A Multidisciplinary Pharmacogenomic Treatment Approach to Reduce Medication Burden and Improve Subject Outcomes in a Rural Developmental Center

Krista N Bohlen,1,2, Bridgeit Bradley,1,2, Eric Kutscher,1,2,4, Erik Ehlı,1,2, Yueshan Hu1,3,4, Timothy Soundy2,4, Gareth E Davies1,2,3,4,5

1Avera Research Institute, Sioux Falls, SD, United States; 2Avera Institute for Human Genetics, Sioux Falls, SD, United States; 3Avera Behavioral Health Center, Sioux Falls, SD, United States; 4University of South Dakota Department of Psychiatry, Sioux Falls, SD, United States; 5South Dakota State University, Brookings, SD, United States; 6Pacific University, Hillsboro, OR, United States

Abstract

Saliva and blood samples were collected from 56 residents at a rural developmental center in South Dakota. The residential intermediate care facility treats about 180 patients ranging in age from 12-77 years old with various disabilities. The residents are mostly Caucasian with a small Native American subset.

The samples were genotyped using the Affymetrix Human Metabolism Enzyme and Transporter (DMET) array. In addition, variable number tandem repeat (VNTR) in various psychiatric candidate genes were also genotyped to assess subject pharmacogenomics (Avera Health IRB 2009-050). Residents of this center suffer from psychiatric disorders, mental retardation, and other debilitating syndromes. The aim of this project is to improve patient outcomes through treatment regimens based on pharmacogenomic analysis.

A multidisciplinary team consisting of a psychiatrist, a medical geneticist, and genetics lab scientists collaborated on this project to provide a database for analysis of DMET SNPs. The pharmacists and psychologist evaluated the current medication regimens, patient results from DMET IV axes, AIMS scores, drug interactions, behavior data, vital signs, and laboratory values for clinical recommendations guided by pharmacogenomic results.

The recommendations were given to the center's interdisciplinary treatment team. The team consists of a psychiatrist, medical residents, physician assistants, a pharmacist, social workers, counselors, and nurses. The Physician Assistants handle the chronic medical issues and day-to-day issues. The treatment team assesses each patient periodically, and for enrolled patients made the final decision for degree of implementation. The medical chart and other data will be reviewed for outcomes with level of incorporation and impact.

Methods

Study Design: non-randomized, retrospective and prospective comparison, proof-of-concept study

48 subjects continue to be in the study. Abstinence resulted when subjects did not pass QC and subjects who previously had not given saliva sample. The variance in results is presented elsewhere.

Ambiguous Results: the medical geneticist and lab staff designed primers for PCR analysis to clarify some of the ambiguous alleles by the DMET array and were able to make clinical recommendations.

Blood: subsequently obtained from subjects who did not pass QC and subjects who previously had not given saliva sample. Awaiting results for 3 subjects for all VNTR results


Recommendations: The first recommendations went to the center February 25, 2011 with intended completion by Dec 31, 2011. Twice a month the treatment team meets and reviews the 2-3 recommendations sent to the center each month. Recommendations were made based off of review of primary literature, book references, and medication interaction review with consideration for pharmacogenomic implications.

Results

<table>
<thead>
<tr>
<th>Gene</th>
<th>Genotype</th>
<th>Possible Clinical Implications</th>
<th>Pharmacogenomic</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2C9</td>
<td>*1/*1</td>
<td>Poor metabolizer</td>
<td>5</td>
<td>1, 2, 3, 4, 7</td>
</tr>
<tr>
<td></td>
<td>*1/*2</td>
<td>Intermediate metabolizer</td>
<td>5</td>
<td>1, 2, 3, 4, 7</td>
</tr>
<tr>
<td></td>
<td>*2/*2</td>
<td>Extensive metabolizer</td>
<td>5</td>
<td>1, 2, 3, 4, 7</td>
</tr>
<tr>
<td></td>
<td>*3/*3</td>
<td>Ultrarapid metabolizer</td>
<td>5</td>
<td>1, 2, 3, 4, 7</td>
</tr>
<tr>
<td>COMT</td>
<td>*1/*1</td>
<td>Alternate</td>
<td>5</td>
<td>1, 2, 3, 4, 7</td>
</tr>
<tr>
<td></td>
<td>*1/*2</td>
<td>Ambiguous</td>
<td>5</td>
<td>1, 2, 3, 4, 7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CYP450 Enzyme</th>
<th>Poor Metabolizer</th>
<th>Intermediate Metabolizer</th>
<th>Extensive Metabolizer</th>
<th>Ultra Rapid Metabolizer</th>
<th>Ambiguous or Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP 2C9</td>
<td>29</td>
<td>12</td>
<td>29</td>
<td>12</td>
<td>29</td>
</tr>
<tr>
<td>CYP 2C19</td>
<td>1</td>
<td>12</td>
<td>20</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>CYP 3A4</td>
<td>4</td>
<td>23</td>
<td>48</td>
<td>1</td>
<td>48</td>
</tr>
</tbody>
</table>

Discussion

Unfortunately, medication interaction software does not incorporate pharmacogenomics despite the extensive publications on their application. Clinical pharmacogenomics is required to evaluate the current patient population’s drug interactions, and the pharmacists should make the best informed decisions possible to alleviate potential complications.

The feasibility of providing extensive reports is a challenge in the physical setting of a rural developmental center. The pharmacists work 2.5 hours per month on data collection, DMET interpretation, medication interaction review and report formulation. Barriers to completion of the report include a paper medical chart, time, ambiguous DMET results, and the complexity and variability of results for each subject.

Most often pharmacogenomics, drug interactions, and drug monitoring parameters were included in the reports. At this time, we can predict the hospitalizations or adverse events prevented, however hope to see subjective improvement in 6 months.

Alongside the barriers to producing recommendations, there are barriers to implementing, especially with difficult and complex patients. The treatment team discusses the report on each subject and uses the past's historical and current notes to describe which recommendations will be implemented. Ongoing the recommendations made so far we expect to see improvement. We anticipate our outcomes will confirm the aim to alleviate medication burden, interactions, duplications, symptoms, and adverse effects. Genetic information integrated into medication therapy may also make a large impact in the gains towards personalized medicine with a software solution linked from an electronic health record (EHR). This approach to care would be feasible if a clinician would only need to review and finalize the report.

Objectives

1. Consider the pharmacogenomic implications on enzyme function and the impact on subjects’ medications.
2. Understand how a multidisciplinary team using genetic data can improve subject medication regimens and outcomes.
3. Recognize the CYP 450 enzymes that can be analyzed with the DMET array which are clinically useful for psychiatric patients and produce known calls.

Outcomes

The outcomes analysis will be complete by June 2012.

References

3. Pharmacogenomics Knowledge Database. www.pharmgkb.org