Professional opportunity for pharmacists to integrate pharmacogenomics in medication therapy

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OVER THE PAST DECADE, THE INTEGRATION OF genetic information into the daily care of patients has led to a redefined concept of individualized medicine and has made significant progress.

Pharmacogenomics (PGx) is becoming one of the pillars of proactive health care and represents the “low-hanging fruit” in the emerging field of genomic medicine, given its potential in predicting medication safety and efficacy.^{1,2}

PGx is the study of how variations in an individual's genetic makeup affect the response to medications. Genetic variants may affect the pharmacokinetics as well as the pharmacodynamics of a medication. For example, genetic variations in the cytochrome P-450 (CYP) isoenzymes can produce differences in enzyme activity that change the amount of drug available in the body. This can have a clinical significance regarding adverse drug reactions, drug efficacy and dose requirements for commonly used drugs, such as antidepressants, opiates, proton pump inhibitors and many more.

For instance, clopidogrel is a prodrug that is metabolically converted by the CYP2C19 gene in the liver to its active metabolite and irreversibly inhibits platelet aggregation. Individuals who have significantly reduced function of the CYP2C19 gene may not respond to clopidogrel therapy because of diminished platelet response and may benefit from alternative antiplatelet therapy such as prasugrel or ticagrelor.³

Regulatory authorities such as Health Canada and the U.S. Food and Drug Administration have recognized the fact that individuals carry genetic variants that have major effects on their response to various drugs and thus require submission of PGx data information for new drug approval, if

it provides evidence of the safety and/or clinical effectiveness of the new drug in the context of its proposed indications. This has led to warnings on labels on more than 140 drugs about PGx variants associated with adverse drug reactions, adjustments of drug dosing or different treatment choices.⁴⁻⁶

In addition to regulatory authority recommendations, recent advertisement and access to direct-to-consumer genetic testing companies (DTC) has increased public awareness of preemptive PGx testing.⁷ Because of an absence of regulatory oversight, DTC report PGx results with varying degrees of interpretation, differences of variants interrogated in each gene, decision support and even unproven and invalid therapeutic recommendations, underscoring significant risks and limitations to the consumer. Also, DTC are not obligated to adhere to genetic privacy policies and thus can use the genetic information in an unauthorized way.⁸ Furthermore, PGx testing provides only one piece of information about safe medication prescribing. Other factors such as lifestyle choices, family medical history, concurrent use of medications and other environmental factors need to be considered. This has raised a number of concerns about the potential for misunderstanding and misinterpreting test results, particularly when pre- or posttest PGx counseling is not provided and/or is insufficient.⁹

As medication therapy experts, pharmacists have a unique opportunity to be at the forefront to incorporate PGx data into individualized clinical care by informing and assisting patients and their health care providers in the interpretation of PGx information that could result in substantial changes in patient care. In light of the changing scope of pharmacy practice, PGx-guided

TABLE 1 Barriers to implementation of pharmacogenomics (PGx)

Test-related barriers	• Availability of PGx tests in regulated clinical laboratory per quality standards • Identifying patients for whom test is appropriate • Reasonable turnaround time for test results • Cost of test and potential lack of reimbursement for test
Knowledge/education barriers	• Insufficient knowledge of PGx data • Uncertainty about PGx genetic test interpretation • Uncertainty about incorporation of PGx test results in patient health record • Uncertainty about drug therapy decision based on PGx test
Evidence barriers	• Lack of randomized controlled trials documenting superiority of PGx-guided treatment approach

medication therapy should be considered part of any therapeutic drug monitoring program and be supported by pharmacists.¹⁰

Indeed, many of the guidelines published by professional societies such as the Clinical Pharmacogenetics Implementation Consortium, the Royal Dutch Association for the Advancement of Pharmacy–Pharmacogenetic Working Group, the Canadian Pharmacogenomic Network for Drug Safety and others have been established and authored by pharmacists to provide actionable recommendations for the use of genomic information in a consistent manner.^{11,12}

Despite several of these positive developments, PGx has been slow to be fully integrated into daily clinical practice because of implementation barriers that require attention (Table 1).¹³

Prospective randomized controlled trials for PGx markers to show evidence of superiority of PGx-guided drug therapy over standard dosing are uncommon, as these studies are often primarily designed to assess the therapeutic effects of drugs, with identification of adverse effects being secondary. Therefore, much of the existing evidence in this field has been based on observational data.¹⁴

Test-related barriers such as access to regulated clinical laboratories with quality standards that offer PGx testing results for clinical use, as well as out-of-pocket expenses for the patient, hinder the use of PGx information in the clinical setting. For now, PGx testing is mostly used as a preemptive approach to support future safe medication prescribing. However, if PGx data are to be considered to guide current medication therapy, quick turnaround time of test results will be critical.

Moreover, the lack of knowledge by health care providers about genetic data interpretation and its clinical implication, as well as identification of

patients for whom testing is appropriate, prohibits seamless incorporation into daily care and is thus holding back the beneficial use of individualized medication administration (Table 1).

Across Canada, however, PGx programs in research institutions such as Western University, University of British Columbia and Université de Montreal and University of Toronto, to name a few, as well as clinical laboratories and community-based pharmacies in collaboration with genetic testing companies, have started to offer PGx testing either on a fee-for-service basis or free of charge when offered in the framework of a research project.^{15–18} Projects like these serve as a test bed to address implementation barriers, develop a blueprint for future PGx services and examine the clinical utility and feasibility of implementing such a test into routine pediatric and adult patient care.

As part of the project scope, pharmacists and pharmacy students should be educated in interpretation of raw sequence data and prediction of drug sensitivity based on these data. Most important, pharmacy students and pharmacists should be trained to identify variants in genes that could represent the needs of the patient population they are serving. This way, pharmacists can make an educated decision when partnering with commercial laboratories for choosing the most relevant pharmacogenomics panel. In addition, pharmacists should play an instrumental role in generating test reports or using external PGx software reports for interpreting and applying test results to patient care and consult patients and their health care providers about the implication of current and/or future drug prescribing in a clinical setting.

The expanding role of pharmacists in delivering health care services and affecting medication

safety at the individual patient level places the pharmacy profession in a perfect position to spearhead this aspect of individualized medicine. PGx-guided medication prescribing complements and supports the service model for medication therapy management delivery by pharmacists, in which identification of the correct medication choice and dosage, in partnership with the patient and their health care provider, not only increases medication safety awareness but also leads to improved outcomes in drug treatments.

It is therefore critical to urge collaboration between all professional pharmacy associations to support an infrastructure that enables pharmacists

in all clinical settings to provide active treatment guidance for patients who have undergone PGx testing. This infrastructure needs to support integrating PGx into the curriculum of all pharmacy students at the university level as well as providing educational materials, including online modules, that allow for continuing education of practising pharmacists in the community as well as hospital settings. It is anticipated that many of the above-mentioned barriers to integrating PGx testing into routine clinical care will soon be overcome. Therefore, pharmacists should begin to position themselves as an integral part of this aspect of predictive and preventative medicine. ■

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