Characterizing Pharmacogenomic Drug Response: A Pilot Study

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Introduction

• Pharmacogenomic testing is a growing topic of interest especially in ambulatory pharmacy practice which may allow pharmacists to make more precise and safer medication recommendations for patients.

• Pharmacogenomic testing will allow the profession to offer more individualized medication therapy for our patients.

• Cytochrome P450 enzymes are essential for the metabolism of many medications. Although this class has more than 50 enzymes, six of them metabolize 90% of drugs, with two most significant enzymes being CYP3A4, and CYP2D6[2]

• Each medication may take a different pathway in metabolism such as degradation or prodrug models and this may affect whether or not a medication is helpful, harmful, or ineffective for a specific patient

Objectives

• Determine the feasibility of performing genetic testing for medication therapy based on genetic markers, specifically CYP2D6

• Determine patients that are rapid, normal, or poor metabolizers in reference to CYP2D6

Methods

Collection

• Determine qualifying patients (>18 years old, on > 2 prescription medication, patient under one of our contracting physicians) and obtain consent from patients

• Perform buccal swab and de-identify using numbers and letters

Isolation

• Remove the DNA from the buccal swabs using PBS and protease solutions from QIAGEN followed by heat shocking to elute DNA and clear contaminants

RT-PCR

• Plating of samples included using MAD mix with the specific allele primer, followed by the pipetting of each sample into an individual well of the plate. 1 plate was completed for each specific allele

• There were 90 patients whose DNA was run in the PCR machine. 6 non-template control wells were used to ensure that the mix being added to the DNA was pure.

• Completed plates were then run through the BIO-RAD CFX96-Real time system (RT-PCR machine) to amplify DNA for each patient for each specific allele.

Results
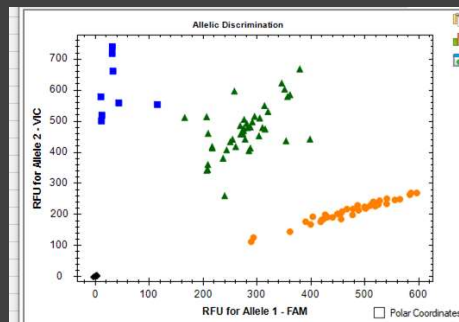
2D6 Allele Variant	Variant Count (N=196)	Variant Frequency
*1	63	0.35
*2	59	0.3278
*3	3	0.0167
*4	31	0.167
*9	6	0.0333
*17	3	0.0167
*33	1	0.0056
*35	14	0.0778
*41	16	0.0889

• The picture is the result of CYP2D6*2 from the RT-PCR

• The table shows the different allele variants and the frequencies among different alleles

• The graph shows the different genotypes of the patients along with their classification
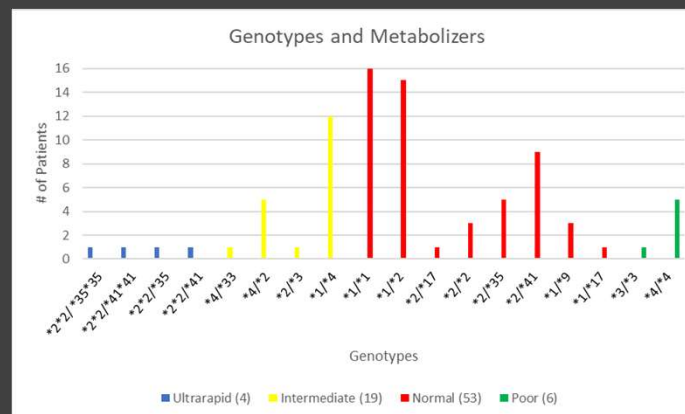
Discussion

• Study weaknesses included: low sample size, multiple researchers isolating samples (increased human error), genotyping costs a great deal of time and money

• Study Strengths: multi-tiered student learning approach, most common alleles were tested for, as well as a few that were unique

• The current processes used are still being optimized and these results are preliminary

Conclusions

• Majority of patients were normal metabolizers, followed by intermediate, poor, then ultrarapid metabolizers as seen in the charts

• In the future, chart review can occur for the patients to determine if they are taking medications that are conducive to their genome.

• Implementation of pharmacogenomic testing such as this into an ambulatory care clinic can help pharmacists and physicians deliver individualized care to patients.

References

1. What is genetic testing?: MedlinePlus Genetics [Internet]. MedlinePlus. U.S. National Library of Medicine; 2020 [cited 2021Mar9]. Available from: https://medlineplus.gov/genetics/understanding/testing/genetictesting/#:~:text=Genetic%20testing%20is%20a%20type,passing%20on%20a%20genetic%20disorder.

2. Lynch T, Neff AP. The Effect of Cytochrome P450 Metabolism on Drug Response, Interactions, and Adverse Effects [Internet]. American Family Physician. 2007 [cited 2021Mar9]. Available from: https://www.aafp.org/afp/2007/0801/p391.html

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