

Clinical Implication of Pharmacogenetics

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Pharmacogenetics indicates the study of the underlying genetic differences that result in variation in an individual's response to drugs. Recent success of the Human Genome project causes the pharmacogenetics to apply to the real clinical practice. Pharmacogenetics and pharmacogenomics lead the use of genetic information 1) to predict the safety, toxicity and/or efficacy of drugs, 2) to enhance drug discovery and development and 3) to improve individual's diagnosis and treatment regimen.

Adverse drug reactions are significant problems which is the 4th leading cause of death and occupies 10 to 30% of hospital admissions in the United States (Lazarou J. et al, 1998). Pharmacogenetics in the clinical practice can contribute to reduce the adverse drug reaction caused by the genetic variations. Although we have not known all the genetic factors determining the adverse reactions, the metabolism of the some drugs are significantly determined by the genetic factors. (Table 1). It indicates the variable response to drugs among patients significantly caused by the variations of the genes related to the drugs.

Table 1. Heritable effects for Pharmacokinetics (example)

Drug	Clearance Measure	Heritability
Phenbutazone	Half-life	0.99
Dicumarol	Half-life	0.98
Aspirin	Plateau levels	0.98
Amobarbital	Elim. constant	0.91
Diphenylhydantoin	Half-life	0.85
Sodium salicylate	Elim. constant	0.85

The genetic variations related to the drug are high among ethnic groups. Therefore genetic variations and frequencies of the each variations needs to be determined for each ethnic groups. For example, our research group found NAT2 gene has a lot of variable polymorphisms among Caucasian, Asian, and African but the number of variation among Koreans are limited compared to the whole variation and the frequencies of the each alleles are quite different from those of Caucasians and some of variations are found only in Koreans from whole gene sequencing of 1000 individuals. Eventually these variations leads to make the patients response to the drugs differently. The optimal regimen needs to be determined according to the genetic variations. I will present the some of the results from the genetic study and pharmacogenetic studies of the drug.