Prevalence of Genetic Variations in CYP2C19 and Their Proposed Role in Pharmacotherapy

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BACKGROUND

Pharmacogenomics studies how an individual's genes affect the way their body responds to a drug, and pharmacogenomic testing may improve the efficacy and safety of medications to lead to better outcomes for patients. CYP2C19 is and enzyme that is responsible for the metabolism of many medications such as certain antidepressants, proton pump inhibitors (PPIs), antiepileptics, and antithrombotics. Genetic variability has been shown in the activity of CYP2C19 among different individuals.

CPIC provides guidelines for pharmacotherapy based on genetic variation in metabolic enzymes. The level of evidence is strongest for antithrombotics and moderate to low for antidepressants and proton pump inhibitors. Research is ongoing and guidelines are updated frequently. Evidence for gene prevalence within the United States is limited.

In this study, we aim to determine if prospective genotyping may be warranted and feasible in a local clinic setting with patients taking medications metabolized by CYP2C19 by comparing genetic variations in the CYP2C19 metabolic enzyme and identifying potential medication targets.

METHODS

•DNA samples were obtained via noninvasive cheek swab at a local outpatient care clinic.

•All samples were de-identified and all patients gave written consent.

•DNA was isolated from cheek swabs using a QIAGEN kit.

•Genotyping Procedure:

- Real-time PCR was performed using the BIORAD CFX96 Real-Time System, and results were quantified using detection of fluorescence.
- This process was done a total of 3 times, once for each allele studied (*2, *3, and *17)
- Those who did not have an allele detected were assumed to have *1, the wild-type allele.

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RESULTS

Study Participant Allele Frequency

2C19 Allele	Frequency (N=180)
*1	110 (61.1%)
*2	26 (14.4%)
*3	0 (0%)
*17	44 (24.4%)

Study Participant Genotypes

2C19 Genotypes	Frequency (N=90)
*1/*1	36 (40.0%)
*1/*2	13 (14.4%)
*1/*17	25 (27.8%)
*2/*2	4 (4.4%)
*2/*17	5 (5.6%)
*17/*17	7 (7.8%)

Study Participant Phenotypes

Metabolism Type	# of patients
Normal (*1/*1)	36 (40.0%)
Poor (*2/*2)	4 (4.4%)
Intermediate (*1/*2 or *2/*17)	18 (20.0%)
Rapid (*1/*17)	25 (27.8%)
Ultrarapid (*17/*17)	7 (7.8%)

CPIC Allele Frequency Vs Study Frequency[1-4]

	CPIC Frequency	Study Frequency
*1	55-79%	61.1%
*2	12-18%	14.4%
*3	0-0.3%	0%
*17	9-21%	24.4%

CONCLUSIONS[1-4]

•For clopidogrel, an antithrombotic, patients who are poor and intermediate metabolizers (24.4% of our participants) are recommended to receive alternative antiplatelet therapy due to decreased platelet inhibition and greater risk of clotting. These patients would likely see the greatest benefit from therapy adjustments.

•Patients taking proton pump inhibitors and who are ultrarapid metabolizers (7.8% of participants) may see a benefit from therapy adjustments. For these patients, a 100% increase in the starting daily dose is recommended due to increased risk of therapeutic failure on a normal starting dose.

•Patients who are ultrarapid (7.8% of participants) and poor (4.4% of participants) may see a benefit from therapy adjustments when taking tricyclic antidepressants and selective serotonin reuptake inhibitors. Ultrarapid and poor metabolizers should avoid use of TCAs and SSRIs due to the potential for suboptimal response to treatment.

•A major limitation of this research project is the number of participants. With only 90 individuals sampled, it is difficult to show a true representation of the local population.

•These preliminary findings should not be used to influence treatment in these patients at this point. Continued research needs to be done to show efficacy and reliability of changing patient therapy based on genotype.

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