SHORT COMMUNICATION

PHARMACOGENOMICS AND THE CONCEPT OF PERSONALIZED MEDICINE FOR THE MANAGEMENT OF HYPERTENSION

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Hypertension poses a significant global burden due to low adherence to antihypertensive medications. Hypertension treatment aims to bring blood pressure within physiological ranges and reduce the risk of cardiovascular disease and organ damage associated with high blood pressure. It is estimated that around 1.13 billion people have hypertension, accounting for 13% of all fatalities worldwide. The World Health Organization aims to reduce this number by 25% by 2025 compared to the baseline year of 2010.[1,2] Despite the availability of effective antihypertensive medications and decreased main risk factors, achieving optimal blood pressure control remains challenging for various reasons, including apparent drug resistance and poor compliance.[3,4] One of the contributing factors to poor blood pressure control is the difficulty in predicting which antihypertensive medication will be most effective for a specific patient. An individualized approach to hypertension treatment, considering risk factors, pharmacokinetic properties, genetic phenotypes, and other patient-specific characteristics, holds promise.

Pharmacogenomics and other 'omics' technologies can help identify genetic signals indicative of a favorable or unfavorable response to specific antihypertensive drugs. By conducting research in this field, we can better understand how to optimize blood pressure response using different classes of antihypertensive medications.[4] Pharmacogenetics studies the genetic basis of medication response variability, particularly the influence of genetic factors on drug metabolism. In recent years, simple nucleotide polymorphisms (SNPs) have emerged as the primary genetic variation markers. High-throughput genotyping approaches can detect SNPs, which are widespread throughout the genome, often involve substitutions, and rarely result in mutations. SNPs in drug-metabolizing enzymes have been reliable indicators for dose-related treatment decisions.

Genetic studies conducted over the past two decades have identified various genetic polymorphisms associated with hypertension, including changes in the number of tandem repeats, microsatellites, single nucleotide polymorphisms (SNPs), and insertions/deletions (I/D). These studies have also revealed significant inter-individual variability in responsiveness to antihypertensive medications, highlighting the importance of pharmacogenomic research and the potential for individualized pharmacological therapy. Genetic factors may contribute to a 30-50% increase in blood pressure.[5] A comprehensive approach is required to advance personalized medicine, incorporating data and insights from genomic, genetic, and proteomic sciences. This applies to both approved medications and therapeutic candidates in various stages of clinical trials. Personalized medicine aims to administer the right drug to the right patient at the right time and dosage. By embracing this concept, we can significantly improve hypertension treatment outcomes.[6]

The goal of personalized therapy for hypertension is to identify the most effective drug for reducing a patient's blood pressure. Conversely, an opposing viewpoint argues that individualized treatment helps eliminate the risks of adverse drug reactions and the use of ineffective medications. The issue of adherence problems further emphasizes the need for modifying hypertension treatment. As a result, personalized medicine, which tailors medical approaches and treatment plans to individual patient characteristics, is projected to become the standard of care in the future.[7]

Antihypertensive pharmacogenomics research aims to improve cardiovascular disease (CVD) outcomes in treated hypertensive patients by identifying genetic factors that influence the variability in antihypertensive response. Although these genetic variables account for approximately 50% of blood pressure variation across populations, specific genes responsible for a significant portion of this variation have yet to be identified. The complexity of the condition is attributed to the influence of alleles at different loci through various pathways and the impact of environmental factors on the manifestation of the blood pressure phenotype.

There is evidence supporting the hypothesis that genetics may contribute to individual variations in how people respond to blood pressure-lowering drugs. By incorporating genetic information, pharmacogenomics can provide insights into personalized treatment approaches. However, further research is needed to uncover the specific genes and pathways involved. Improving our understanding of the genetic basis of antihypertensive response

variability holds excellent potential for optimizing hypertension treatment. Personalized medicine, driven by pharmacogenomics, can revolutionize the management of hypertension and enhance patient outcomes.[8]

A previously published study revealed that the response to angiotensin-converting enzyme (ACE) inhibitors was less favorable in black participants than in Caucasians. The study involved 56 white patients (aged 22 to 51) with untreated essential hypertension from the East Anglia region of the United Kingdom. These patients were alternately administered four major antihypertensive medications (beta-blockers, diuretics, calcium antagonists, and blockers). The study demonstrated that only 22 out of 56 patients initially achieved the target blood pressure with their initial treatment. However, when the best response was considered, the number increased to 41 out of 56 patients, supporting the notion that each patient's response to antihypertensive treatment is unique. This study highlighted that ethnicity alone is insufficient to indicate who will benefit from a particular therapy.[9]

Genetic differences in relation to several antihypertensive medications and their efficacy have been investigated. Two recent studies examined the ACE insertion-deletion (ID) variant, one focusing on blood pressure response and the other on myocardial infarction (MI) and stroke. Neither study found significant pharmacogenetic associations with the use of ACE inhibitors. These findings were consistent with prior research on lisinopril, but a previous study on fosinopril reported significant associations between fosinopril and ACE (ID) regarding blood pressure response. Establishing a firm scientific foundation is essential but insufficient for developing clinically useful antihypertensive pharmacogenetics. Clinicians must adopt a new paradigm to appropriately and routinely utilize genetic information in the clinical setting.[10,11]

The concept of pre-prescription genotyping is gaining attention in the treatment of various conditions. For example, by detecting CYP450 gene variants, pre-prescription genotyping can help determine the optimal dose of serotonin reuptake inhibitors. This approach can enhance treatment outcomes and minimize adverse reactions by tailoring medication regimens to individual patients.[12,13] Further research and a shift in clinical practice are necessary to fully realize the potential of antihypertensive pharmacogenetics and personalized medicine in optimizing hypertension treatment and improving patient care.[14]

Two recent European studies examining the perspectives of healthcare professionals and patients revealed generally optimistic expectations regarding the potential benefits of genetic testing in terms of customizing drug dosages and minimizing side effects. However, some patients expressed concerns about the stress and anxiety associated with testing, as well as potential violations of confidentiality. Patients also emphasized their preference for pharmacogenetic services provided by experts confident in their ability to interpret and apply the results. Therefore, the perception of risk-benefit must align for individualized therapy to be effective in the initial treatment of hypertension.

The rise of direct-to-consumer genetic screening has made genetic information more accessible to individuals without involving healthcare professionals initially. As this industry develops, it may help people become more comfortable with pharmacogenetics, viewing their genetic information as a tool for optimizing therapy. However, research collaborations and study designs need to be adapted to fully harness the potential of personalized medicine. Comprehensive biobanks and registries that provide accessible data, standardized phenotyping methods, and analytical tools are essential. Incorporating novel information from investigator-initiated studies into ongoing clinical trials and cohorts based on demographic data would further enhance these resources.[15,16]

Enhancing the understanding of "-omics" technologies is crucial for biomedical researchers, physicians, patients, legislators, healthcare organizations, and consumers to develop and implement personalized medicine, reducing the burden of hypertension on the public health system and its associated complications. Targeted educational initiatives in the field of "-omics," focusing on both new and experienced scholars, should emphasize team approaches by involving subject matter experts from related fields. Early achievements in this field would help construct a compelling narrative for personalized medicine that all stakeholders can easily understand. This shift would promote greater reliance on prediction models, facilitating the integration of personalized medicine as a cornerstone of medical education, surpassing traditional case studies.[17-19] By addressing these considerations and fostering interdisciplinary collaboration, personalized medicine can revolutionize the management of hypertension and improve patient outcomes.

REFERENCES

1. Ashiq K, Ashiq S, Shehzadi N. Hyperuricemia and its association with hypertension: risk factors and management. Pakistan Heart J. 2022;55(2):200-1.
2. Shahbaz SAZ, Nazar MS, Umar A, Tariq MA, ul Haq I, Junaid M. Evaluation of hypertension awareness among general population in Bahawalpur, Pakistan: a cross sectional study. Int J Pharm Integ Health Sci. 2023;4(1):100-17.
3. Savoia C, Volpe M, Grassi G, Borghi C, Agabiti Rosei E, Touyz RM. Personalized medicine—a modern approach for the diagnosis and management of hypertension. Clin Sci. 2017;131(22):2671-85.
4. Cooper-DeHoff RM, Johnson JA. Hypertension pharmacogenomics: in search of personalized treatment approaches. Nat Rev Nephrol. 2016;12(2):110-22.
5. Bhardwaj S, Balgir PP, Goel RK. Pharmacogenomics and personalized management of hypertension. J Crit Rev. 2015;2(2):1-6.
6. Oliveira-Paula GH, Pereira SC, Tanus-Santos JE, Lacchini R. Pharmacogenomics and hypertension: current insights. Pharmacogenomics Pers Med. 2019:341-59.
7. Byrd JB. Personalized medicine and treatment approaches in hypertension: current perspectives. Integr Blood Press Control. 2016;9:59-67.
8. Turner ST, Bailey KR, Fridley BL, Chapman AB, Schwartz GL, Chai HS, et al. Genomic association analysis suggests chromosome 12 locus influencing antihypertensive response to thiazide diuretic. Hypertension. 2008;52(2):359-65.
9. Dickerson JC, Hingorani AD, Ashby MJ, Palmer CR, Brown MJ. Optimisation of antihypertensive treatment by crossover rotation of four major classes. Lancet. 1999;353(9169):2008-13.
10. Filigheddu F, Argiolas G, Bulla E, Troffa C, Bulla P, Fadda S, et al. Clinical variables, not RAAS polymorphisms, predict blood pressure response to ACE inhibitors in Sardinians. Pharmacogenomics. 2008;9(10):1419-27.
11. Schelleman H, Klungel O, Witteman J, Breteler M, Hofman A, Van Duijn C, et al. Interaction between polymorphisms in the renin–angiotensin–system and angiotensin-converting enzyme inhibitor or β-blocker use and the risk of myocardial infarction and stroke. Pharmacogenomics J. 2008;8(6):400-7.
12. Arnett DK, Davis BR, Ford CE, Boerwinkle E, Leiendecker-Foster C, Miller MB, et al. Pharmacogenetic association of the angiotensin-converting enzyme insertion/deletion polymorphism on blood pressure and cardiovascular risk in relation to antihypertensive treatment: the Genetics of Hypertension-Associated Treatment (GenHAT) study. Circulation. 2005;111(25):3374-83.
13. Stavroulakis GA, Makris TK, Krespi PG, Hatzizacharias AN, Gialeraki AE, Anastasiadis G, et al. Predicting response to chronic antihypertensive treatment with fosinopril: the role of angiotensin-converting enzyme gene polymorphism. Cardiovasc Drugs Ther. 2000;14:427-32.
14. de Leon J, Arranz MJ, Ruano G. Pharmacogenetic testing in psychiatry: a review of features and clinical realities. Clinics Lab Med. 2008;28(4):599-617.
15. Fargher EA, Eddy C, Newman W, Qasim F, Tricker K, Elliott RA, et al. Patients' and healthcare professionals' views on pharmacogenetic testing and its future delivery in the NHS. Pharmacogenomics. 2007 Nov;8(11):1511-9.
16. Ho D, Quake SR, McCabe ER, Chng WJ, Chow EK, Ding X, Gelb BD, Ginsburg GS, Hassenstab J, Ho CM, Mobley WC. Enabling technologies for personalized and precision medicine. Trends Biotechnol. 2020;38(5):497-518.
17. Ashiq S, Ashiq K, Shabana SU, Qayyum M, Sadia H. Prevalence and role of different risk factors with emphasis on genetics in development of pathophysiology of coronary artery disease (CAD). Pak Heart J. 2020;52(4):279-87.
18. Ashiq S, Ashiq K. The association of apolipoprotein-E (APOE) gene polymorphisms with coronary artery disease: a systematic review and meta-analysis. Egyptian J Med Human Genetics. 2021;22(1):1-8.
19. Ashiq S, Ashiq K. Genetic perspective of the congenital heart disease. Pak Heart J. 2020;53(3):210-2.

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