New Oxycodone Drug Interactions

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Oxycodone is a commonly used opioid analgesic, often used as a combination product with acetaminophen, aspirin, or ibuprofen. It was synthesized almost a century ago but only recently have some of its drug interactions been discovered. Attention to these new interactions will help patients maximize oxycodone efficacy and minimize adverse outcomes.

In patients starting oxycodone therapy, check the patient's drug regimen for CYP3A4 inhibitors or inducers.

What Are the New Oxycodone Interactions?

In a recent report, healthy subjects were given a single dose of oxycodone with and without concurrent administration of multiple doses of voriconazole. Voriconazole dramatically increased oxycodone plasma concentrations and also increased the pharmacodynamic effects of oxycodone.[1] Oxycodone area-under-the-curve values increased almost 4-fold; with multiple oxycodone doses, this would likely lead to adverse effects in at least some patients. Oxycodone is metabolized primarily by the cytochrome P450 (CYP450) enzyme CYP3A4. Voriconazole is a known CYP3A4 inhibitor, so it appears that voriconazole inhibits oxycodone metabolism.

Another recent report found—as one would expect—that increased CYP3A4 activity through enzyme induction has the opposite effect from voriconazole; it reduces oxycodone plasma concentrations. In a study of healthy subjects, multiple doses of the enzyme inducer rifampin dramatically reduced plasma concentrations of oxycodone.[2] The bioavailability of oxycodone was reduced by rifampin from 69% to 21%. This would very likely render oxycodone ineffective in many patients.

What Are the Implications of These New Findings?

Given that oxycodone appears to be highly susceptible to changes in CYP3A4 activity, it is likely to interact with any other drug that inhibits CYP3A4. CYP3A4 inhibitors include other antifungals, such as fluconazole, itraconazole, ketoconazole, and posaconazole; antibiotics, such as clarithromycin, erythromycin, quinupristin, and telithromycin; AIDS drugs, such as amprenavir, atazanavir, darunavir, delavirdine, indinavir, nelfinavir, ritonavir, and saquinavir; and miscellaneous CYP3A4 inhibitors, such as conivaptan, cyclosporine, diltiazem, grapefruit, imatinib, lapatinib, and verapamil. These drugs vary in their ability to inhibit CYP3A4, so depending on the drug, dose, and patient, they may produce a greater or lesser effect on oxycodone compared with voriconazole.

Drugs that increase CYP3A4 activity (enzyme inducers) are likely to reduce oxycodone plasma concentrations in a manner similar to rifampin. Rifampin is one of the most potent enzyme inducers, however, so in most cases, the interaction of enzyme inducers with oxycodone will be less than that observed with rifampin. Nonetheless, oxycodone effect is likely to be reduced by enzyme inducers, such as barbiturates, bosentan, carbamazepine, efavirenz, nevirapine, oxcarbazepine, phenytoin, primidone, rifabutin, rifapentine, and St. John's wort.

Recommendations

In patients starting oxycodone therapy, it would be prudent to check the patient's drug regimen for CYP3A4 inhibitors or inducers. If CYP3A4 inhibitors are found, the patient may be more sensitive to the effects of oxycodone and more likely to suffer side effects. If the prescription directions allow for discretion on the part of the patient, consider suggesting that the patient use conservative doses to start.

If the patient is receiving CYP3A4 inducers, he or she may not respond adequately to the oxycodone. If this becomes a problem, the patient may need to increase the oxycodone dose within the recommended doses on the prescription. Alternative opioid analgesics could be tried, but many of them are probably also affected by enzyme inducers. For example, alfentanil, fentanyl, and sufentanil are metabolized by CYP3A4; methadone and tramadol are partially metabolized by CYP3A4; morphine and codeine may not be affected by increased CYP3A4 activity, but their analgesic effect is probably reduced by enzyme inducers through other mechanisms. ■

▶ For a list of references, go to www.PharmacyTimes.com.