Opioid-Related Genetic Polymorphisms of Cytochrome P450 Enzyme After Total Joint Arthroplasty: A Focus on Drug-Dose Gene Interactions with Commonly Co-Prescribed Medications

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Introduction

Genetic polymorphisms in the CYP 450 enzyme system correlate to immense variability observed in opioid analgesic metabolism and its consequent sequelae. However, the impact of CYP polymorphisms on opioid metabolism following TJA, both in terms of drug efficacy and associated side effects, has yet to be delineated. This article focuses on three categories of CYP metabolizers (EM: extensive metabolizers, PM: poor metabolizers, and NM: non-metabolizers), in terms of drug efficacy and adverse reactions witnessed in the use of various pain analgesics and other commonly prescribed drugs [1]. This paper hopes to highlight the necessity of pharmacogenomic testing as a part of orthopedist’s pre- and postoperative pain management repertoire for TJA. Utilization of genetic testing may serve clinical utility in minimizing adverse drug reactions while maximizing response rates for hopes in improving postoperative patient satisfaction.

Although the theoretical link between drug interaction and genetic polymorphisms is tangible, evidence-based relevance is limited. However, some clinical cases have been reported and with increasing knowledge of pharmacogenomics it may soon be possible to identify subgroups of patients at greater risk of adverse reactions and poor response rates to certain medications. We hope that the orthopedic community can benefit from our analysis by understanding the genetic basis of pain response and the opioid interaction. We aim to provide the reader with a greater understanding of the etiological complexity associated with drug-interactions in order to develop evidence-based approach to prescribing opioids.

Methods

We conducted a search on DrugStats database for the 50 most common prescribed medications in the United States within the 1st quarter of 2020. This database is a standardized version of publicly available data provided by the U.S. Government [2]. This database is updated yearly and includes more than 3 billion outpatient prescription fills per year. In addition, we used PharmGKB database to perform a detailed search for the metabolic pathways and relevant genetic polymorphisms of both opioids and the other identified commonly prescribed drugs in TJA patients [3]. The relevant polymorphisms are highlighted in the subsequent sections below, as well as in Table II: Pharmacogenomic Interactions Between Top 50 Prescribed Drugs and Pain Medications.

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Table II: Pharmacogenomic Interactions Between Top 50 Prescribed Drugs and Pain Medications

<table>
<thead>
<tr>
<th>Gene</th>
<th>Variant</th>
<th>Drug</th>
<th>Genotype</th>
<th>Evidence</th>
<th>Type</th>
<th>Phenotype Effect</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2D6</td>
<td>*1/*1</td>
<td>Oxycodone</td>
<td>T/A</td>
<td>Toxicity/AD</td>
<td>Increased risk refractory cardiac arrest, renal impairment, respiratory insufficiency</td>
<td>(2)</td>
<td></td>
</tr>
<tr>
<td>CYP2D6</td>
<td>*1/*2</td>
<td>Oxycodone</td>
<td>T/A</td>
<td>Toxicity/AD</td>
<td>Increased risk refractory cardiac arrest, renal impairment, respiratory insufficiency</td>
<td>(2)</td>
<td></td>
</tr>
<tr>
<td>CYP2D6</td>
<td>*1/*3</td>
<td>Oxycodone</td>
<td>T/A</td>
<td>Toxicity/AD</td>
<td>Increased risk refractory cardiac arrest, renal impairment, respiratory insufficiency</td>
<td>(2)</td>
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</tr>
<tr>
<td>CYP2D6</td>
<td>*1/*4</td>
<td>Oxycodone</td>
<td>T/A</td>
<td>Toxicity/AD</td>
<td>Increased risk refractory cardiac arrest, renal impairment, respiratory insufficiency</td>
<td>(2)</td>
<td></td>
</tr>
<tr>
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<td>*1/*5</td>
<td>Oxycodone</td>
<td>T/A</td>
<td>Toxicity/AD</td>
<td>Increased risk refractory cardiac arrest, renal impairment, respiratory insufficiency</td>
<td>(2)</td>
<td></td>
</tr>
</tbody>
</table>

Results

The management of pain is challenging, as drug intervention is usually the first-line therapy for resolving pain. Personalizing analgesia during the perioperative period to maximize pain relief while minimizing adverse events can help in postoperative pain optimization. Genetic factors may be major influences on how patients respond to a specific treatment. Genetic factors such as modulatory proteins that are involved in pain perception, analgesic metabolism, and receptor signaling [4]. Focusing on genetic evaluation can help to long term investigate patients’ compatibility with specific medications.

Conclusion

The management of pain is challenging, as drug intervention is usually the first-line therapy for resolving pain. Personalizing analgesia during the perioperative period to maximize pain relief while minimizing adverse events can help in postoperative pain optimization. Genetic factors can be major influences on how patients respond to a specific treatment. Genetic factors such as modulatory proteins that are involved in pain perception, analgesic metabolism, and receptor signaling [4]. Focusing on genetic evaluation can help to long term investigate patients’ compatibility with specific medications.

References