A Novel Gene-Drug Interaction Guide (G-DIG) for Computer-assisted Polypharmacy Decisions in Psychiatry

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Background

In the US, about 75% of adults aged 45 and older use ≥ 5 drugs. Drug-drug interactions, side effects, and environmental interactions are important risk factors for polypharmacy that must be considered to avoid standard drug dispensing-support tools. The efficacy, exposures, and the safety of medicines are modulated by drug-metabolizing enzymes, especially the CYP450 system. In 2017, prescribing information of >400 U.S. licensed drugs, including >30 psychotropic drugs, contain cautions, precautions or warnings with respect to specific pharmacogenetic (PGx) metabolizers. The need for more accurate, less error-prone algorithmic approaches to aid clinicians in suggesting the need for tests that integrate drug-gene-drug interactions.

Top 100 drugs: Drug-Drug or Drug-Gene Agency Guidance

Objective and Methods

• To create a practical, digital drug-gene-environment interaction machine for use at the point of care.
• We systematically reviewed information on drug-metabolization from multiple publicly available databases, including FDA labels, Pharmacogenomics, and PubMed searches. These data were utilized to design an algorithm in a custom-designed SQL database. Readily interpretable icons, including warnings, help to assess the results. Disparities in the published drug-metabolism are manually curated consensus of experts based upon best interpretation of the literature and scientific information. The output of the tool was prediction of a drug-metabolizing phenotype, and drug-gene-drug interactions expressed as no effect/low risk/moderate risk/higher risk.

Data Sources

• FDA label
• CPIC: Clinical Pharmacogenetics Implementation Consortium; DPWG: Dutch Pharmacy Working Group; https://cpicpgx.org/
• https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm

Methods

• High-throughput screening of >240 U.S. licensed drugs, including >25 psychotropic drugs, containing enzymes, especially the CYP450 system. In 2017, prescribing information of >400 U.S. licensed drugs, including >30 psychotropic drugs, contain cautions, precautions or warnings with respect to specific pharmacogenetic (PGx) metabolizers. The need for more accurate, less error-prone algorithmic approaches to aid clinicians in suggesting the need for tests that integrate drug-gene-drug interactions.

Results

• The G-DIG Interface

• Arimiprazole: G-DIG Guidance

• Venlafaxine: G-DIG Guidance

Discussion

• We developed a practical, novel support tool for computer-assisted polypharmacy decisions. Its feasibility in reducing errors, with prescribing practices was demonstrated in a validation set of psychiatric patients. Future research will focus on demonstrating clinical validity and economic benefits of this tool, and expanding to a wider spectrum of drug-metabolizing enzymes. Availability of U.S. licensed pharmacogenetic and additional environmental factors will be incorporated.