Pharmacist Responses to Potential Drug Interactions

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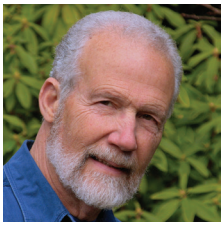
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WE ARE OFTEN ASKED HOW TO RESPOND to a potential drug-drug interaction (DDI) in a specific patient. Identifying a potential DDI is fairly easy, some would say too easy, but deciding how to proceed requires the consideration of multiple factors, both drug and patient specific. Although there is no single best way to accomplish this, the following are intended to provide a structured approach to selecting an appropriate response to a DDI.

OBJECT AND PRECIPITANT DRUG DOSAGE

The magnitude of change in the object drug for most potential drug interactions depends on the dose. Larger doses of precipitant drugs are more likely to produce clinically important changes in object drug plasma concentration.[1] For example, fluconazole is an inhibitor of CYP3A4, but doses below 200 mg daily have only modest effects on the metabolism of CYP3A4 substrates.[2,3] Patients receiving lower doses of fluconazole are unlikely to experience an adverse response to an interaction with a CYP3A4 substrate.

Potential interactions based on the precipitant drug adsorbing an object drug in the gastrointestinal track require that both drugs be simultaneously present in the gut. Quinolone or tetracycline adsorption by di- and trivalent cations (eg, aluminum, calcium, iron, and magnesium) reduce an antibiotic's plasma concentration and, perhaps, efficacy. Counsel patients taking this combination of drugs to separate the doses of the drugs. Administering the antibiotic 2 hours before or at least 6 hours after the cation will minimize the magnitude of the interaction.

Sometimes a DDI alert will occur when one of the drugs is being administered as needed. In these cases, interactions based on inhibition or induction of drug elimination are unlikely to be of clinical consequence. The occasional use of an antacid during a quinolone treatment is not likely to alter the antibiotic's efficacy.

ASSESSING THE RISK TO THE PATIENT

The assessment of potential DDIs is intended to prevent patients from suffering adverse events. An important consideration when assessing the risks to patients is the therapeutic range of the object drug. Interactions involving drugs with small differences in their efficacy and toxicity (eg, cochicine, digoxin, theophylline, and warfarin) present a greater risk to patients and should be given enhanced consideration. Similarly, DDIs that have the risk of serious adverse events need particular attention. Potential DDIs with these drugs often require consultation with a prescriber to manage the risk.

MODIFIERS OF PATIENT RESPONSE TO DDI

We have previously addressed common drug and patient factors that can modify the outcome of a potential DDI. These include drug dosage, concurrent diseases,[4,5] genetics,[6] complementary and alternative medicines,[7] and gender.[8] Depending on the interacting drug pair, one of these, or other factors, may either decrease or increase the risk of patient harm from the interaction. Discussing these modifiers helps to accurately assess the risk and plan an appropriate response.

PROVIDING A RECOMMENDATION

Once the above factors have been considered, the pharmacist can formulate a recommendation that will mitigate the risk presented by a potential DDI. For interactions with low risk of harm, this may simply be a brief conversation with the patient explaining the issue and providing instructions to avoid the potential DDI. When a DDI has the potential for a serious adverse event, consultation with the prescriber may be indicated.

Depending on the DDI, the pharmacist may recommend therapeutic alternatives that will not interact, dosage adjustment, and/or monitoring approaches. When physicians respond to DDIs, monitoring the patient is a common choice, in which case the pharmacist should be prepared to describe appropriate monitoring options, such as watching for the physical signs and symptoms associated with altered object drug concentrations or laboratory tests that could signal the onset of clinically important DDI-induced changes in patient response.

CONCLUSION

Pharmacists play an important role in identifying and managing DDIs. By considering drug and patient features, it is possible to better assess the potential risk of patient harm and offer appropriate management options. ◆