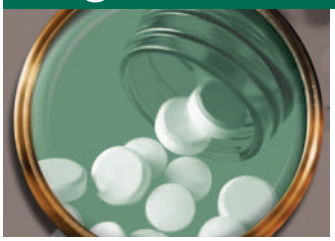

"Classy" Drug Interactions

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Drug interactions often are purported to occur across all members of a drug class. Drug classes are often based on the drug's primary pharmacologic activity. For example, all thiazide diuretics, macrolide antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and tricyclic antidepressants have been considered by some to have similar interaction potential within the class. This method of assigning drug interactions was adopted some years ago when the mechanisms responsible for most interactions were unknown and the number of drugs in a class was often limited to 2 or 3 agents. Because data were not available for all members of a class of drugs, the conservative approach was to assume that all members of the class would interact in a similar manner.

With increased knowledge about the mechanisms involved in drug interactions, the idea that all members of a similar pharmacologic class will interact in the same manner has become passé. Yet, one can still find examples of drugs listed as interacting based only on their membership in a certain class.

It is important to remember that drug interactions are divided into 2 fundamental types, based on the mechanism of the interaction, pharmacokinetic interactions, and pharmacodynamic interactions. Grouping pharmacokinetic drug interactions by pharmacologic class rarely results in an accurate classification. For example, all macrolide antibiotics often are listed as inhibitors of CYP3A4. Yet, this is only true for erythromycin, clarithromycin, and troleandomycin, not for azithromycin. Similarly, listing all of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, or statins, as interacting with CYP3A4 inhibitors is incorrect, but still occurs. The selective serotonin reuptake inhibitors represent another large group of pharmacologically related drugs that frequently are considered to demonstrate equivalent potential interactions despite much evidence to the contrary.

Some pharmacodynamic interactions do indeed affect all members of a class. Hyperkalemia due to coadministration of angiotensin-converting enzyme inhibitors and potassium-sparing diuretics may occur with the combination of any member of either drug class. Interactions due to simple additive pharmacodynamic effects, as may occur when 2 drugs with sedative or hypotensive effects are coadministered, serve as another example in which classification based on the drug's pharmacologic class often accurately predicts potential pharmacodynamic interactions. Of course, most practitioners do not need to be reminded that such pharmacodynamic interactions may occur. Furthermore, the selection of drugs with similar pharmacologic effects is the basis for the selection of most drugs used in combination.

Often small differences in the pharmacology of drugs in a class create subgroups of interacting and noninteracting agents. Examples of drug classes with subsets of drugs that have a different interaction potential from the other members of the class include cardioselective beta-blockers, calcium channel blockers that slow cardiac conduction or inhibit CYP3A4, and cyclooxygenase-2 NSAIDs.

The problems of incorrect assignment of potential interactions based on drug class include the listing of interactions that are unlikely to occur. These false-positive interaction listings are quite common in most computerized databases and cause users to become desensitized to potential interactions that offer real risk to the patient. Interaction alerts based on false-positive reports may lead to inappropriate changes in drug therapy or patient monitoring. Class grouping also may eliminate consideration of a useful alternative drug for one of the pair of truly interacting drugs.

Knowledge of noninteracting drugs with similar pharmacology is the key to selecting alternative drugs to substitute for one drug of an interacting pair. For example, the substitution of pravastatin, fluvastatin, or rosuvastatin for lovastatin or simvastatin in a patient prescribed ketoconazole would prevent possible excess accumulation of the statin. Alternatively, an antifungal agent without CYP3A4 inhibition (eg, terbinafine) could be considered for patients taking lovastatin or simvastatin. The selection of a noninteracting drug with similar efficacy is often the best approach to managing a potential drug interaction.

Until drug interaction listings are purged of inappropriate interaction pairs based only on the drug's pharmacologic class, pharmacists must rely on alternative sources to evaluate potential interactions. When a true interaction is identified, the pharmacist should try to identify an alternative drug for either the object or the precipitant drug. If it is necessary to contact the prescriber regarding a potential interaction, offering several noninteracting alternative drugs with similar therapeutic efficacy will assist the prescriber in selecting an appropriate management strategy. PT