An Interactive Pharmacogenetics Lesson Using PharmGKB To Individualize Pharmacotherapy Recommendations

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Abstract
PharmGKB is a user-friendly, online pharmacogenomics database that simulates clinical guidelines for prescribing drug therapy based on patient genotypes. The majority of guidelines in PharmGKB are based on the interindividual variability in cytochrome P450 (CYP) enzyme responsible for metabolizing drugs. By individualizing patient therapy according to CYP genotypes, there is potential to improve pharmacotherapy outcomes and minimize the risk of adverse events. Although there is growing interest amongst educators and students to integrate pharmacogenetics into their curricula, it is challenging to provide non-pharmacogenetics students with guidelines to help them understand how to utilize such resources. The purpose of this study was to assess and disseminate an interactive, team-based interactive lesson on pharmacogenetics-based drug dosing principles that uses PharmGKB. Seventy-one high school students participated in a two-hour, Zoom session as part of a broader, interactive curriculum designed to teach pharmacogenetics. A total of 71 students were divided into pharmacogenetics-focused groups for two didactic sessions. Case questions focused on both in silico (PharmGKB) and in vivo (cytochrome P450) scenarios. Exemplars included the use of codeine for analgesia (CYP2D6) and digoxin for atrial fibrillation (CYP3A4). Assessment of student understanding was measured by percent gain in correct answers between pre- and post-test polling questions. The first question focused on pharmacology concepts while the last two focused on genotoxic concepts. Students were asked to use PharmGKB to annotate a case question having marked these concepts earlier in the program. For the additional two questions, there was a positive gain (100%) demonstrating an increase in knowledge during the lesson. Seventy-eight percent of students would be extremely likely or very likely to recommend this activity. We propose that an interactive, group-based activity can be used to teach basic principles of pharmacogenetics and empower students and educators to effectively use online drug resources.

Learning Objectives
- Students will be able to:
  - Explain the pharmacogenomics and pharmacodynamics of a drug.
  - Discuss the importance of understanding clinical pharmacogenetics concepts.
  - Derive possible CYP genotype combinations of offspring when provided parental genotypes.
  - Describe how different CYP phenotypes impact clinical responses to drugs (both effectiveness and toxicity).
  - Utilize the PharmGKB website as a source of a genotypic and phenotypic database.
  - Work collaboratively to optimize drug therapy for a hypothetical patient based on genotypic data.

Lesson Overview
- Primer on Genetics, Pharmacokinetics, and Pharmacodynamics in a Virtual Summer Program for High School Students (n=71)
- Overview of the PharmGKB Website
- Team-based Case Studies using PharmGKB in Breakout Rooms
- Students are Brought Back Together For Case Presentations

Main Takeaway
An interactive, team-based activity can be used to teach pharmacogenetic principles and connect students and educators to online drug dosing resources.

Clinical Cases for Student Groups

<table>
<thead>
<tr>
<th>Case</th>
<th>Clinical Indication</th>
<th>Drug</th>
<th>Pharmacogene</th>
<th>Role of CYP in Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Depression</td>
<td>Chlorpromazine</td>
<td>CYP2C19</td>
<td>Clearance/Excretion</td>
</tr>
<tr>
<td>2</td>
<td>Anaglogia</td>
<td>Citalopram</td>
<td>CYP2D6</td>
<td>Bioactivation</td>
</tr>
<tr>
<td>3</td>
<td>Transplantation</td>
<td>Tacrolimus</td>
<td>CYP3A4</td>
<td>Clearance/Excretion</td>
</tr>
<tr>
<td>4</td>
<td>Anticoagulation</td>
<td>Warfarin</td>
<td>CYP2C9</td>
<td>Bioactivation</td>
</tr>
<tr>
<td>5</td>
<td>Visceral Infarction</td>
<td>Iloprost</td>
<td>CYP2D6</td>
<td>Clearance/Excretion</td>
</tr>
<tr>
<td>6</td>
<td>Cancer</td>
<td>Tamoxifen</td>
<td>CYP2D6</td>
<td>Bioactivation</td>
</tr>
<tr>
<td>7</td>
<td>Fungal Infection</td>
<td>Voriconazole</td>
<td>CYP2C19</td>
<td>Clearance/Excretion</td>
</tr>
<tr>
<td>8</td>
<td>ADHD</td>
<td>Atomoxetine</td>
<td>CYP2D6</td>
<td>Bioactivation</td>
</tr>
</tbody>
</table>

The table lists the relevant pharmacokinetic information associated with the pharmacogenes for each patient case. For some drugs, the CYP-mediated metabolism impacts clearance or removal of the drug from the body thereby decreasing its activity. In other cases, the CYP enzyme is needed to bioactivate or convert the drug to an active form. Notably for atomoxetine, both the parent drug and its metabolite are active in the body.

Assessment of Participant Knowledge

How likely would you recommend this session to your colleague?

1. Extremely Likely
2. Very Likely
3. Somewhat Likely
4. Not Very Likely

Assessment of Lesson

Use one word to describe what you learned today

1. Collectively
2. Interpersonal
3. Collaborative
4. Individual

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