Pharmacogenetics - Strengthening the Clinical Medicine

With a lengthy and wide-ranging history of Pharmacogenetics, the researchers to this date are still discovering more and more about how the genetic variability of individuals affect the response to the drugs. The terminology of pharmacogenetics was not introduced until 1957. How an individual's genetic makeup affects his response to drugs is an emerging field which helps in predicting about the effectiveness of the drug for that particular individual. This field is growing day by day, which is helping the world develop effective and safe drugs.[1]

Everyone doesn't respond to the same drug in the same way, though most of the drugs available today are prescribed as "one size fits all". It is not easy to predict who would be benefitted from the drug and who wouldn't. A clinician's decision regarding prescription is mostly based on factors like age, weight, sex, liver and kidney functions of the patient. This is a conventional practice in clinical medicine where judgment of the clinician and continuous patient observation contributes towards establishing a working dosage of drug regimen for a vast number of the drugs.[2] However; there are a few drugs that have a narrow therapeutic index that need a careful titration of dose so that the desired clinical effect is achieved. With time genetic testing came into picture, where when the genetic variation gets associated with a particular drug response, there comes a potential to make a clinical decision on the basis of genetics in the larger interest of the patient in terms of selecting the best dose and best drug for each patient. Prior to this link between the genetic profile and optimum dose of the drug, a process of continuous monitoring of the response of the patient to the drug was in practice, which was rather a trial-and-error kind of approach. Warfarin,[3,4] irinotecan,[5] and atomoxetine,[6] are among such drugs where the genetic testing guided the starting dose, thus accelerated the overall process of reaching at the optimum drug dosage with least adverse effects.

Throughout the world, adverse drug reactions are one of the prominent causes of mortality.[7] Moreover these days the researchers have identified and linked genetics as a basis to these adverse effects caused by the drugs. Thus, the awareness of the genetic makeup can predict the possibility of an unwanted effect and help the clinicians go for an alternative drug if necessary and available. Abacavir is one such example, there if the HIV patients do not carry the HLA-B*57:01, then the patients won't experience abacavir-induced hypersensitivity. However, if the patients carry this allele, then they carry a risk of a potentially fatal reaction because of which the clinicians always opt for some other alternative as a part of good clinical practice. Thus, in HIV patients, this screening of HLA-B*57:01 prior to starting abacavir have been found successful in decreasing the incidence of abacavir induced hypersensitivity in HLA-B*57:01 carriers by replacing this drug with non-abacavir-containing drugs.[8] The approach of targeted therapies genuinely contributes towards improving effectiveness of a treatment and minimizes the unintentional mortality which thus considerably reduce the burdens on health care systems.

Genetic testing helps in identifying who will respond to the drug and who won't. So far this is becoming a keystone while deciding treatment of diseases including cancers and infectious diseases. One such example is that of Trastuzumab, a drug prescribed for breast cancer patients who are specifically HER2-positive. This drug has improved survival and reduced relapse of cancer by nearly 10%.[9] In contrast to this, the same drug has been ineffective in patients who are HER2-negative. A genetic testing when precisely determines an effective treatment, strengthens a patient's confidence especially the ones who are facing devastating and mentally distressing conditions like cancers. In such conditions one faces not only a rapid detoriation in quality of life but also has to pay a high price for a treatment that itself is not only harmful but at same time may have a doubtful efficacy.

While studying the response in individuals to drugs, researchers have been focusing on two major aspects: the pharmacokinetics and dynamics. Pharmacokinetics takes into consideration how much of a drug will reach its target in the body, dealing more with absorption, distribution, metabolism and excretion of the drug. Of all these the drug metabolism is one of the best studied areas of pharmacogenetics. Since metabolism takes place through enzymes encoded by genes, so their genetic variations are likely to affect the drugs being metabolized through them, ultimately defining the response in an individual.[10] The second aspect being considered is how well the target cells respond to the drug and that is pharmacodynamics. These target cells being protein in nature and encoded by genes are again subject to genetic variations which modulate

the drug response. Though the findings from these studies are not always in complete agreement, the researchers have been relying on both pharmaco-kinetics and pharmacodynamics while considering pharmacogenetic studies.

So far most of the research is focused on the impact of variations in the single nucleotide polymorphisms (SNPs) on drug's response in an individual. Profiles of these SNP variations may enable tailored prescription of drugs so as to specifically accommodate the needs of each individual. Extensive data from different developed populations is already available publicly and the developing ones are on their way. How the researchers will manipulate these findings to human advantage is still in progress.[11]

It is the fact that pharmacogenetics drastically decreases the burden on health care systems. With these testing one can go for cheaper drugs like abacavir and simvastatin, rather than going for costly alternatives like tenofovir and alirocumab. As these costly drugs invite redundant expenses onto the health-care system. They also increase the risk of more unusual adverse effects. Likewise, when one goes for the inexpensive substitutes free-handedly, they increase the risk of morbidity while compromising quality of life because of the adverse effects. The more the clinicians become knowledgeable about the individual genetic profiles of their patients, the more they will be able to assign costlier alternatives only to those who would not withstand the inexpensive drugs, and this can save a substantial amount of economy of the health care system even with the cost of genetic testing prior to treatment included.[1] Such larger advantages of the pharmacogenetic testing however get overshadowed by the higher costs of these tests on individuals.

Because of its tangible benefits, today pharmacogenetics is regarded as an essential area for scientific research. If it gets implemented correctly, it will promise a targeted treatment in accordance to the genetic makeup of each individual. With more research and advancements in this field, there are chances that more clarity and understanding of this subject will guide towards prescribing drugs that will guarantee more effectiveness while simultaneously reducing adverse effects. A lot more research however, has to be embarked upon and a number of practical concerns need to be addressed prior to integrating pharmacogenetics into health care systems. It is expected that with time more definitive and convincing research in this field will set the motion of its incorporation into medical practice, thus will improve the health care systems on the whole.

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