The Importance of Gene-Drug-Drug-Drug-Interactions in Pharmacogenomics Decision Support

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Pharmacogenomics (PGx) Decision Support

PGx test raw results $\rightarrow$ Genotype $\rightarrow$ Predicted phenotype $\rightarrow$ Predicted drug response $\rightarrow$ Dosing recommendation

CYP2D6*1/*2xN
CYP2D6 Ultrarapid metabolizer

Increased risk for adverse drug reactions when prescribed standard dosage of tramadol
Reduce dosage of tramadol by 30%

Genetics is not the only factor influencing drug response!
The intake of other prescription drugs can alter the activity of enzymes and transporters whose function PGx tests aim to predict!
Example: Prescription of Tramadol

PGx result: **CYP2D6 Ultrarapid metabolizer**

PGx recommendation: **Reduce dose by 30%**

Also receiving Fluoxetine: a **strong CYP2D6 inhibitor**

→ Dosage??

Pharmacogenomic dosing guidelines consider only SINGLE gene-drug interactions!
How frequent are such problematic co-prescriptions?

**PGx drugs**
(= drugs for which dosing can be optimized based on PGx guidelines)

Drugs that **inhibit** or **induce** the activity of the respective enzymes or transporters
We screened Austrian claims data for concomitant prescriptions of 4,440 distinct interaction pairs.

55 PGx drugs across 7 genes
193 inhibitor / inducer drugs

GAP-DRG database operated by the Main Association of Austrian Social Security Institutions

1,587,829 Austrian insurance holders
393,476,104 prescriptions (years 2006 and 2007)
58.8% of our study population received at least one PGx drug

On average, every 4th patient who was treated with a PGx drug concomitantly received an inhibitor or inducer of the respective enzyme or transporter!

In half of the cases, co-prescriptions of moderate (47.3%) or strong (7.3%) inhibitors or inducers
How can gene-drug-drug interactions be addressed in PGx decision support?

Future perspective:

• Development and incorporation of more sophisticated dosing algorithms based on pharmacometric data

Interim solution:

• Use a minimum-set of high-relevance gene-drug-drug interaction to alert healthcare providers of potential interactions
Gene-drug-drug interactions are not uncommon.

Addressing them in PGx decision support helps to increase medication safety!

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