Pharmacogenomics In Practice: Case Studies

David Bankes, PharmD
Background

- **Pharmacogenomics**: study of how individual variations in genome affect disposition and response to drugs
- Ability to metabolize most medications is based on type of metabolic protein enzymes inherited from mom & dad
- Cytochrome (CYP) P450 Enzyme System
  - Activate pro-drugs
  - Prepare drugs to be excreted
- Evidence based vs. individual based medicine
Case 1:
Pain Control

CYP 2D6
Case 1: CYP2D6

- 61 year old female
- PMH:
  - Severe MDD, GAD, borderline/ dissociative personality disorder
  - Obese, diabetes type II, hypertension, dyslipidemia
  - Chronic pain from OA
    - Percocet 7.5/325 QID (scheduled, in MAC)
  - CrCl 80mL/min
CASE 1

- Patient is complaining of breakthrough pain
- Scheduled QID Percocet isn’t holding the pain from dose to dose
  - “Never really did much”
  - Reports 10/10 pain
- Decision made to start OxyCONTIN 10mg q12h in addition to QID Percocet in MAC-Pack
  - After 10 days of therapy, no significant relief
Relevant PGx Results

• PGx tested upon admission to PACE
• Gene: CYP2D6
• Genotype: *2/*4
• Phenotype: “Intermediate metabolizer”
Opioid Metabolism

- Prodrug
  - Codiene
  - Oxycodone
  - Hydrocodone
  - Tramadol

- CYP 2D6

- Active Drug
  - Morphine
  - Oxymorphone
  - Hydromorphone
  - O-desmethyltramadol

Janicki PK. Comprehensive treatment of chronic pain. 2013
CASE 1

• OxyCONTIN d/c’ed at end of July
• Fentanyl (Duragesic) patches prescribed
• Patient reports no need for breakthrough dosing
  – No breakthrough dose dispensed in 1.5 months since conversion to fentanyl
  – Patient has been reporting 3/10 pain
Case 2

CYP 2D6: Behavioral And Psychiatric Symptoms in Dementia
Case 2
CYP2D6

- 87-year old male with a PMH of early onset Alzheimer’s dementia
- Over a 4 week period, he was becoming increasingly delirious, agitated
  - Wandering
  - Auditory hallucinations/ paranoia
- No significant psychiatric history other than depression
PGx Results

• Tested January 2015
• CYP2D6 *2/*7 → “Intermediate”
• PharmD consult March 10th 2015
  – At date profiled, no profiled medications affected by genetic make-up
  – Provided list of potential target medications
Case 2
CYP2D6

- March 26\textsuperscript{th}: Patient started on:
  Risperdal 0.25mg BID x 1 month

- March 30\textsuperscript{th}: Risperdal discontinued
  – Profound dizziness, sedation, and hypotension
Antipsychotic Comparison

<table>
<thead>
<tr>
<th></th>
<th>Risperdal</th>
<th>Abilify</th>
<th>Seroquel</th>
<th>Zyprexa</th>
<th>Haldol</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2</td>
<td>++++</td>
<td>++++</td>
<td>+</td>
<td>++</td>
<td>+++++</td>
</tr>
<tr>
<td>M1</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>++++</td>
<td>-</td>
</tr>
<tr>
<td>α-1</td>
<td>++++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>5HT-2c</td>
<td>++++</td>
<td>++</td>
<td>-</td>
<td>++++</td>
<td>-</td>
</tr>
<tr>
<td>H-1</td>
<td>++</td>
<td>++</td>
<td>++++</td>
<td>++++</td>
<td>-</td>
</tr>
<tr>
<td>Renal</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>CYP 2D6</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>CYP 3A4</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

http://primarypsychiatry.com/antipsychotics-pharmacology-and-clinical-decision-making/
Lexi-comp for each drug listed
CASE 2
CYP 2D6

• Abilify prescribed next
  – 2mg QD → 10mg QD → 15 mg QD
  – D/c due to “ineffectiveness” about 2 months later
    • Multiple injections of haldol given from E-box

• Then...Haldol therapy initiated
  – 1mg QHS
  – PRN order for 1mg IM q8h
Thank you!!

Any questions?