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Empowering Patients: The Role of Pharmacogenomics in Personalized Medicine

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ABSTRACT

Pharmacogenomics is a branch of science that focuses on the systematic identification of human genes, their products, and inter-individual and intra-individual variation in expression and function. Personalized medicine, also known as precision medicine, aims to provide patients with prescriptions for drugs based on their genetic, environmental, and lifestyle characteristics. This approach represents a paradigm shift away from "one drug fits all" and towards personalized care. Pharmacokinetics and pharmacodynamics play a major role in pharmacogenomics drug development. DNA-based technology is quicker but has not thoroughly explored the relationship between genotype and phenotype for many genetic variants. Inter-individual heterogeneity in drug response is crucial in cancer treatment, as genetic variants can alter the drug's metabolism, affecting toxicity and efficacy. Artificial Intelligence (AI) plays a critical role in empowering healthcare providers by improving and encouraging the application of pharmacogenomics. Machine learning (ML) integrates deep learning to create artificial neural networks (ANNs) that influence DNA-influenced phases in the pharmacogenomics process. Pharmacists are uniquely suited to advance personalized medicine as a clinical tool due to their knowledge, skills, and abilities in pharmacokinetics, pharmacodynamics, and clinical pharmacology. In this review, we compiled a number of articles spanning a wide range of pharmacogenomics topics. These include genetic variations, pharmacogenomics in drug development, genotype, phenotype, pharmacogenomics markers, challenges, implementation, AI in pharmacogenomics, and the role of pharmacists in pharmacogenomics.

INTRODUCTION

Pharmacogenomics is a branch of science that deals with the systematic identification of all human genes, their products, and inter‑individual and intra‑individual variation in expression and function.[1] It may be possible to base treatment decisions on genetics when a gene mutation is linked to a patient's particular drug reaction, such as changing the dosage or selecting a different medication. Similar to how they assess gene variations linked to disease, researchers discover genetic loci linked to known drug responses and then test people whose response to the drug is unknown in order to assess gene variants affecting an individual's response. Multi-gene analysis and whole-genome single nucleotide polymorphism (SNP) profiles are two contemporary techniques that are just now being used clinically for medication development.[2] Pharmacogenomics that will result in safer and more efficient drug treatment, help improve drug therapy compliance, reduce hospitalizations, and enhance overall health care.[19]

The inability to taste phenylthiocarbamide was the first instance of inherited differences in response to foreign chemicals or xenobiotics. In the 1950s, patients with a glucose-6-phosphate dehydrogenase deficiency experienced severe hemolysis when exposed to the anti-malarial drug primaquine. Classical pharmacogenetic traits altering amino acid sequence led to prolonged paralysis after succinylcholine administration and peripheral neuropathy in patients treated with isoniazid. These early observations led to the founding of the scientific field of pharmacogenetics, which studies heredity and medication response.[16] The term "pharmacogenomics" first appeared in the medical literature at the end of the 1990s. Although the phrase "pharmacogenomics" and the term "pharmacogenetics" are frequently used interchangeably, there is currently no agreement on the term's working definition.

The European Agency for the Evaluation of medicinal products (EMEA), 2002) defines pharmacogenetics as studying inter-individual variations in DNA sequence related to drug response, while pharmacogenomics studies gene expression variability at cellular, tissue, individual, or population levels. This aligns with the widely used definition of pharmacogenomics as genomic-scale evolution.[3] In recent years, pharmacogenomics has made use of a new generation of technologies known as the 'omics' technique, which has resulted in a revolution in our understanding of disease susceptibility and pathophysiology.[9]

Personalized medicine, sometimes known as precision medicine, involves giving patients prescriptions for drugs that are right for them based on their genetic, environmental, and

lifestyle characteristics. This method, made possible by molecular diagnostics, differs from the conventional practice of treating all patients with the same aliment with the same medication and dosage.[5] Personalizing care and predicting the clinical results of various treatments in various patients are the two main aims of personalized medicine. One of the key components of customized treatment is pharmacogenomics. The fundamental idea is that inter-individual multiple factors, such as genetics, epigenomics, the environment, and a patient's characteristics, such as gender, age, and/or concurrent medications, all contribute to heterogeneity in drug response.[9] The ultimate goal of precision medicine is to perfectly match each treatment action with the patient's molecular profile. Modern sequencing tools have propelled the study of human genetics for the past twenty years, helping us to better understand how genetic diversity and human health are related. Precision medicine has made extensive use of genetics, and one of its more recent uses is pharmacogenomics-informed pharmacotherapy, which adjusts drug choice and dosage based on a patient's genetic characteristics.[4]

Several pharmacogenetic guidelines have lately been published by international scientific consortia, but there hasn't been much success in putting them into practice in clinical settings. Numerous coordinated international initiatives are being carried out to overcome the current barriers preventing the utilization of pharmacogenomic research. However, the validated pharmacogenomic indicators that are currently available can only partially account for the observed clinical variation in therapeutic outcomes. There is a need for new investigative methods, such as the analysis of the immune system’s pharmacogenomic involvement and previously overlooked uncommon genetic variation, which are said to be responsible for a significant portion of the inter-individual variability in drug metabolism. Significant challenges in everything from implementation to basic pharmacogenomics research have been identified. To advance our understanding of pharmacogenomics, it is necessary to investigate previously unrecognized uncommon genetic variations and to confirm their functional and clinical effects through the creation of pre-clinical models and in silico techniques. On the other, continuing global coordinated initiatives established to remove the current obstacles to pharmacogenomic implementation will offer fresh tools and insights into the clinical application of pharmacogenomics, paving the road for its wider adoption.[4]

In precision medicine, pharmacogenomics serves two key functions.

- It aids drug research and discovery in pharmaceutical businesses.

- It helps physicians select the best medication for patients based on their genetic makeup, steer clear of adverse drug reactions, and prescribe the optimum amount of medication to maximize drug efficacy.[5]

Pharmacogenomics is a sign of personalized medicine because it represents a paradigm shift away from "one drug fits all" and towards the idea that "the right drug for the right patient at the right dose and time". This does not imply that each person will receive unique treatment that would be impractical from an economic standpoint. Based on genetic and other markers that forecast illness development and response to treatment, patients are split into groups. In pharmacological therapy, it's important to prevent toxicity or poor response. A medicine has a more favorable risk or benefits ratio and might become the first choice treatment, increasing its market share, if the frequency of an adverse event can be decreased from 5 to 2% by removing 10%of the population. The characteristic of personalized medicine, better treatment outcomes for individual patients, might be anticipated as a result of an increasing tent to relate the introduction of new pharmaceuticals to diagnostic markers, frequently genetic markers.[6]

The conventional approach to drug development that characterized the 20th century was predicated on finding treatments that target a broad population. However, through time, we have learned that patients have unique familial qualities that influence how they respond to therapy, and we have developed customized treatments based on these traits. In today's medicine, patients, health, and diseases are approached in a way that is more predictive, preventive, interactive, and individualized. Although this so-called P4 medicine faces many obstacles and problems, it also presents numerous opportunities for enhancing treatment and care outcomes.[7] The rapid growth in FDA approvals of biomarker-based tailored therapies demonstrates the importance of pharmacogenomics. Molecularly focused cancer therapies serve as a lighthouse for all therapeutic modalities by showcasing current developments in drug development and clinical use. Multi-component biomarker panels that take into account genetic, psychological, and environmental characteristics can help diagnose patients and direct treatments. These panels are increasingly using artificial intelligence to handle the extremely complex data that they generate. However, there are significant obstacles to clinical application, such as a lack of knowledge about the validity across ethnic groups, inherent bias in healthcare, and real-world validation.[8]

The rapid increase in the human population, environmental changes, and genetic adaptability have led to increased disease progression and treatment. The innate immune system has evolved to protect against infectious diseases, but overactive immune systems can lead to autoimmune and inflammatory disorders. Rapid population growth accelerates genetic acclimatization, affecting reproductive success but not always preventing chronic diseases. Drug therapy often fails due to genetics, environment, behaviors, and social factors. Adverse drug effects are a major source of morbidity and mortality. [10]

DISCUSSION

Genetic variations:

About 20,500 genes make up the human genome, and 99.5% of them are similar. The remaining 0.5 percent consists of variants that determine an individual's blood type, eye color, susceptibility to certain diseases, etc. Single nucleotide polymorphism (SNP) is the most prevalent type of DNA sequence variation observed in the human genome. Deletions, insertions, tandem repeats, inversions, and copy number variations (CNV) are examples of another type of variation known as structural variants (SV). In the human genome, there are roughly 11 million SNPs, one for every 1,300 base pairs. SNPs serve as biological markers that predict a person's response to specific medications, vulnerability to environmental dangers like pollutants, and likelihood of contracting diseases.[5]

Pharmacogenomics in drug development:

Pharmacogenomics clearly plays a significant role in the development of new drugs. Numerous pre-candidate genes perhaps appropriate for drug discovery have already been found as a result of SNP data analysis. Drug discovery will also make use of knowledge gained by understanding the behavior of genes, their relationships, their function in organic pathways, as well as their heterogeneity among the population. Working out of gene expression changes from normal tissues through the onset of disease among unusual populations provides potential targets for therapeutic development. Sooner or later, goal setting will need to be genetics-focused rather than the currently prevalent target validation. Utilizing methods for goal determination that are genetically supported must limit the testing of too many hypotheses that can ultimately be confirmed Success in discovery is measured by reducing attrition and improving a product's return on investment.[14]

Individual variability in drug efficacy and drug safety is a major challenge in current clinical practice, drug development, and drug regulation.[23] When researching how drugs affect people, scientists pay close attention to two key factors:

- How much of a drug is required to reach its target in the body, and
- How well the target cells, such as heart tissue or neurons, respond to the drug.

Pharmacokinetics and pharmacodynamics are the scientific names for these two determinants, and both are very important factors in the field of pharmacogenomics.[2]

Pharmacokinetics:

Absorption, distribution, metabolism, and excretion are the four processes included in pharmacokinetics and are frequently referred to as ADME. When a medicine is administered intravenously, absorption, which often refers to how a substance enters the bloodstream following consumption of a tablet or inhalant, is avoided. After absorption, the drug travels to many locations, and its distribution defines how much of the drug reaches the target spot. The term metabolism describes how a drug is broken down in the body. This process can occur instantly through the action of an enzyme in the stomach, and it occasionally results in end products that have their own pharmacologic effects. Last but not least, excretion outlines how medications exit the body.[2] Pharmacokinetic studies are crucial for drug therapy in pregnant women, as they take various medications and face higher side effects risk.[21]

Pharmacodynamics:

The molecular action of a drug on its target, whether it be a cell surface target, an ion channel, or an intracellular target (such as an enzyme or regulatory protein), is known as pharmacodynamics. For example, beta-agonists for the treatment of asthma and beta-blockers for the treatment of hypertension both target the beta-2 adrenergic receptor, and this receptor possesses polymorphisms that have been linked to the responsiveness to these medications.[2]

Use of pharmacogenomics in improving pk and pd balance:

PK problems are responsible for 40% of drug development failures. More than 170 genes, more than half of which are known to be polymorphic, are known to play a role in the disposition of drugs. Pharmacokinetic processes exhibit inter-individual heterogeneity and are influenced by host- and environment-specific variables like physiology and genetics. In any of the ADMEs, genetic polymorphisms, which are mostly in charge of inter-individual variability, might have the following effects:

- changes in the production of active metabolites due to differential absorption/clearance
- modifications to medication interactions
- Ethnic differences and drug reaction.[5]

Genotype and phenotype

Diagnostic tests that directly measure the phenotype rather than a genetic mutation may be more accurate if there are several mutations that can result in similar susceptibilities to ADRs Although DNA-based technology may be quicker and only needs one blood sample from a patient, the relationship between genotype and phenotype for many genetic variants has not been thoroughly explored. The phenotype is what the doctor is interested in learning, but sadly, the current DNA-based diagnostics may not accurately capture the whole spectrum of phenotypic variance. As a result, developing trustworthy, affordable, high-throughput genotyping platforms is a huge barrier for companies designing DNA-based diagnostics, and determining complete, therapeutically meaningful genotype-phenotype correlations is a major challenge for pharmacogenomic science [2]. Inflammatory bowel illness, acute lymphoblastic leukemia, and organ transplant recipients are all treated with thiopurine medications (Weinshilboum & Wang, 2004). These medications are helpful, but they are also toxic, and there is very little window for dosage that will produce the intended therapeutic benefit without also causing toxicity. The primary toxicity of thiopurines is potentially fatal. Thiopurine S-methyltransferase (TPMT), a metabolic enzyme that is expressed by a polymorphic gene, inactivates thiopurines. The gene variant TPMT*3C, which has a cytosine in position 3, is widespread in Asian groups, whereas TPMT*3A is more prevalent in Caucasians. Two distinct SNPs in TPMT*3A change the encoded amino acids in various ways. People homozygous for this allele have little to no detectable TPMT protein in their tissues because the gene product that TPMT*3A encodes is rapidly destroyed.[2]

Loss of function of thiopurine S-methyltransferase (TPMT) results in severe and life-azathioprine.[24] Therefore, when receiving conventional thiopurine medication doses, people who are homozygous for TPMT*3A are at significantly higher risk for myelosuppression which could be fatal. However, such patients can be treated with these medications at about a tenth of the recommended amount, but only under close observation. Thiopurine dosage in the treatment of acute lymphoblastic leukemia is evaluated using genetic variation in the TPMT gene as a diagnostic tool. Red blood cell testing in a lab can also be used to detect TPMT activity as an alternative to genotyping. The test can find those uncommon mutations

that the DNA level could overlook. The genotype (DNA) and phenotype (enzyme activity) of TMPT have a high degree of concordance, according to a recent study (in a sample of healthy Europeans) (Schaeffler et al., 2004). The authors came to the following conclusion: "Genetic testing for TPMT is worthy of adoption into clinical practice because all these parameters show values higher than 90% in our large-scale study".[2]

Metabolizer phenotype:

The quantity and kind of functional alleles that a patient possesses for specific genes determines the metabolizer phenotype, which reflects the patient's capacity to metabolize specific medications. The CYP enzymes, which make up the majority of this pamphlet, are encoded by these genes most frequently. The phenotype of a metabolizer can range from "poor," which refers to patients with little to no functional activity of a particular CYP enzyme, to "ultra-rapid," which refers to patients with noticeably elevated activity of a particular CYP enzyme. Therapeutic medication response is frequently unsatisfactory and depends on the type of CYP variation present, the patient's metabolizer phenotype, and the type of drug. Poor metabolizers, for instance, are unable to metabolize some medications well, leading to the accumulation of an active drug that could be hazardous or the failure to convert a pro-drug into an active metabolite. A pro-drug is swiftly digested, causing a rapid commencement of therapeutic effect, while an active drug is promptly inactivated by ultra-rapid metabolizers, resulting in a sub-therapeutic response.[22]

Pharmacogenomics markers in drug labeling:

The information on a scientific product label must be sufficient to understand the product and how to use it. For the purpose of illustration, drug labels are "planned to present an abstract of the substantive scientific knowledge necessary for the practical and comfortable administration of drugs." FDA mandates that product labeling be consistent, accurate from a scientific standpoint, and no longer deceptive, as well as that healthcare professionals get clear instructions regarding the ordering and/or administration of medications. A result should be labeled as PM that will be most effective and reliable in particular subpopulations or that must be administered in extraordinarily high doses to a particular subpopulation. Choosing pharmaceutical responders and non-responders, preventing adverse events, and adjusting drug dosage are all possible uses for pharmacogenomics. The information on drug labels may only include knowledge of genetic biomarkers and may describe: Variability in clinical response and medication disclosure; risk of negative outcomes; and genotype-specific

mediating factors Structures of drug action Polymorphic drug target and natural gene sequences 121 of the 1200 medicine labels for FDA-approved medications in the USA from 1945 to 2005 indicated that they included pharmacogenomics information. In the present, pharmacogenomics biomarker expertise is mentioned on the labels of more than 141 FDA-approved medications. Drugs having pharmacogenomics expertise in their labeling and FDA approval. The labeling of certain products, but not all, now includes concrete trials to gather the biomarker data. Depending on the activities, pharmacogenomics knowledge can display certain elements of the labeling in a different way. There is only one consultant product specified for drugs that may be available in multiple dosage ranges, salts, or mixes. In the case of combination goods, the agent stated is the only one connected to the biomarker, unless the agent is most operatives approved as a combination product. [14]

A list of endorsed products is published by the U.S. Food and Drug Administration (FDA). Medicines with pharmacogenomic labeling that includes advice on dose, cautions, and indications for usage. Abacavir, a medication used to treat Human Immunodeficiency Virus (HIV), for instance, comes with a warning for those who have the HLA-B*5701 allele because some of these people experience severe hypersensitivity reactions to the medication. The annual proportion of new FDA drug approvals with pharmacogenomic labeling has climbed nearly threefold, from 10.3% in 2000 to 28.2% in 2020, illustrating how significant pharmacogenomics has become.[12]

Interaction in combining drug therapy:

In the treatment of complicated diseases like cancer and HIV/AIDS, single-drug regimens that target a single receptor are no longer seen as ideal. However, when numerous medications are taken at once, the likelihood of drug-drug interactions increases, which could result in unanticipated side effects that are challenging to identify. Ritonavir is an effective membrane transporter inhibitor, such as Pgp (MDR1), and a robust CYP3A4 mechanism-based inhibitor. As a result, the dose of additional antivirals that are also carried by Pgp and processed by CYP3A4 can be decreased, but the dose titration becomes unpredictable. To combat the lipodystrophic side effects of the antivirals, the majority of patients are also treated with antibiotics, antidepressants, and statins. Polymorphisms in genes associated with ADME are likely responsible for determining the frequency and severity of the resulting high rate of severe adverse effects. With one gene, one drug strategy, it may be challenging to determine a causal relationship because effects are dispersed across a network of interactions.

Instead, integrating overall negative effects with functional variations in numerous genes requires a systems approach.[6]

Role of Pharmacogenomic in adverse drug reaction

Unwanted side effects might occur as a response to medications. When these can be positively linked to a particular treatment, the preferred term is "adverse drug reactions" (ADRs). ADRs are significant contributors to morbidity and mortality, and genetic variation significantly increases the likelihood of developing them. Adverse drug reactions can be divided into Type A (pharmacological) or Type B (idiosyncratic) categories in their most basic forms. Pharmacological responses have a dose-dependent occurrence, may be understood and possibly predicted given the drug's known targets, and result from an unfavorable response to the known mechanism of action. Examples of highly penetrant risk alleles within drug-metabolizing enzyme genes include CYP2D6 and opiate-induced respiratory depression or CYP2C9 and bleeding on warfarin treatment, which show how genetic variation contributing to pharmacokinetic mechanisms may be relevant for these ADRs. Contrarily, idiosyncratic ADRs are more uncommon and are not anticipated from the drug's established pharmacological profile but they can be fatal and result in significant organ damage numerous of these ADRs have been linked to immunological mechanisms, and the majority of recommendations link them to polymorphisms in immune response genes, particularly the HLA system. These findings demonstrate the possibility of creating ADR prediction systems to enhance patient safety and resource efficiency. It has been estimated that at least 65% of primary care patients are exposed to medications with pharmacogenomic indications over a 5-year period (Kimpton et al., 2019), in which genomic data could be used to prevent or minimize adverse drug reactions. These medications are slightly overrepresented among those prescribed in routine care (Barbarino et al., 2018). With the possibility of standardizing pharmacogenomic variance being saved on routine health records and added to warning and monitoring systems to aid prescribing decisions, the utility of this information is currently being studied at scale.[11]

Pharmacogenomics in cancer treatment:

Inter-individual heterogeneity in drug response is crucial in cancer treatment due to limited therapeutic indices. Genetic variants may even create minor modifications in an anticancer drug's metabolism, which can have significant effects on the drug's toxicity and efficacy.[3] The outcomes of a bioinformatic review of a TCGA dataset of ovarian cancer patients who

underwent radical resection and received adjuvant platinum-based therapy. The study focuses on somatic copy number alteration and tumor tissue genetic modifications, demonstrating a markedly distinct pattern of genomic amplification in platinum-resistant individuals compared to platinum-sensitive patients. Additionally, it highlights the excellent chance provided by the vast amount of genetic data generated by international consortia like TCGA that might be processed to uncover creative pharmacogenomic markers.[4] Researchers developed a diagnostic kit using real-time PCR techniques to study 21 genes in breast cancer and paraffin-preserved tissue samples (paik et al., 2004). The kit predicts outcomes and genetic factors in patients, based on their risk categories. The kit also assessed therapy benefits, finding that chemotherapy had a significant positive effect on high-risk individuals, reducing cancer recurrence by 28%. [2]

Pharmacogenomics: A road ahead for precision medicine in psychiatry:

Insights into the nature of psychiatric disorders are being provided by psychiatric genomics, which over time should help develop new medication targets and enhance patient care. The global burden of psychiatric disorders remains high, despite improvements in communicable and non-communicable diseases. Factors contributing to this include incomplete understanding of pathogenesis, faulty medicines, and poor mental healthcare availability. Only 20% of European and North American patients have effective therapy, and this gap is likely wider in low- and middle-income nations. Fewer than 50% of patients with major mental health disorders receive effective therapy, leading to treatment decisions based on generic adverse-reaction profiles. Adverse drug reactions and lack of effectiveness are common reasons for discontinuing psychiatric medication. Long-term treatment requirements and the need for long-term care further exacerbate these issues, resulting in a large fraction of patients failing to benefit from current care standards. Common care in high-income nations disregards genetics, with psychiatric pharmacogenomics testing available before antidepressant prescriptions. A future scenario with genetic data and electronic health record access before medication prescriptions.[14]

According to Trevio et al. (2017), the study makes the following assumptions about depression patients: 79% of them are initially prescribed pharmacotherapy, 60% stop taking their first antidepressant within three months, and 40% of those who stick with it don't see any therapeutic improvement. Additionally, PGx testing is free and adheres to genotype-dosing recommendations. Furthermore, 62.4% of the population carries a PGx actionable

variant for routinely taken antidepressants. Therapeutic benefit and treatment adherence is improved by 1.7 times with PGx-informed treatment (Jessel et al., 2020). Due to frequently obtained personal and exposure data in clinical decision-making, PGx-guided care's therapeutic improvement in eHR-driven healthcare grows to 2.5 times, and even standard prescriptions would be more effective (1.5 times) (Denny and Collins, 2021).[11] Recently, many major pharmaceutical companies have but all abandoned drug discovery efforts for mental illness, and left behind the era of blockbuster drugs designed to treat large segments of the population.[25]

Pharmacogenomics in children:

Pediatric cancer pharmacogenomic research focuses on the side effects of therapy, but clinical implementation remains challenging due to conflicting results and confusion. Ototoxicity linked to cisplatin is a concern, particularly for young children. Gene studies have identified variations in genes affecting cisplatin-induced ototoxicity risk. The reproducibility of initial findings is a significant issue, as the correlation between ototoxicity and polymorphisms in COMT and TPMT in diverse cohorts is limited. TPMT was confirmed in two comparable cohorts, but the connection with COMT was the opposite in one. Lack of knowledge on their contribution to cisplatin-induced ototoxicity is another issue.[30]

Pharmacogenomic guidance improves outcomes

Pharmacogenomics is important in cancer therapy because it aids medical professionals in selecting the best medications and avoiding drug toxicity. For instance, 5-fluorouracil (5-FU) is frequently used to treat colorectal cancer, although there are still issues with toxicity and drug resistance. In 3% to 5% of people, the DPD gene has been found to have different forms, and those who lack the DPD enzyme are known to be more hazardous to 5-FU. Another illustration is how variations in the GSTM1 and GSTT1 genes, which are involved in the detoxification of cancer medications, might affect the effectiveness of cisplatin, carboplatin, and oxaliplatin. Additionally, pharmacogenomic indicators have become a crucial tool for predicting the recurrence of mood disorders. In 1,737 individuals, pharmacogenetic-directed therapy produced significantly better results, with patients 1.7 times more likely to experience symptom remission compared to patients who did not receive this guided therapy, according to a new meta-analysis.[12]

Using questionnaires to gauge depressed symptoms, multicenter, randomized controlled trials have assessed the effectiveness of genotype-guided antidepressant prescription prescribing. Combinatorial pharmacogenomic techniques were used in this research to propose antidepressants based on patient genotypes and panels that interrogate numerous genes (e.g., CYP2D6, CYP2C19, SLC6A4, HTR2A, and HTR2C). When compared to patients receiving normal clinical therapy, those who were randomly assigned to genotype-guided treatment performed noticeably better in terms of standardized depression rating scores or response and remission rates. Pharmacogenomic-guided antidepressant drug selection may improve clinical results as well as decrease the use of healthcare resources and medication-related expenses of antidepressant therapy.[13]

Clinical use of pharmacogenomics:

There is compelling evidence that the reaction to more than 60 pharmaceuticals may be influenced by variations in roughly 20 genes. Evidence-based, peer-reviewed guidelines are available from the Clinical Pharmacogenetics Implementation Consortium (CPIC), an initiative funded by the US National Institutes of Health to help clinicians interpret the results of genomic tests and apply them to patient care. Several examples of pharmacogenomic testing implementation have been described, with approaches varying from preemptively testing everyone with gene panels to testing particular genes before prescribing specific medications. Regardless of the implementation strategy, however, institutions and physicians alike face difficulties in developing the infrastructure necessary to preserve genetic data that may be important for the duration of a patient's life.[13] Only a limited subset of pharmaceuticals have FDA labeling requiring pharmacogenetics testing, and there is scant evidence of the therapeutic value of this technique. There are not many instances where pharmacogenomics affects clinical utility, despite its enormous potential.[28]

Addressing challenges to pharmacogenomic testing:

Conducting randomized clinical studies to evaluate pharmacogenomics' utility is challenging due to the need for large sample size and the need to accurately reflect all ethnic groups due to certain pharmacogenetic variants. White persons performed better in the European Pharmacogenetics of Anticoagulant Therapy (EU-PACT) experiment, which compares fixed warfarin dose to genotype-guided dosing. The Clarification of Optimal Anticoagulation Through Genetics (COAG) trial compared warfarin doses based on clinical variables and genetic data, with 30% of participants being black. Results showed no improvement in

anticoagulation control, and African ancestry patients had worse control due to decreased-function alleles. Two trials show divergent results due to different dosing approaches, suggesting genotype-guided dosing may not be preferable. The Genetics Informatics Trial (GIFT) randomized elderly patients to either a genotype-guided algorithm based on clinical variables alone or one incorporating CYP2C9, CYP4F2, and VKORC1 genetic data. The study found that the genotype-guided warfarin dosing arm reduced major bleeding, international normalized ratio, venous thromboembolism, and death. This suggests that when relevant genetic variations are included, a genotype-directed algorithm outperforms a clinically guided algorithm.[13]

Pharmaceutical research addresses personalized therapeutics with pharmacogenomics:

Clinical trials conducted by pharmaceutical corporations use DNA microarrays, and the use of biomarkers in drug development is widespread.[27] Genomic technologies have already gained traction and are having an effect on the pharmaceutical sector. In order to quickly identify the gene targets that start the drug discovery process, high-throughput sequencing and transcript profiling were applied to disease-based disease models in cells, animals, and human tissues.[15]

Pharmacogenomics is used in pharmaceutical research to determine who will respond favorably or negatively to prescribed medication by addressing individualized treatments. Finding that highly polymorphic enzymes like CYP2D6 often metabolize the most repulsive substances. Therefore, if genetic differences between individuals are taken into account when prescribing medications, some ADRs are in fact avoidable. Pharmacogenomic biomarkers with >150 gene-drug pairings of clinical relevance have been put together by the FDA in the meantime. However, the acceptance of these genetic biomarkers in clinical settings has been notably slow, in part because each given genetic variant often only contributes a small amount to the genetic influence on treatment outcomes. The integration of many genomic markers with all other aspects impacting a person's reaction is thus necessary for individualized therapies, although this task has not yet been accomplished successfully.[10]

Implementation:

Genetic information is increasingly used in clinical disciplines to predict treatment response and adverse drug reactions, requiring a framework of genetic, phenotypic, and environmental information for effective personalized medicine.[26] The implementation of individualized health care is a laborious process since it encounters significant challenges and moves

painfully slowly when translating medical advancements into the very complicated, chaotic reality of contemporary society. The biggest obstacle to global healthcare improvement is providing advantages to all facets of human society. Thus, we face great challenges in a time of disruptive technological and social change that happens more quickly. Pharmaceutical scientists who live up to these standards will be crucial in realizing the advantages of individualized healthcare.[10]

The technology behind pharmacogenomics:

Cell biology is essential for understanding pharmacogenomics technology. Each living organism has a unique genetic makeup, consisting of genes that direct protein development. Three types of proteins affect drug metabolism: receptors, which control substances entering and exiting cells, and proteins that change drug molecules' forms. Geneticists can identify specific markers in a person's genetic profile associated with drug interactions, enabling doctors to provide the right prescription without causing adverse effects or unnecessary therapy.[17]

Artificial intelligence in pharmacogenomics:

By improving and encouraging the application of pharmacogenomics, Artificial Intelligence (AI) plays a critical role in empowering healthcare providers. Machine learning (ML) integrates deep learning to create artificial neural networks (ANNs), influencing DNA-influenced phases in the Pharmacogenomics process, and different types of ANNs can play a significant role in drug uptake, drug-receptor drug breakdown, and targeted drug development.

AI is essential for developing the development of tailored treatments for numerous fatal diseases. Several methods of using AI are;

- AI-powered robotics: AI-driven robots improve biomedical engineering by enhancing efficiency and accuracy in tissue scaffold production through electrospinning.

- 3D printing: 3D printing offers precise interventions, with the first FDA-approved 3D-printed medication in 2015. Smart drug delivery systems improve treatment efficacy using genetic testing, using techniques like ink-jet deposition and photo-polymerization.

- N-of-1-trails: Treatment created, N-of-1 trials conducted, AI-based pattern identification aids in advanced patient outcomes.

- AI-based stimulation studies: These investigate, foresee, and anticipate potential directions that a treatment plan might go.[18]

Role of pharmacist in personalized medicine:

Pharmacists are uniquely suited to advance personalized medicine as a clinical tool due to their knowledge, skills, and abilities in pharmacokinetics, pharmacodynamics, and clinical pharmacology. They individualize drug therapy based on patient factors like age, size, organ function, treatments, diet, allergies, and disease states. Additionally, pharmacists offer dose customization through therapeutic medication monitoring. Despite their extensive experience, personalized medicine and pharmacogenetics remain emerging areas of patient care, with unclear roles and responsibilities for pharmacists. Professional pharmacy organizations, such as the American Society of Health-System Pharmacists, American Pharmacists Association, and Pediatric Pharmacy Advocacy Group, support pharmacist involvement in pharmacogenetics. These responsibilities include clinical application, testing recommendations, interpretation, and designing patient-specific drug and dosage regimens. Pharmacists with specialized education and experience are encouraged to assume leadership roles in advancing safe, effective, and cost-effective medication practices.[29]

CONCLUSION:

In conclusion, the studies compiled in this volume highlight the potential of molecular approaches, including multi-locus genotyping, to identify genetic determinants of inter-individual variability in the effects of drugs in a number of significant clinical settings, including cancer and psychiatry. It is possible to explain the predictable sources of inter-patient variability in drug effects by combining multiple layers of pharmacological information, including variation in genetic, phenotype, genotype pharmacodynamics and pharmacokinetic processes, as well as information obtained through cutting-edge statistical and bioinformatic approaches. If properly implemented, this will lead to precision therapy. The process of putting personalized health care into practice is difficult because it runs into many obstacles and proceeds excruciatingly slowly while trying to apply medical discoveries to the incredibly complex, chaotic reality of modern society.

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