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Journal of Pharmacogenomics & Pharmacoproteomics

EDITORIAL

Clinical Pharmacogenomics

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INTRODUCTION

Geographical Pharmacogenomics tests for genetic variations in genes that are responsible for drug metabolism, transport, and targets of drug action. Variations can increase the risk for drug toxicity or poor efficacy. Pharmacogenomics can, therefore, be used to help select the best medication or aid in dosing. Pharmacogenomics tests for genetic variations in genes that are responsible for drug metabolism, transport, and targets of drug action. Variations can increase the risk for drug toxicity or poor efficacy. Pharmacogenomics can, therefore, be used to help select the best medication or aid in dosing.

In the following sections, drug-gene pairs with clinical guidelines and a high level of evidence in conditions commonly treated by the nephrologist are presented. The focus is on cardiovascular disease and transplantation versus an exhaustive list of drugs and genes. Readers are encouraged to investigate the primary literature described herein as a means to further learn about pharmacogenomics in relevant therapeutic areas.

Cardiovascular disease is a leading cause of death for patients suffering from CKD. Hallmarks of cardiovascular disease secondary to CKD are cardiac remodeling, atherosclerosis, and arteriosclerosis (17). Pharmacogenomics of cardiovascular disease is an active area of research and clinical implementation, with evidence-based guidelines for antiplatelets, anticoagulation, and hyperlipidemia (16,18,19).

Diabetic nephropathy is a leading cause for CKD and ESKD (55). As such, nephrologists treat many patients with comorbid type 2 diabetes mellitus who are managed on metformin. Although there are no clinical guidelines for the use of pharmacogenomics to tailor therapy with metformin, evidence has been growing that supports the use of the SNP rs11212617 in an intergenic (nongene) region of the genome called the chromosome 11 open reading frame 65 region. At this SNP, the presence of at least one "A" allele is associated with decreased response to metformin (56). In the future, this variation or others affecting pharmacokinetics (e.g., transporters) may be useful for predicting which patients will require altered doses of metformin for adequate hemoglobin A1c control.

Several barriers prevent more widespread pharmacogenomics clinical implementation in everyday practice (Figure 4). Providers need to understand pharmacogenomics concepts for successful precision medicine clinical decision making, specifically whether they can apply the pharmacogenomics data within their current practice model, how the data should be integrated with other clinical parameters, and if a referral to a specialist should be made (e.g., pharmacist, medical geneticist, or genetic counselor) (57). The addition of these data also creates a growing need for provider education. Strategies to train practicing providers and health care students to use pharmacogenomics in practice have been reviewed elsewhere (58) and range from clinical decision support at the point of care to education courses that allow learners to undergo personal genomic testing as a means of learning with one's own data (59).

Unique challenges and opportunities to integrating pharmacogenomics into the care of patients with kidney disease also exist. CKD is known to alter pharmacodynamic and pharmacokinetic relationships of several medications, particular those that rely on kidney elimination. In general, this scales with CKD stage and can be especially challenging in patients receiving dialysis (69). Nephrologists must also consider the systemic changes in patients with CKD, such as the changes in hepatic drug metabolism and other nonkidney clearance pathways that occur in patients with CKD

Nephrologists care for patients with significant comorbidities and are challenged by wide interpatient variability in medication responses. They are ideally positioned to champion integration of pharmacogenomics to achieve precision medicine in the many disease areas affected by kidney disease. As pharmacogenomics knowledge expands, nephrologists will need to have familiarity

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Received: July 08, 2021; Accepted: Aug 12, 2021; Published: Aug 20, 2021.

Citation: Shufeng Zhou. (2021) Clinical Pharmacogenomics. J Pharmacogenomics Pharmacoproteomics.

with the state of the pharmacogenomics science, available pharmacogenomics resources and guidelines, contemporary application of pharmacogenomics data for specific drugs, and clinical decision-making approaches to using pharmacogenomics data.

ACKNOWLEDGEMENT

The author is very thankful to all the associated personnel in any reference that contributed in/for the purpose of this research.

CONFLICT OF INTEREST

The authors have declared that no competing interests exist.