Pharmacogenetics: The Solution for All Future Challenges?

Around 15 years ago pharmacogenetics was predicted to revolutionize pharmacotherapy. Patients would no longer be treated with standard drugs in a standard dosage. Instead, the right drug in the right dose would be selected for each individual based on a genetic test. Individuals likely to experience adverse events would be identified prior to drug treatment, and personalized medicine would be within close reach. Unfortunately, this prediction has not materialized. Although pharmacogenetic studies have found correlations between pharmacokinetic parameters and gene polymorphisms for a large number of drugs, very few physicians have ordered pharmacogenetic tests for their patients outside clinical trials. Technical advances have outpaced clinical implementation. The time needed to genotype, and the cost associated with these tests, have been reduced to a level that is no longer prohibitive for widespread use. Not only detection of single-nucleotide polymorphisms (SNPs), but also more extensive whole-genome sequencing is now widely available.

The FDA has included pharmacogenetic information in the labels of more than 150 approved drugs. To assist physicians, the Royal Dutch Association for the Advancement of Pharmacy established a Pharmacogenetics Working Group that developed pharmacogenetics-based therapeutic (dose) recommendations following a systematic review of the literature [1]. In order to facilitate clinical application, the dose recommendations are now being integrated into electronic prescription systems, with the assumption that this type of clinical decision support will encourage physicians to use the available information [2, 3]. In addition, these recommendations were integrated with the Pharmacogenomics Knowledge Base for each investigated drug and can be found under the 'Clinical PGx' heading [4].

Many factors influence the between-patient variability in drug response. Besides comorbidities, interacting comedication and environmental factors the genetic variability is just one of the factors that may influence the outcome of treatment. In pediatric patients also the ontogeny in drug transporters and drug metabolizing enzymes need to be taken into account. For the vast majority of drugs this contribution of pharmacogenetics is below 20% and unlikely to lead to a useful pharmacogenetic test. Yet, there are drugs for which the contribution of pharmacogenetics to overall variability is substantial, and we should carefully consider implementing these tests into our daily practice.

In my presentation I will examine the evidence that pharmacogenetic information can predict the pharmacokinetics or the pharmacodynamics. The potential impact of these data on clinical practice will be discussed.

Conflict of Interest

Teun van Gelder has received lecture and consulting fees (paid to the Erasmus MC) from Astellas Pharma, Roche Diagnostics and Novartis, as well as grant support (paid to the Erasmus MC) from Chiesi Pharma.

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