An Interactive Pharmacogenetics Lesson Using PharmGKB To Individualize Pharmacotherapy Recommendations

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Abstract

PharmGKB is a user-friendly online pharmacogenomics database that annotates clinical guidelines for optimizing drug therapy based on patient genotypes. The majority of guidelines in PharmGKB are based on the interindividual variability in cytochrome P450 (CYP) enzymes 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 pharmacogenetic content into health science curricula, there is a lack of educational resources that teach students how to utilize resources such as PharmGKB to inform clinical decision making. The purpose of this study was to assess and disseminate a case-based interactive lesson on pharmacogenetic-based drug dosing principles that uses PharmGKB. Seventy-one high school students participated in a two-hour Zoom session as part of a four-day Toxicology, Health, and Environmental Disease Program. The lesson was divided into a didactic lecture on pharmacogenetics followed by a group-based analysis of hypothetical case scenarios. Case questions focused on genetic variation in *CYP* enzymes in the context of different clinical scenarios. Examples included the use of codeine for analgesia (CYP2D6) and clopidogrel for stroke prevention (CYP2C19). Assessment of student understanding was measured by percent gain in correct answers between pre- and post-lesson polling questions. The first question focused on pharmacology concepts while the last two focused on genetics concepts. Students had high pre-test scores on the pharmacology question having learned these concepts earlier in the program. For the additional two questions, there was a positive gain (42%) 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 pharmacokinetics and pharmacodynamics of a drug.
- Demonstrate their understanding of basic pharmacogenetic 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 data.
- Work collaboratively to optimize drug therapy for a hypothetical patient based on genetics.

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

Case	Clinical Indication	Drug	Pharmacogene	Role of CYP in Drug Therapy[1]
1	Depression	Citalopram	CYP2C19	Clearance/Excretion
2	Analgesia	Codeine	CYP2D6	Bioactivation
3	Transplantation	Tacrolimus	CYP3A5	Clearance/Excretion
4	Anticoagulation	Clopidogrel	CYP2C19	Bioactivation
5	Viral Infection	Efavirenz	CYP2B6	Clearance/Excretion
6	Cancer	Tamoxifen	CYP2D6	Bioactivation
7	Fungal Infection	Voriconazole	CYP2C19	Clearance/Excretion
8	ADHD	Atomoxetine	CYP2D6	Bioactivation

The table lists the relevant pharmacokinetic information associated with the pharmacogene for each patient case. [1]For some drugs, the CYP-mediated metabolism causes 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.

PART 1

Review Patient Clinical Case and Pharmacodynamics/ Pharmacokinetics

Activity: Identify the mechanism of action (pharmacodynamics) and *CYP* pharmacogene (pharmacokinetics) for prescribed drug in the clinical case.

PART 2

Consider Parents' Diplotypes for *CYP* Pharmacogene

Activity: Determine the 4 possible genotype combinations after inheriting one allele from each parent and characterize the corresponding phenotype (poor, intermediate, extensive, or ultrarapid metabolizer).

PART 3

Learn Patient's Diplotype and Develop Therapeutic Recommendations

Activity: Use the tools within PharmGKB, including CPIC guidelines, to evaluate the phenotype associated with the patient's genotype and recommend a course of therapy.

Assessment of Participant Knowledge

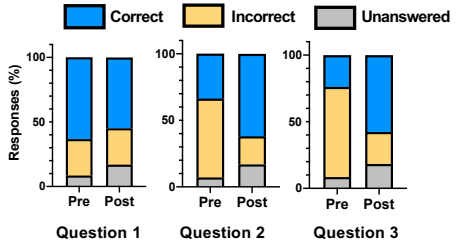

Figure 1. Pre- and Post-Assessment of Participant Knowledge. Students were asked three polling questions at the start and the end of the didactic and interactive sessions. Students had approximately 1 minute to answer each question. N=71 participants.

Assessment of Lesson

How likely would you recommend this session to your colleague?

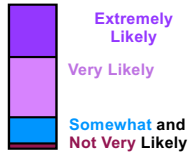

Figure 2. Post-Assessment of Activity. Students were asked the likelihood they would recommend this activity to their colleagues (scale: extremely likely, very likely, somewhat likely, not very likely, not at all). N=55 respondents.

Use one word to describe what you learned today

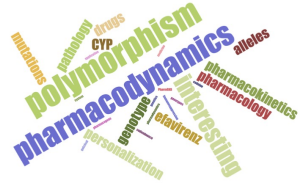

Figure 3. Collective Student Learning. Students were asked to use one word to describe what they had learned after the lesson. Answers were inputted into a word cloud generator from www.jasondavies.com. The text is a visual representation of the frequency of the words used by the participants. The more frequently a word is used, the larger the size of the text.

Acknowledgments

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