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Short communication

Pharmacogenetic Clinical Decision Support in Patients with Multi-Drug Regimens

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Introduction

We had reported our experience in a comprehensive medication management service for mental health with an algorithmic and heuristic Clinical Decision Support system (MEDtuning, Genomas Inc.) [1] based on the combinatorial genetic profile of CYP2D6, CYP2C19 and CYP2C9 [2]. This system provides a drug proscriptive warning if a patient's CYP450 phenotype (derived from the genotypes) is functionally abnormal for an isoenzyme constituting the primary or sole metabolic pathway for a given medication. The CDS tool has previously proven very useful for diagnosing pharmacogenetic vulnerabilities of psychiatric patients and supporting drug selections to minimize risk [3-5]. Multi-drug regimens (i.e., polypharmacy) have the greatest potential for bringing drug-related adverse events and harmful drug interactions in patients with cardiometabolic and neuropsychiatric co-morbidities.

Table 1: CDS results from 2,470 US patients of different ethno-geographic regions. The first 2 columns classify the cohort by number of different drugs prescribed and the number of patients receiving each amount. *The italicized columns indicate the prescription of high-risk drugs, and the number of patients receiving these for each of the drug regimens.* The last column provides the percentage of patients in each of the drug regimens receiving at least 1 high risk drug.

#Different Drugs Prescribed	Number Patients Given	*Number of Patients Given #Different Drugs with High CYP450 Risk*							%Patients at Risk w 1 or more Drugs
		0	*1*	*2*	*3*	*4*	*5*	*6*	
1	**378**	***314***	***64***						**16.9**
2	469	*360*	*91*	*18*					23.2
3	420	*288*	*102*	*26*	*4*				31.4
4	344	*241*	*70*	*27*	*5*	*1*			30.0
5	250	*153*	*55*	*34*	*8*				38.8
6	183	*106*	*41*	*21*	*13*	*2*			42.1
7	135	*75*	*27*	*20*	*8*	*4*	*1*		44.4
8	97	*56*	*18*	*15*	*6*	*2*			42.3
9 to 11	163	*95*	*30*	*17*	*10*	*8*	*2*	*1*	41.7
12 to 15	31	*16*	*2*	*6*	*2*	*3*	*1*	*1*	48.3
Grand Totals	2470	*1704*	*500*	*184*	*56*	*20*	*4*	*2*	31.0%

[Table 1] Illustrates the application of the pharmacogenetic CDS to 2,470 patients of diverse ethno-geographic backgrounds (including Hispanics) referred to the clinical laboratory. Nearly half of the patients (49%) was prescribed 4 or more drugs. The number of patients given high-risk drugs identified by the CDS system steadily increased as the number of prescribed medications rose. The percentage ranged from 17% of patients being given a high-risk drug when only one medication was prescribed up to 48.3% of patients being given high risk drug(s) when given 12-15 medications. Altogether, 31% of patients in the cohort had been prescribed at least 1 high risk medication.

In the future, it should be possible for the pharmacist to apply the genotype data to selected CDS models from various sources and achieve a consensus based on clinical judgment. This proscriptive global model could complement specific clinical guidance's available for selected drug-gene pairs from learned bodies [6-9]. These models can enable comprehensive medication management, as no single pharmacogenetic guidance model is likely to encompass the multiple drug regimens overseen by the pharmacy profession.

Acknowledgement

Patients signed an informed consent agreeing to DNA testing and use of deidentified information for validation, research, and accreditation purposes. This project was supported by Genomas internal research funds.

Conflict of interest

GR was Medical Director of Genomas when patients were referred.

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