Pharmacogenetics: promise or reality?

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A common problem in medicine is that there are differences in how patients repond to drugs. Whereas most individuals will tolerate the standard dosages well, certain patients may either experience severe toxicity on the same dose, or may eventually show to be subtherapeutically treated. Since the 1960s, we are aware that individuals may differ in metabolizing capacity, due to genetic polymorphisms encosing drug metabolizing enzymes.

Examples are NAT2 polymorphisms and isoniazide (used to treat tuberculosis), TPMT and azathioprine/6-mercaptopurine (Crohns disease, Acute Lymphatic Leukemia) and cytochrome P450 2D6 (CYP2D6). Yet, this knowledge has not resulted at that time in a large implementation for patient care. In the last 5 years, however, important improvements have been made, both in availability of genotyping techniques as in knowledge about translating genotypes to phenotypes.

Interesting new applications are CYP2D6 testing for tamoxifen therapy (breast cancer), CYP2C9/VKORC1 analysis for anticoagulation, HLA-B5701 testing for abacavir (HIV treatment) and CYP2C19 analysis for clopidogrel (anticoagulation). Because of these examples, there seems to be a growing acceptance of pharmacogenetic testing. How far are we at this moment? Can we integrate pharmacogenetic testing already in routine diagnostics, or are we still too early?

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