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A BRIEF REVIEW ON PHARMACOGENOMICS

Pranav Upadhyay, Pranjul Shrivastava*, Rashmi Pandey, Rupali Bharti Sao, Sandip Prasad Tiwari
Faculty of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh India (492101)

*Corresponding Author's E mail: pranjul.shrivastava@kalingauniversity.ac.in
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ABSTRACT

Pharmacogenomics is the study of genes and how a drug's effects on a person's response. Pharmacogenomics is a rapidly developing field of medicine that combines the fields of genomics, which studies genes, and pharmacology, which studies drugs, to create safe, effective doses of medication that are specific to each patient's genetic preferences. One of the most important programs in which scientists are creating and learning about the relationship between genes and how the body reacts to drugs is the Human Genome Project. Variations in genetic composition contribute to variations in drug efficacy and can be used to forecast future therapeutic efficacy for a given individual as well as investigate the occurrence of adverse drug reactions. Pharmacogenomics is still in its infancy, despite advances in science and technology. Pharmacogenomics is not widely used, although new methods are continually being tested in clinical settings. Pharmacogenomics will soon make it possible to create specialized medications to treat common health issues like HIV, cancer, asthma, neurological diseases, and cardiovascular disorders.

Keywords: Pharmacogenomics, Gene Sequencing, Genotyping, Phenotyping.

INTRODUCTION

The study of pharmacogenomics focuses on how a person's genetic makeup influences how their body reacts to medications. The phrase refers to the area where genetics and pharmacology converge. It is derived from the terms pharmacology and genomics. Pharmacogenomics offers hope that medications may eventually be customized to a person's unique genetic composition. Although a person's environment, food, age, lifestyle, and health can all affect how they react to medications, it is believed that knowing a person's individual gene composition will be essential to developing tailored drugs that will be more effective and safer. A person's drug response, which encompasses both positive and negative reactions, is a complicated characteristic regulated by numerous genes. It has proven challenging for scientists to create

genetic tests that could forecast an individual's reaction to a given treatment because not all the genes implicated in drug response are known [1,2].

Pharmacogenomics in the treatment of cancer

Pharmacogenomics appears to be more potent in the realm of oncology than anywhere else. Since a medication must interact with two genomes in this situation, somatic or tumor-specific gene alterations as well as hereditary or germline mutations can affect a drug's effects. With a few notable exceptions, a prevalent paradigm is that somatic variants have a noteworthy effect on clinical efficaciousness and germline mutations significantly influence metabolism.

Pharmacogenomic testing in the treatment of cancer includes- Colorectal cancer-

Camptosar (Irinotecan) is one form of a chemotherapy that is frequently used by doctors for the management of colon cancer. Genetic mutations can result in a deficiency in the UGT1A1 enzyme in certain individuals. This is the enzyme that is in the charge of irinotecan metabolism [3].

Acute lymphatic or lymphoblastic leukemia (ALL)- For small children with ALL, pharmacogenomic testing is used by doctors. A genetic difference in the enzyme thiopurine methyltransferase affects about ten percent of the population. TPMT is in charge of processing ALL chemotherapy. Chemotherapy doses are reduced for small children with lower TPMT levels. This lessens the chance of serious negative side effects [4].

Importance of pharmacogenomics

The horror of experiencing a serious adverse reaction to a prescription medication is not well conveyed by adverse drug reactions. However, such unfavorable responses are still possible. In the United States, adverse drug reactions (ADRs) accounted for over 2.2 million serious cases and over 100,000 fatalities in 1994, making them one of the leading causes of hospitalization and mortality, according to a hospitalized patient study from 1998 that was released in the American Medical Association Journal.

If the doctor had known beforehand about the patient's DNA profile, which dictates the medication reaction, many of the mortality could have been prevented. Because there is currently no easy way to predict whether a patient would react to a treatment well, poorly, or neither at all, pharmaceutical industries are forced to design medications based on a one-size-fits-all approach. A strategy to deal with the matter of ADRs before they occur is what's required [5].

Advantages of pharmacogenomics

Pharmacogenomics can be defined as an integration of annotated understanding of proteins, genes, and variants in single nucleotides with traditional medicinal sciences like biochemistry. These are some benefits-

(1) **More powerful medicines**- It will be possible for pharmaceutical companies to develop medications based on the RNA molecules, proteins, and enzymes connected to genes and illnesses. This will speed up the searching process of new drugs and enable producers to manage medical treatments that are more specialized to particular illnesses. This precision will reduce harm to neighboring healthy cells while also optimizing therapeutic benefits.

(2) **Better and safer drugs for the first time**- Physicians will have the ability to evaluate a patient's genetic information and recommend the optimum therapy from the start, replacing the current trial-and-error approach for matching population with the appropriate medications. This will not just eliminate uncertainty from selecting the appropriate medication, but it will also expedite recuperation and enhance security by removing the possibility of negative responses [6,7].

BARRIERS TO PHARMACOGENOMICS PROGRESS

A vast amount of information on numerous potentially clinically significant genetic factors of medication efficacy and toxicity has been obtained through basic research in recent decades. More recently, larger, genome-wide searches for factors influencing medication reaction has been made feasible by the quick development of genomic technologies. Collectively, these developments are extensively marketed as the cornerstone of a novel age of customized drug-based therapies. It is evident that in order to effectively utilize genomic advancements in the therapeutic context, a number of progressively intricate obstacles must be removed [8,9].

Clinical implementation of pharmacogenomics

Pharmacogenomics may have an impact on clinically significant drug dose, which may lead to recommendations for further research. Pharmacogenomics has yielded conflicting results for medications. One likely explanation is that the degree to which genetic and nongenetic factors influence a drug's therapeutic relevance depends on both of them. The restrictions and difficulties of applying pharmacogenomic tests in practice are further compounded by issues related to legal, and societal concerns, issues related to cost effectiveness, provider knowledge, practicality, utility, and degree of evidence [10].

Genotyping and phenotyping

The technical capacity to precisely assess genotypes the variation in DNA sequence at particular genetic loci or regions is necessary for the development of pharmacogenomic research and its therapeutic application. The majority of variations in germline DNA belong to the class of single base-pair modifications, or SNPs, that have some relative prevalence in the human population (e.g., a G/A polymorphism, which is a shift in DNA strand composition from guanine (G) to adenine (A) in more than 1% of all persons).

Genetic variation and their effect in drug response

Pharmacokinetic variation- Two examples show how pharmacokinetic effects resulting from single gene variations can have very significant impacts. The first involves giving a prodrug—a pharmacologically inactive material—whose therapeutic benefits are dependent on drug metabolism's bioactivation. These bioactivation routes often include a enzyme that broaks down the drugs; genetic variations that cause these enzymes to become dysfunctional can reduce or completely stop the effects of drugs [11].

Pharmacodynamic variations- Pharmacodynamic pathways play their role in some of the earliest well-defined pharmacogenetic disorders, as was previously indicated. Variants in RYR1 or CACNA1S mediate the risk of malignant hyperthermia following exposure to inhaled anaesthetics or succinylcholine.

Role of pharmacogenomics in the drug development

Fewer and fewer medication candidates that start clinical trials go on to receive regulatory approval. The hypothesis that medications whose targets have been verified by human genetic researches are likely to be successfully marketed than those that do not has substantial support from the available data. As a result, gathering this evidence is becoming a more crucial step in the creation of new drugs. Adding to GWAS, other methods that are being investigated might include EHR-based phenome scanning, which looks at the connection between certain variants in putative medication target genes and symptoms found throughout the EHR [12,13].

Conclusion

One of the main objectives of pharmacogenomics is personalized or custom therapy. Due to variations in how a medicine reacts when administered, inheritance-related factors also influence individual treatments. Physicians can now accomplish therapeutic individualization because to numerous recent advancements in the fields of genetics and pharmacology.

The fields of pharmacogenetics and pharmacogenomics have the potential to contribute to the realization of personalized medication treatment plans. Individual variation in drug response is influenced by a

multitude of factors other than inheritance. However, recent advances in pharmacological and genomic science have raised the possibility that we could be able to give thedoctor objective information that could help customize drug selection and/or dose to the patient's likely response to that particular drug class, that particular agent, or that dose based on their unique genetic makeup.

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