How Common are Drug and Gene Interactions? 
Prevalence in a Sample of 1143 Patients with Known CYP Genetics

BACKGROUND

- Drug-drug interactions (DDIs) are a major cause of adverse drug reactions. 
- There are two other newly-described important types of interactions: drug-gene interactions (DGIs) and drug-drug-gene interactions (DDGIs).

DGIs: A drug-gene interaction occurs when a patient’s genetic metabolic type (for example, CYP2D6 poor metabolizer) affects that patient’s ability to clear a drug.

DDGIs: In a drug-gene interaction, two patient-specific factors affect that individual’s ability to clear a drug: 1) the patient’s genetic metabolic type, and 2) another drug in the patient’s regimen, such as a potent CYP2D6 inhibitor.

METHODS

- The investigators conducted a retrospective analysis of 1143 individuals whose CYP2D6, CYP2C9, and CYP2C19 genotypes were known. Using each individual's medication list and a software tool called YouScript, the prevalence of potential DDIs, DGIs and DDGIs was calculated.
- The study population included all patients 18 to 80 years of age who provided a current medication list and submitted a DNA cheek swab sample for CYP polymorphism testing at Genelex Corporation during 2 months in 2012. Patients across the United States participated.
- Standard CYP nomenclature was used: poor metabolizer (PM), intermediate metabolizer (IM), normal metabolizer (NM), rapid metabolizer (RM), and ultra rapid metabolizer (UM).1,4
- The software tool used in the study was designed to analyze cumulative drug-gene and drug-drug interactions based on both data from the literature and a predictive algorithm. By evaluating multiple simultaneous interactions from both drug and gene sources, the software provides a cumulative estimate of pharmacokinetic interactions. In addition, the software alerts users about pharmacodynamic interactions.

OBJECTIVE

This pilot study reports the frequency of potential Drug Drug Interactions, Drug-Gene Interactions, and Drug-Gene-Gene Interactions in a sample of 2460 cytochrome-tested individuals.

RESULTS

The study population of 1143 patients had a mean age of 60 (range 18 to 89) and patient medication count contained a mean of 6.4 drugs (range 1 to 44).

Overall Frequency of Potential Interactions

- 31% of participants had a potential Drug-Drug Interaction, while 12% had a potential Drug-Gene Interaction, and 12% had a potential Drug-Drug-Gene Interaction.

Frequency of Potentially Significant Interactions

- 43% of participants had potentially significant interactions (categorized as Major or Substantial).
- Potential Drug-Gene Interactions and Drug-Gene-Gene Interactions were quite common in the study population accounting for 33.9% of all potentially significant interactions (DDIs, 66.1%; DGIs, 14.7%; DDGIs, 19.2%).
- Most of the potential major interactions were DDGIs (64.5%), followed by Drug-Gene Interactions (21.5%), and Drug-Gene Interactions (13.9%); the type distribution was similar for potentially significant interactions (Figure 2).

CONCLUSIONS

Potential Drug-Gene Interactions and Drug-Gene-Gene Interactions accounted for 33.9% of all of potential clinically significant interactions identified in this study.

In the study population, potential Drug-Drug Interactions were more common than Drug-Gene Interactions.

When compared to potential DDIs alone, potential Drug-Gene Interactions and Drug-Gene-Gene Interactions increased the number of potential clinically significant interactions by > 50%.

REFERENCES


In the future, identifying potential Drug-Gene Interactions and Drug-Gene-Gene Interactions may lead to a more comprehensive and effective method for predicting which patients are most likely to experience adverse drug reactions.