

Prevalence of CYP450 drug-drug exposures among oxycodone CR patients

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Purpose

Patients taking at least one cytochrome P450 (CYP450)-metabolized opioid analgesic agent concurrent with another CYP450-metabolized medication experience a drug-drug exposure (DDE) with the potential to cause a pharmacokinetic drug-drug interaction (PK DDI). Oxycodone controlled-release (CR), a commonly prescribed, long-acting opioid, used in the management of moderate to severe chronic pain, is metabolized by the CYP450 system. The objective of this study was to evaluate the prevalence of CYP450 DDEs in patients using oxycodone CR in a commercially insured population. Since the oxycodone CR package insert indicates that it is metabolized by both CYP450 3A4 and CYP2D6, we compared the prevalence of DDE in both enzyme systems.

Method

This was a retrospective database study using claims data from the MarketScan Commercial Database (Thomson Reuters). Patients aged 18 to 65 years were identified between 7/1/2006 and 9/30/2009. Patients were included if they had filled a prescription of oxycodone CR for ≥ 30 days and had continuous insurance enrollment during the 6 months before and after the first 30-day supplied dispensed date. Subjects were excluded if they were pregnant or had health maintenance organization enrollment during the study period. DDE is defined as the dispensing of a prescription for oxycodone CR concurrently with another CYP450-metabolized medication with \geq one-day overlap in days supplied during the 30-day window immediately following the index date. DDE prevalence was reported by CYP2D6 alone and CYP2D6 plus CYP3A4.

Results

A total of 32,208 patients were included after applying all inclusion and exclusion criteria. Forty-seven percent of the sample was male, while females accounted for 53% with the overall mean age of 50 years old. Using the DDE definition associated with medications metabolized by CYP2D6 enzymes, the overall prevalence of DDEs for oxycodone CR was 29.4% (or 9476 patients). When CYP3A4 inhibitors and inducers were included as part of the DDE definition in addition to CYP2D6, the prevalence of DDEs increased to 37.6% (or 12,103 patients). Of these DDEs, 93.7% were 2D6 and 3A4 inhibitors, 3.7% were 3A4 inducers and 2.7% were others. Among patients taking oxycodone CR, the most common potentially interacting drugs included diazepam (19.4%), duloxetine (19.2%), venlafaxine (9.6%), bupropion (9.6%) and escitalopram (9.3%).

Conclusions

This study used a paid claims database to analyze DDEs in patients receiving prescriptions for oxycodone CR. Using a CYP450 2D6 definition alone, the overall prevalence of exposures was 29.4%. When including CYP450 3A4-metabolized medications, the prevalence of DDE was 37.6%. Physicians should consider the possibility of DDEs with the potential to cause PK DDIs when selecting an opioid analgesic to treat patients with chronic pain.