

1. Comprehending the concept and significance of pharmacogenomics.
2. Comprehending how genetic variations affect the response to drugs.
3. Comprehending the important gene–drug interactions.
4. Comprehending the different uses of pharmacogenomics in the various fields of therapy.
5. Comprehending the significance of pharmacogenomics in the prevention of adverse drug reactions.
6. Comprehending the significance of pharmacogenomics in Indians.
7. Comprehending the use of artificial intelligence in pharmacogenomics.
8. Comprehending the important issues in pharmacogenomics.

9. Comprehending the future perspectives of pharmacogenomics.

METHODOLOGY

In the current review paper, information has been gathered from recently published research articles and reviews in various areas such as pharmacogenomics, personalized medicine, pharmacovigilance, genetics variations, and their clinical uses.

Literature search has been done to get information about important pharmacogenomic genes, drug-gene interactions, clinical use, genetic variations in particular population, and new technologies. In particular, those studies which have been done in the area of pharmacogenomics in the Indian population and the role of genetic information in the prevention of adverse drug reaction.

The information obtained has been classified as below: Principles of pharmacogenomics, drug-gene interactions, clinical uses, Indian population, pharmacovigilance, clinical uses, limitations and future perspectives.

Pharmacogenomics and Genetic Variation

Genetic variation is one of the key elements which explains why different people have different responses to the same medication. Genotype determines individual differences, thus leading to changes in the functioning or deactivation of proteins. There are different enzymes involved in drug metabolism, so it is important to pay attention to the enzymes involved in it. Enzymes from cytochrome P450 group (CYP2D6, CYP2C19 and CYP2C9) play an important role in drug metabolism. Any changes in the structure of these enzymes lead to the changes in their activity rate. For example, in case a drug needs to be activated through metabolism, the fast metabolism rate will negatively affect the effectiveness of the drug, while the slow metabolism rate increases the concentration of the drug in the body. Low rate of drug metabolism results in the increase of drug concentrations in the body. Moreover, pharmacogenomics deals with transporters and drug target genes. In several ways, genetic variation affects pharmacokinetics and pharmacodynamics of the drug. The poor, intermediate, normal, rapid and ultrarapid metabolizers classification is one of the characteristics



of pharmacogenomics. Patients are classified according to the rate of their drug metabolism. This helps to understand why some people have high and low concentrations of drugs even if they take equal amounts of the medications. However, genetic variation is not the only element which affects the drug response of the body. Such elements as age, organ function, drug interactions, smoking, etc. affect the drug response of the body.

Examples of Clinical Relevant Gene-Drug Interactions

There are examples of clinical relevant gene-drug interactions which have arisen due to pharmacogenomics.

• CYP2C19 and Clopidogrel

The above-mentioned anti-thrombotic drug should be activated through the metabolism. The information concerning pharmacogenomics of CYP2C19 variability should be considered in the case of using clopidogrel.

• CYP2C9/VKORC1 and Warfarin

Warfarin is the anti-coagulant drug with the narrow therapeutic index and the dosing depending on the patient. The variability of the genes CYP2C9 and VKORC1 will affect the effectiveness of the treatment with warfarin. Therefore, both clinical and pharmacogenetic information can be used in defining the individual dose of warfarin.

• DPYD and Fluorouracil

Fluoropyrimidines and their analogs are widely used in the cancer therapy. DPYD variability influences the metabolism of these drugs and increases the risk of adverse effects. Thus, identification of this genetic variation will decrease the risk of the adverse side effects of the treatment.

• TPMT and NUDT15 with Thiopurines

Variability of TPMT and NUDT15 will affect the metabolic pathways of mercaptopurine and azathioprine and the risk of adverse effects. Thus, genetic testing can be done in case of treatment of thiopurines.

• HLA-B and Drug Hypersensitivity

Variability of the HLA-B allele causes immune-mediated adverse drug reaction. Identification of HLA-B variability is one of the genetic tests used for detection of increased risk of adverse effects.

• SLCO1B1 and Statins

SLCO1B1 gene encodes the protein which transports drugs including statins. SLCO1B1 variability will influence the efficacy of statins and cause the risk of adverse effects. These are examples of pharmacogenomics application in the case of gene-drug interaction.

Application of Pharmacogenomics

• Cardiovascular Diseases

Cardiovascular diseases represent one of the most important aspects in studying pharmacogenomics.

There exist some drugs like clopidogrel and warfarin which demonstrate high level of variability in metabolism in terms of their genetic characteristics. It is known that the efficacy of clopidogrel depends on the patient's genetic characteristics whereas the dose of warfarin should be determined according to the patient's genotype. Thus, the results obtained in the process of researching pharmacogenomics are useful for making appropriate decisions related to treatment.

• Cancer Treatment

Treatment of cancer is one of the most interesting applications of pharmacogenomics.

Generally speaking, anticancer drugs have narrow therapeutic windows thus, individual differences in genetics may cause increased side effects due to metabolic variations. Interaction between DPYD gene and fluoropyrimidines represents just one example. Application of pharmacogenomics enables predicting dangerous side effects and choosing treatment carefully. Furthermore, pharmacogenomics helps in promoting targeted treatment because of understanding the role of genetics in treatment.

• Neurological and Psychiatric Disorders

Individual variations in treatment results in people suffering from psychological disorders are important as well.



Change or modification of treatment of patients taking antidepressants becomes necessary because of their low effectiveness and side effects. Recent studies revealed that such genes as CYP2D6 and CYP2C19 are important for determination of the influence of antidepressants whereas CYP2B6 influences serotonin reuptake inhibitors. Currently, there is enough information about pharmacogenomics that can be applied in case of mismatch between the patient and drug. However, there is not enough information about the necessity of conducting comprehensive genotyping in order to determine the right drug. Thus, pharmacogenomics can be considered only as supportive tool.

• Prevention of Adverse Drug Reactions

Prevention of adverse drug reactions is one of the most interesting applications in pharmacogenomics.

Information about reasons for adverse reactions helps to change treatment regimen and even replace medicines if necessary. In this way, pharmacogenomics turns pharmacovigilance into prevention.

Pharmacogenomics in the Indian Population

To start with, India is a unique region where it is possible to work on the development of pharmacogenomics due to the presence of a great number of genetically variable individuals in the country. Various gene variations related to the drug response are found in the Indian population with different prevalence. A great number of pharmacogenomics resources have been developed using data obtained from European and North American individuals. Consequently, the use of data about pharmacogenomics in the context of the Indian population is sometimes wrong because of differences in genetic variation between India and other countries. The scoping review conducted in 2025 focused on pharmacogenomic variants that might be used by the Indian doctors. This scoping review was done according to the data provided by WHO about essential medicines and medicines for neonatal intensive care, Association for Molecular Pathology and IndiGenomes database. As a result, it became possible to identify 24 genes associated with the drug response in the case of 57 medications. Therefore, it became evident that there is a need to collect more information about pharmacogenomics in India. The collection of genetic data

about Indians would help to determine the special variants that would be useful for them. However, another important issue is the question of access to the test results. Genetic tests should be available to everyone in order to make pharmacogenomics effective.

Pharmacogenomics and Precision Pharmacovigilance

Pharmacovigilance can be defined as efforts aimed at detecting, assessing, and preventing adverse drug reactions. Pharmacogenomics assists in pharmacovigilance since it identifies people prone to such reactions in every individual case. Normally, pharmacovigilance involves adverse reaction reports of drugs and their explanations. With the help of pharmacogenomics and real-world evidence, we can develop a framework of precision pharmacovigilance that employs genomics, clinical data, electronic health records (EHR), and others to monitor safety of medications. Artificial intelligence could be used for identifying patterns in data gathering and analysis. The discussion could involve such points as data standardization, genomic analysis, regulatory and ethical issues, and pharmacogenomics education.

Artificial Intelligence and New Technologies

AI will help in analyzing the data and establishing relationships between genotype variations, drug intake, and the patient's response. AI can also assist in making clinical decisions, including all necessary pharmacogenomics data in prescribing a certain drug. The key aspect here will be the integration of various types of biological data. In the future, genomic data may be combined with transcriptomic, proteomic, metabolomic, and clinical data to provide a more precise explanation of the effect of the drug on the patient. However, one should properly apply new technologies, since very sophisticated models do not always function successfully.

Implementation of Pharmacogenomics in Clinical Settings

The move from the bench to the bedside poses one of the biggest challenges in the field of pharmacogenomics. Having a genetic test does not necessarily mean that such a test would improve patient care. There



are different things to consider in implementing pharmacogenomics. They include carrying out the tests in a good laboratory setting, interpreting results, guidelines, electronic health records and the right professionals. A pharmacist can greatly contribute to the implementation process of pharmacogenomics because the pharmacist is knowledgeable in pharmacology, pharmacokinetics, and medication issues. The test for pharmacogenomics can be carried out before there is need for medication - this is referred to as preemptive testing, or in reference to certain drugs - this is referred to as reactive testing.

Limitations and Challenges

There are many limitations in applying the pharmacogenomics nowadays.

• The Lack of Population-Specific Data

The lack of genomic data acquired from several populations is one of them. In case of India, this problem is especially relevant due to its population diversity.

• Expensive and Unavailable Testing

Genetic testing can be expensive and can be unavailable. The costs of testing, lab facilities and interpreting test results can prevent people from using it.

• Interpreting Results

Not all the information regarding genetics can be easily interpreted. A specific variation of a certain gene can influence drug action, however, clinical relevance of this information will depend on the specific drug, dose and patient's characteristics.

• Insufficient Awareness

Doctors usually don't have enough knowledge regarding pharmacogenomics. To improve the situation, pharmacogenomics should be included in the education process of pharmacists and doctors-to-be.

• Privacy, Ethical and Data Storage Issues

The genetic information can become confidential and require special protection. The issues of privacy, ethical use and storage, patient's consent should be considered.

• The Lack of Clinical Relevance of Genes-Drugs Associations

Not all of the associations between genes and drugs are clinically well-founded. Recently conducted studies in the sphere of psychiatry showed that there was more evidence regarding specific associations based on CYP enzyme rather than general commercial panels used for classification of drugs. Therefore, testing should be done according to clinically relevant data.

Future perspectives

Among the future perspectives in the field of pharmacogenomics is increased use of these findings in regular medical practice. With expanding genomic databases, it is expected that new drug-gene interactions with practical value will be identified.

In the nearest years, pharmacogenomic data may become a part of electronic medical records (EMR) of patients. Then, it will be possible to use a patient's genetic data at all steps of his/her treatment process, rather than repeating this test whenever there is need to prescribe a new medicine.

Besides that, clinical decision support systems might start giving alerts in the case of prescribing a medicine to a patient that might interact with the patient's genome. Thus, the systems will help healthcare providers to adjust the dose of medicines, choose other drugs, and/or conduct additional monitoring if necessary.

With the use of artificial intelligence and real-world evidence, it is possible to analyze genomic and clinical data in a better way. However, the transparency and interpretability of clinical information in future systems should be maintained.

Recent studies about pharmacogenomics of antidepressants suggest that the most realistic perspective is not an approach when genetics will define the optimal medicine for a patient. On the contrary, pharmacogenomic data will become one part of the algorithm of decision-making that also will take into account clinical data of a patient, his/her concomitant medicines, history of adverse effects, and other factors.



The expansion of population-specific databases would be very important for India. Additional research will help to identify relevant genetic markers.

CONCLUSION

Pharmacogenomics can be viewed as a revolution in finding out how drug responses vary in various people. Pharmacogenomics represents a change from the approach when all people received the same kind of drugs to more individual treatment interaction between genes and drugs in connection with CYP2C19, CYP2D6, CYP2C9, DPYD, TPMT, NUDT15, HLA, and SLCO1B1 emphasizes the importance of pharmacogenomics and its implementation in cardiology, oncology, psychiatry, neurology, and pharmacovigilance. Nevertheless, pharmacogenomics can be seen only as one of steps which help solve the problem of personalized drug treatment. Analysis of the results of genetic testing should consider not only genetic features of patients but also their past, co-morbidities, conditions. Problems connected with high costs, lack of population-specific data, difficulties in interpreting tests, patient privacy, and low knowledge still need to be solved. Consequently, in connection with genetically highly diverse population as it can be found in India, development of the genomics database specifically for the certain population becomes an important step. Researches, guidelines about pharmacogenomic tests, educational programs for pharmacists and health care providers, artificial intelligence may become helpful in the process. In conclusion, pharmacogenomics provides a possibility of obtaining the safe and individual drug therapy. However, the future of pharmacogenomics depends on the discovery of the new interactions between drugs and genes and use of genomic information in practice.

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