The Pharmacist's Perspective on Pharmacogenetics Implementation

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KEYWORDS

- Pharmacogenetics • Pharmacokinetics • Pharmacodynamics
- Drug–gene interaction • Personalized medicine

KEY POINTS

- Pharmacists have the chance to apply and incorporate drug knowledge in collaboration with physicians and other health care providers using pharmacogenetics.
- This will not be just in a general broad context, but will be personalized for each patient reflecting that patient's drug–gene metabolic pathway.
- Patients with this approach benefit with enhanced therapeutic outcomes that could lead to more streamlined drug approaches, fewer follow-up visits, cost savings, and shorter times to achieve therapeutic outcomes.
- Drug–gene metabolic pathways will allow the providers to avoid drug failures, customize doses and schedules, alert drugs using the same pathway, and prevent duplication of therapies.
- The time will arrive when no medication order can be processed without the knowledge of the patient's drug–gene metabolic pathway.

INTRODUCTION

Every pharmacist has a goal to maximize medication therapy success and minimize medication therapy failure. Currently, pharmacists review the patient's renal status, allergies, hepatic function, weight, gender, and other parameters to optimize medication response and minimize and adverse drug reactions that may occur. This all occurs within an institutional drug formulary with the goal of successful patient outcomes and

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cost controls. Pharmacogenetics adds another tool for the pharmacist to enhance successful outcomes and minimize untoward effects. Knowing a patient's drug–gene metabolic pathway allows the pharmacist to aid the provider with that ability to avoid medications metabolized by the liver that will not result in the desired outcome. Adverse drug reactions (ADRs) are one of the leading causes of death in the United States.[1] If the drug–gene metabolic pathways are identified before implementation, up to almost 60% of ADR risk could be identified and managed[2] (**Table 1**). Having this knowledge gives the provider and the pharmacist the ability to select medications that would give a greater chance of success and avoid those medications that genetically would be impaired. This ability to identify patient variability genetically helps to illuminate why certain patients respond better than others and also why others fail to achieve the desired effects. This variability then can be viewed as a function of the patient's unique genetic makeup and used to enhance the personalization of medications. The impact is better medication selection, resulting in safer administration, quicker drug response, and cost savings by avoiding other risky medications and fewer follow-up provider visits to monitor outcomes. Idiosyncratic reactions now can be explained partially with an increasing knowledge of the drug–gene metabolic pathways, reflecting the variations that exist among individuals. This personalized approach to medicine reflecting pharmacogenetics gives the pharmacist a special opportunity to understand on a molecular level each patient and their predicted response.

PHARMACOGENETICS IS MORE THAN JUST DRUG METABOLISM

Pharmacogenetic variants affect modulators of both pharmacokinetic (PK) and pharmacodynamic (PD) processes, and have very different consequences on drug safety and efficacy. Pharmacology is broken down into 2 equal sides for every drug: the PK effect and the PD response. Genetic variants in both PK and PD mechanisms can affect drug safety and efficacy, but they do so by very different mechanisms.

Pharmacokinetics

PK is what the body does to the drug. It is the process of drug disposition—absorption, distribution, metabolism, and excretion—that sets the concentration of drug delivered to the target receptor site. Absorption reflects the administration of the drug by injectable, oral, subcutaneous, rectal, and transdermal routes with the fraction of drug available in systemic circulation termed *bioavailability*. If the drug undergoes metabolism or elimination before entering the circulation, or absorption is reduced, then the bioavailability is reduced. When drugs are given by rapid intravenous injection, the peak concentration occurs earlier and higher than when the same dose is administered by a nonintravenous route. Chemical properties such as insolubility, destruction at the site of administration, or incomplete release from the drug medication form may also reduce the amount absorbed. Deliberately slowing absorption is the goal of extended release or sustained release formulations, which results in minimizing plasma drug level fluctuations between doses. A *steady state* occurs with continuous intravenous infusion whereas, in oral administration, plasma concentrations vary during the dosing interval and steady state is achieved in 5 half-lives when given consistently. The distribution of drugs for a 70-kg human is about 20 L extracellular water, blood volume of about 5.5 L, and a plasma volume of 3 L. Many drug factors can affect volumes of distribution. For example, tricyclic antidepressants and digoxin are highly bound to tissues for a high volume of distribution, whereas warfarin is protein bound in plasma and reflects a much lower volume.