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PHARMACOGENOMICS – A REVIEW

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ABSTRACT

Pharmacogenomics, the use of genomic techniques in the study of pharmacological function, drug disposition and drug action, will allow a better understanding of drug response on an individual level. This is the main basis for a move towards a more individualized medicine, which is commonly referred to as personalized medicine. The long-term future of pharmacogenomics-based drug development looks something like Lead compounds coming out of preclinical pharmacogenomics testing will ideally be chosen based on the fact that they are metabolised and eliminated by several alternative pathways. The Present Review is based on overall concept of pharmacogenomics and its importance in today's scenario.

KEYWORDS

Pharmacogenomics, Genetic testing and Personalized medicine.

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INTRODUCTION

To better understand individual medication reactions, pharmacological genomics applies genetic approaches to the study of pharmacological function, pharmacokinetics, and drug action. This is the main rationale behind the shift to personalised medicine, as it is more popularly known. To more clearly convey the idea of identifying subgroups via pharmacological genomics (rather than individuals). The phrase "layered medicine" has just been coined by researchers. Terms are still being established in the fast developing medical field of pharmacological genomics. It's crucial to comprehend the terminology used in scientific and regulatory documentation if you're thinking about

adding pharmacological genomics into international drug development efforts. In certain instances, personalised treatment has been seen to have caught the newest trends, attracted the attention of the general public and brought news and media coverage[1,2].

What part do genes play in how medications work?

Our genes partially influence how our body reacts to medications, just as they do when it comes to determining the colour of our hair and eyes. A gene is a DNA instruction that directs the synthesis of a protein molecule. The same gene might exist in several forms in different persons. The DNA sequence varies somewhat between each variant. These variations come in both common and uncommon forms. Additionally, there are health consequences, such as genetic abnormalities linked to specific diseases.

It is well recognised that specific proteins affect how medications work. Pharmacological genomics is the study of these proteins' genetic variations. These proteins contain liver enzymes that alter the chemical make-up of the medication.

The medicine may be partially or fully activated in the body by chemical changes. The safety and effectiveness of the medication can be significantly impacted by even the smallest variation in the genes encoding these liver enzymes. The liver enzyme referred to as One-fourth of all prescription medicines are impacted by CYP2D6. For instance, it changes codeine, a painkiller, into morphine, which is the active substance. The CYP2D6 gene comes in more than 160 different forms. Many just have one unique DNA sequence change between them. Larger adjustments are made by others. The majority of these variations have little impact on how people react to medications.

The average person has two copies of each gene. The CYP2D6 gene is present in some individuals in hundreds or even thousands of copies. The CYP2D6 enzyme is overproduced and the drug is processed swiftly in those having an extra copy. As a result, their bodies can swiftly and totally convert codeine to morphine, making ordinary doses dangerous.

On the other hand, some CYP2D6 variations result in inactive enzymes. People with these mutations absorb codeine slowly, if at all, and have little to no pain alleviation. You may be given a different medication by the doctor[4].

Pharmacological genomics: The basics

The metabolic disease alkaptonuria was the target of the first pharmaceutical genomics-based therapies. Since 1902, research has revealed a hereditary foundation for the problem[3]. African-American soldiers were more likely to experience hemolysis after malaria treatment during World War II, and certain enzymes were discovered to be hereditary factors[4].

The idea of "multiple genomes, one medication" is influenced by pharmacology genetics, which focuses on the genetic variety of genes. Patient variety is needed in order to produce the desired outcome. Pharmacological genomics, in contrast, is predicated on the idea of using many medication molecules to choose a specific genome, leading to "many drugs, one genome[5]". Both adjust to a person's unique medication metabolism and drug reactions to lessen adverse effects[6], while the pharmaceutical industry uses the idea of pharmacogenomics more broadly as a tool for compound selectivity[7].

Short-term advantages

An estimated 3 million of the 3 billion prescriptions written annually are incorrect or invalid, and American Depositary Side Effects (ADRs) claim the lives of more than 100,000 people each year[8,9]. Between the fourth and sixth most common reasons for mortality. Since medications are currently given to treat the disease, you can administer medications to those who have this propensity without anticipating their reactions. Only 40–60% of the general population actually benefits from the blockbuster medicine, a widely used general group drug[10].

Long-term advantages

A more effective healthcare system is what pharmacological genomics is supposed to produce. Incorporating the patient's medical history and genetic predisposition increases the likelihood that

doctors will formulate sound advice. Patients' health behaviours can be improved by having more faith in the healthcare system. Today, half of all patients stop taking their medications for chronic conditions after a year because there are so many ineffective prescriptions being written[11].

negative effects of genetic testing

The first kind of genetic testing tracks a person's drug use, from consumption to distribution to excretion. The second test type is concerned with pairing people with particular medicinal molecules to boost or increase efficacy.

Finally, genetic testing identifies those who are more likely to have specific illnesses[12]. A person can learn more about their health or predisposition to a specific disease or condition through genetic testing. An individual can determine their risk of contracting a particular disease or condition by learning which precise genetic region is known to encode that tendency. Despite the fact that the outcomes are independent of the surroundings, some are worried about delivery methods because the way people react to this information might encourage or prevent behavioural changes[13].

By miscontextualizing an individual's risk in relation to the broader population, results given by individuals may accidentally over emphasise the danger of tendency, which can cause an individual to over interpret and overreact. On the other hand, people may feel relieved if genetic testing does not confirm certain outcomes they were expecting based on their family history, although they may still be dubious of the results[14,15].

Pharmaceutical sector Result in enhancing the billions of dollars-a-year output pipeline of the conventionally successful company model[16]. Pharmaceutical corporations are compelled to provide drugs for the general public, especially for long-term use, by concentrating on a small number of mass-produced items. The typical development process and timeline are depicted in the following figure. To arrive at a single sturdy end product that is the patented active ingredient of the medicine, around 10,000 parent compounds must progressively progress through the drug research and development process[17].

Candidate medications can be isolated and identified for possible development more quickly by developing methods like high-throughput screening and the usage of microarrays. Preclinical testing is the process' rate-determining stage since only candidates that have undergone rigorous in vitro and animal testing have been shown to be sufficiently safe to be used in people. The effectiveness of the medicine is evaluated in phase II clinical trials, which are conducted on a carefully chosen volunteer population, eliminating the elderly, adolescents, and patients with other disorders. Data where the association between efficacy and/or safety and biomarkers is significant can be found by incorporating pharmacogenetics. Using this information, you can adjust a compound's active ingredients or reduce the population to potential responders. Phase 3 the largest and most comprehensive clinical trials[18].

Altering the business plan of the pharmaceutical sector

Pharmacogenomics is anticipated to play a substantial part in traditional medical practise during the next ten years. This tactic prevents smaller enterprises from encroaching on the clientele of larger ones. Because they have more capacity for subsequent clinical studies, large pharmaceutical businesses commonly work with smaller biotech companies to outsource research and schedule when the study will be sent to a larger company for clinical testing and sale[19]. Pharmaceutical corporations claim that pharmacogenomics enhances traditional drug development by weeding out non-viable candidates early on[20]. Pharmacogenomics is a promising approach for discovering new applications for medicines. By recommending a medicine to a specific demographic, this strategy would revive prior commercial or biologic failures[21].

How are prescribing recommendations and drug development and design being impacted by pharmacogenomics?

Drug safety in the US is monitored by the Food and Drug Administration (FDA). The labels of about 200 drugs now contain pharmacogenomic data. The recommendations on dosage, potential adverse effects, or variations in effectiveness for people with particular gene variants can help clinicians customise medicine prescriptions for individual patients.

Pharmacogenomics is also being used by pharmaceutical corporations to create and sell medications for patients with particular genetic profiles. Medicine companies may be able to accelerate the development of a drug and enhance its therapeutic benefit by only testing it in patients who are likely to benefit from it.

Additionally, if researchers are able to pinpoint genes that result in harmful side effects, doctors might only recommend those medications to those who do not possess those genes. As a result, some people could obtain potentially life-saving medications that might otherwise be prohibited because they provide a risk to other people.

How does pharmacogenomics impact medical care?

Currently, a patient's age, weight, sex, liver function, and renal function are the main considerations when a doctor prescribes a medication. Researchers have discovered gene variations for a few medications that influence how people react. For each patient in these situations, doctors can choose the optimum drug and dosage[22,23].

Finding out how patients react to drugs also aids in identifying the various disease kinds they are dealing with.

Pharmacogenomics benefits

Drugs are more effective: Drugs target specific disorders with less adverse effects than earlier medications since they are specially developed for the proteins, RNA molecules, and enzymes linked to their genes.

Increasing the potency of vaccines: Vaccines that strengthen the immune system without increasing the danger of infection can be created using DNA and RNA.

Unlike the previous trial-and-error method, medicines may now be matched to the genetic make-up of the patient so that the patient will be provided the proper medication without any side effects. Because the drug has been precisely prescribed, patients recover swiftly.

Problems with pharmacogenomics

Finding gene variants that affect medication responsiveness is challenging: Finding SNPs that affect medication responsiveness is like searching for a needle while wearing blinders. Finding the correct SNPs is an extremely time- and money-consuming operation because we don't know which genes affect drug responsiveness. Which might impede the growth of pharmacogenomics. The issue with pharmacogenomics is that, depending on your genetic makeup, there will be hundreds or perhaps thousands of extremely identical medications available. This will make choosing and dispersing recipes much more difficult.

The fact that they will develop into "designer medications" that prevent many less fortunate individuals and nations from receiving the best care raises a number of ethical concerns. The wealth disparity widens as a result of it.

If major pharmaceutical corporations don't accept the concept of pharmacogenomics, this could become a significant issue.

The use of genetically engineered animals, sometimes known as "pharming," to manufacture essential human medications is another significant ethical problem. Pharming would definitely subject domestic animals to cruel treatment on a scale never before seen in medicine. Because the fight against animal testing is already quite strong.

CONCLUSION

Amazingly, there are many different therapy choices accessible today. However, selecting the ideal medication for every patient continues to be a challenge. Only 50% of the time do doctors choose the "correct" first medication, and ADR is still unexpected. Even affluent nations like the United States cannot afford to treat all patients due to the high cost of new biologics. The creation of clinical instruments for patient assessment has been made possible by the completion of the Human Genome Project. Pharmacogenomics enables the identification of patients who stand to gain the most from a given course of therapy and of those whose expenses and hazards outweigh their potential gains. Drug therapy could be made safer and more effective. In the future, genotyping can be used to personalize the drug treatment of a large number of patients, reduce the cost of drug treatment, and increase the effectiveness of the drug.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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