Exposure to Potential CYP450 Pharmacokinetic Drug-Drug Interactions Among Osteoarthritis Patients: Incremental Risk of Multiple Prescriptions

Joseph V. Pergolizzi¹, Sumedha A. Labhsetwar², R. Amy Puenpatom³, Seongjung Joo³, Rami H. Ben-Joseph⁴, Kent H. Summers⁵

¹Johns Hopkins University School of Medicine, Baltimore, MD, United States, ²NEMA Research, Naples, FL, United States, ³Endo Pharmaceuticals, Chadds Ford, PA, United States

Purpose

Patients taking more than one drug metabolized through the cytochrome P450 (CYP450) enzyme system experience a drug-drug exposure (DDE) which puts them at risk for a potential pharmacokinetic drug-drug interaction (DDI), defined as two or more drugs interacting in such a way that the effectiveness and/or toxicity of one or all drugs are changed. Any patient subjected to a DDE is at risk for a potentially serious DDI, the epidemiology of which has not been thoroughly studied. Many drugs are metabolized primarily via the CYP450 enzyme system, including certain opioids used to manage moderate to severe chronic pain.

Method

We conducted a retrospective analysis of a large commercial claims database and a Medicare database to assess the prevalence of DDEs among patients with osteoarthritis taking CYP450-metabolized opioids.

Results

The overall prevalence of DDEs in this population was 26%, with females more likely to experience DDEs than males (28.4% vs. 21.0%, respectively). The number of unique concurrent prescriptions at baseline, sex, age, and Charlson Comorbidity Index (CCI) were statistically significant predictors of DDEs (p<0.05). This study challenged previous assumptions about DDEs in that advanced age was not positively associated with the risk of DDE and the number of concurrent medications at the time of DDE was not a risk factor, although a risk factor was the number of prescriptions the patient received in the 90-day window prior to index date. For patients taking at least two medications in the 90-day period prior to the index date, every additional prescription taken increased their risk for a DDE during the observation period by 138% (on average). The risk of DDE during the study period was three-fold greater for patients with one medication in the 90-day period before index date compared to similar patients with no prescriptions in that same period before the index date.

Conclusions

DDEs are more common than may be generally believed in patients with osteoarthritis, regardless of age, and can occur even in patients taking few medications. When selecting an opioid analgesic to treat osteoarthritis, physicians should consider the potential for exposure of these patients to drugs that could interact unfavorably.