Indian Journal of Clinical Anaesthesia 2023;10(1):110–112

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical Anaesthesia

Journal homepage: www.ijca.in

Brief Communication

Application of pharmacogenetics in the practice of anaesthesia

Pallavi Ahluwalia[1,*], **Bhavna Gupta**[2]

[1]*Dept. of Anaesthesia, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India*
[2]*Dept. of Anaesthesia, All India Institute of Medical Science, Rishikesh, Uttarakhand, India*

ARTICLE INFO

Article history:
Received 25-01-2023
Accepted 07-02-2023
Available online 09-03-2023

Friederich Vogel first used the word "pharmacogenetics" in 1959 to describe a newly emerging field of study that aims to investigate the effect of inherited characteristics over the diversity of drug responses by combining genetic and pharmacological knowledge and research techniques.[1] European Agency for the Evaluation of Medicinal Products (EMEA) defines "pharmacogenetics" as "the study of interindividual differences in DNA sequence associated to drug response" and "pharmacogenomics" as "the study of the variability of the expression of individual genes relevant to disease susceptibility and medication response at the cellular, tissue, particular or population level."[1] Because of this, many genetic variables that can predict the toxicity and the body's reaction to pharmacological therapies have been found. Pharmacogenetic and pharmacogenomic tests may aid clinicians in selecting the most effective course of treatment and the least hazardous dosage for each individual patient in the not-too-distant future. Polymorphism is defined as a variation in the DNA sequence that has an allelic frequency of one percent or higher in a population, whereas mutation is defined as a variation that has a lower frequency overall in the population. Gene mutations and polymorphisms are responsible for the production of enzymes with unique metabolic activities or receptors that have varying degrees of affinities for different drugs. They alter the pharmacological response in individuals, and in the case of variants found in certain racial and ethnic groups, they can even alter the response in a population. Many people believe that expanding the use of pharmacogenetic testing would present an amazing opportunity to enhance the safety and effectiveness of the medication. This pattern is being driven by the fact that adverse drug responses are responsible for 106,000 deaths and 2.2 million serious events each year in the USA, which is the residence of a highly advanced healthcare system.[1] The most recent findings in the field of pharmacogenetics have ushered in the era of personalised medicine, which is based on the notion that everyone possesses a variant of the human genome that is unique to them. An individual's health is not just influenced by genetic variation, but also by the behaviors they engage in and the factors they are exposed to in their environment. Recent developments in customised medicine are dependent on technology that verifies a patient's fundamental biology, such as their DNA, RNA, or protein, which, in the end, leads to the diagnosis of disease.[1]

In the field of pharmacogenomics, genomic data is analysed to better understand how individuals react to various medications. When a gene variant is linked to a specific drug reaction in a patient, clinical decisions can be made using genetic information. These decisions could involve changing the patient's dosage or selecting a new medication, for instance. Scientists assess gene variants that influence a person's response to drugs in the same way that

* *Corresponding author*.
E-mail address: pallaviahluwalia22@gmail.com (P. Ahluwalia).

https://doi.org/10.18231/j.ijca.2023.020

they assess gene variants associated with diseases. They start by identifying genetic loci associated with known drug responses, and then they test people whose responses are unknown. Single nucleotide polymorphism (SNP) profiles are an example of a modern technique; these approaches are just beginning to find application in clinical settings for medication discovery and development. [1,2]

There are an infinite number of benefits that may be gained through personalised medicine, which, as it continues to advance, will cause a shift in the way that conventional care is conducted. One of the issues that people have with the methods that are being used to provide medical care in the modern era is that there are no concrete guidelines that specify how medicine should be carried out. The development of customised medicine will lead to the creation of a treatment strategy that is more unified and specific to the individual as well as their genome. The use of personalised medicine raises the possibility of more accurate diagnoses, which could lead to early treatment, as well as faster medication discovery and more effective treatments.

Anaesthesiologists are now able to select anaesthetic agents and determine appropriate dosages because of the advancement of fundamental principles in the fields of pharmacokinetics and pharmacodynamics, respectively. Because these ideas can be applied to a wide range of therapeutic settings and patient types, it is now possible to individualise the dosage, which in turn reduces the likelihood of experiencing any consequences. The practice of determining a patient's dosage based on empirical methods, such as calculating it in milligrams per kilogram of total body weight, is going to be phased out of the anaesthesia field as scientists learn more about the dramatic variations in medication reactions that can occur. The administration of anaesthesia has been regarded as both an art and a science for a very long time. The fact that individual patients' responses to drugs might vary greatly from one another is not the exception but the rule. Historically, variations in patient response have been linked to a variety of factors, including age and sex, prior disease and comorbidities, drug interactions, operation type, and nutritional state. Even though anaesthesia has been at the forefront of the discovery of pharmacogenomic disorders such as pseudocholinesterase deficiency, malignant hyperthermia (MH), and thiopental-induced porphyria, many anaesthesia providers have limited knowledge of the topic beyond these specific disorders. Medicine and the development of new drugs are making greater use of pharmacogenomics as a method for predicting how a patient will respond to treatment. Pharmacogenomic considerations offer the potential to improve therapeutic results and individualise drug therapy while avoiding adverse effects and treatment failure. This promise can be realised through the expansion of the knowledge base of anaesthesia physicians. Considering the possibility that pharmacogenomics does not fully explain the diversity in drug response, the use of pharmacogenomics should be done in conjunction with traditional anaesthetic concerns. For a drug to be effective, it must interact with a specific target that is either located on the cellular membrane, in the cytoplasm or plasma. Changes to these effectors that are either qualitative (for example, in the sequence of amino acids) or quantitative (for example, in the amounts of gene expression) are what generate the biological diversity that is so widely observed, but they can also produce genetically defined diseases. The administration of a drug that is safe and effective in the general population may cause severe adverse effects in individuals who carry the disease gene and may also cause a subclinical alteration, as it occurs in a relatively rare but clinically important syndrome such as long QT syndrome. This is true in both scenarios (LQTS). Genetic changes in ion channels that control the ventricular repolarization phase cause congenital LQTS. These mutations can be passed down through either parent. LQTS increases a person's risk of developing potentially fatal cardiac arrhythmias such as torsade de pointes, as well as the risk of dying unexpectedly.1 An increasing number of laboratories are assisting anaesthesiologists in personalising patient care by using pharmacogenetic testing to predict a patient's response to postoperative opioid therapy, treatment for postoperative nausea and vomiting with a variety of anti-emetics, and perioperative thrombosis risk. These tests are used to determine how a patient's genetic makeup will react to opioid therapy after surgery. Patients whose genetic profiles indicate a propensity to react poorly to specific drugs, such as opioids, or to metabolise them too quickly, can benefit from these predictions because they can help anaesthesiologists choose the best treatments for those patients.

In the field of pharmacogenomics, genomic data is analysed to better understand how individuals react to various medications. It is possible to make clinical decisions depending on genetic information when a gene variation is shown to be connected with a certain drug reaction in a patient. These decisions could involve changing the patient's dosage or selecting a new medication, for instance. Scientists assess gene variants that influence a person's response to drugs in the same way that they assess gene variants associated with diseases. They start by identifying genetic loci associated with known drug responses, and then they test people whose responses are unknown. Modern methods, such as multigene analysis or whole-genome single nucleotide polymorphism (SNP) profiles, have only recently begun to be used in clinical settings for drug discovery and development. [3,4]

When researching the effects of drugs on humans, scientists mostly concentrate on two primary determinants:

(1) the amount of medicine that must be taken for it to reach its destination in the body, and (2) the degree to which the cells at the destination, such as those in the heart or the neurons, respond to the drug. These two factors are referred to as pharmacokinetics and pharmacodynamics in the scientific community. Within the realm of pharmacogenomics, both of these factors are considered to be essential concerns.[5]

1. Drug Safety

The anticipation of life-threatening adverse drug reactions is an important goal of pharmacogenomic research. Certain antidepressant, antiarrhythmic, and antipsychotic medicines, for instance, are broken down and their effects are stopped by an enzyme called CYP2D6, which belongs to a set of enzymes found in the liver that is responsible for drug metabolism.[6] The gene responsible for coding this enzyme has been the subject of molecular cloning and characterisation studies, which have resulted in the description of more than 70 variant alleles. However, few alleles have gene deletions or duplications that can contribute to enhanced enzyme activity. One or more point mutations are present in these alleles; however, only a subset of those mutations affects enzyme activity. Extensive metabolizers are people who are homozygous or heterozygous for wild-type or normal activity enzymes (75-85 percent of the population). Individuals who carry two alleles that reduce enzyme activity are intermediate (10-15%) or poor (5-10%) metabolizers.[7] Ultrarapid metabolizers (1% to 10%) have duplicated genes. DNA chip microarrays can identify the most common alleles, allowing the majority of patients to be classified into a specific phenotypic category.

Because of recent discoveries and ongoing studies, the fields of pharmacogenetics and pharmacogenomics are expected to have an increasingly significant bearing on the processes of drug discovery and development, clinical testing, and everyday clinical work. In the latter case, the doctor will have an easier time personalising treatment options because the description of each individual's genetic makeup will add another relevant factor to the mix of non-genetic considerations. We anticipate that clinical application software, such as anaesthesia information systems, will incorporate additional pharmacogenomic data as well as decision support in the not-too-distant future.

References

1. Mini E, Nobili S. Pharmacogenetics: implementing personalized medicine. Clin Cases Miner Bone Metab. *Clin Cases Miner Bone Metab*. 2009;6(1):17–24.
2. Karczewski KJ. Progress in genomics according to bingo: 2013 edition. *Genome Biol*. 2013;14:143. doi:10.1186/gb4148.
3. Lemmens HJ, Stanski DR. Individualized dosing with anesthetic agents. *Clin Pharmacol Ther*. 2012;92(4):417–9.
4. Lotsch J, Skarke C, Liefhold J, Geisslinger G. Genetic predictors of the clinical response to opioid analgesics: clinical utility and future perspectives. *Clin Pharmacokinet*. 2004;43(14):983–1013.
5. Fishbain DA, Fishbain D, Lewis J, Cutler RB, Cole B, Rosomoff HL, et al. Genetic testing for enzymes of drug metabolism: does it have clinical utility for pain medicine at present? A structured review. *Pain Med*. 2004;5(1):81–93.
6. Gardiner SJ, Begg EJ. Pharmacogenetics, drug-metabolizing enzymes, and clinical practice. *Pharmacol Rev*. 2006;58(3):521–90.
7. Ingelman-Sundberg M, Rodriguez-Antona C. Pharmacogenetics of drug-metabolizing enzymes: implications for safer and more effective drug therapy. *Philos Trans R Soc Lond B Biol Sci*. 2005;360(1460):1563–70.

Author biography

Pallavi Ahluwalia, Professor https://orcid.org/0000-0001-8730-3730

Bhavna Gupta, Assistant Professor https://orcid.org/0000-0002-3108-0408

Cite this article: Ahluwalia P, Gupta B. Application of pharmacogenetics in the practice of anaesthesia. *Indian J Clin Anaesth* 2023;10(1):110-112.