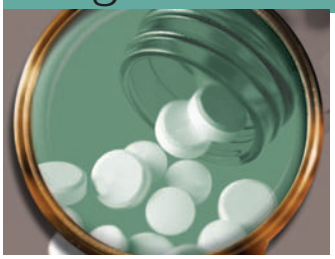

Drug Interaction Classification Systems

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Anyone who uses any compendium of drug–drug interactions—a book, a personal digital assistant (PDA), or a computer-based screening program—is familiar with the various schemes that have been devised to classify drug interactions. These classification systems were developed during a time when little was known about the mechanisms of drug interactions and even less was known about the potential to cause patient harm. As a result, a variety of parameters have been included in the schemes, such as the "quality" or quantity of the published data concerning the interaction. Because interactions generally could not be predicted, one had to wait for a report of an interaction to appear in the literature.

Today, most interactions can be predicted based on simple pharmacologic properties. The need for interaction documentation is reduced to defining the magnitude of the effect of the precipitant drug on the object drug. In addition, although some of the classification systems are based on very different criteria, most users assume that the systems are the same and are surprised that the use of different criteria result in different classifications of the same interaction. It is important that one read and understand the criteria employed to determine the interaction classifications in the compendium one uses.

There is an innate desire to simplify the whole issue. No one can possibly memorize all the potential drug interactions that have been identified to date, and new interacting drug pairs are identified every month. This fact has led to the common assumption that most drug classes have homogeneous interaction profiles, when such is actually quite a rare occurrence. "Just tell me the 10 most significant drug interactions" is a pleading we often hear. Unfortunately, we are never going to be able to list the 10 or even the 100 most significant drug interactions. The large interpatient variability in the magnitude of the effect makes predicting the clinical outcome of an interaction in any one patient nearly impossible.

It is common for drug interaction studies done in healthy individuals under controlled conditions to demonstrate a 5- to 7-fold difference in effect between participants. This variability would be expected to increase with the addition of different doses, routes of administration, formulations, sequences of drug administration, genetics, and other modifiers of drug elimination or response (eg, food, environment, disease).

Knowledge of the mechanisms of drug interactions has increased markedly in the past few years, yet almost nothing is known about their epidemiology. Thus, developing comprehensive, sophisticated, "expert" systems to classify drug interactions for which almost no data exist seems to be, at best, a futile effort. At worst, it may lead to errors of interpretation.

When a classification system is applied to a collection of drug interactions, users immediately make generalizations regarding the importance of the interactions. For example, some computerized screening systems are adjusted so that only interactions with the most severe rating are flagged for pharmacist review. There are, of course, no data to support such arbitrary delineation of interaction alerts, and there exists a real medicolegal risk if a patient is harmed by a "low-risk" interaction that was ignored. In other installations, pharmacists routinely override drug interaction alerts, knowing that most of the time the patient will not suffer an adverse outcome. The unpredictability of drug interaction outcomes hinders one's ability to generalize interaction severity classifications.

Pharmacists must learn to think about every drug interaction that has a potential to cause patient harm. How does one know which interactions will cause a particular patient harm? One simply cannot know. Until data are available on the risk of an adverse outcome from an interaction, one must err on the side of patient safety. Consideration of the therapeutic range of the object drug, dosages of the drugs, concurrent disease state(s), patient demographics, and many other variables is necessary to estimate the risk to the patient. No book, PDA, or computer-based classification system can replace the pharmacist's informed evaluation. An interaction that is likely to cause an adverse outcome in one patient may have no effect on a different patient.

Here are some tips for pharmacists:

- Learn to recognize the factors that alter a patient's risk for an adverse event when he or she is exposed to interacting drug pairs
- Consider the risk of the potential interaction against the benefit of administering the drugs
- If the risk to the patient appears to be greater than the expected benefit, identify a suitable alternative for one of the drugs

Drug interaction classification systems should be used for general guidance. One should find a classification system that uses appropriate criteria to guide one's response to a potentially interacting drug pair. One should understand the classification system's limitations and then regard each interaction–patient pair as unique. By evaluating the risk and benefit of a potential drug interaction to a patient, the pharmacist can decide on a suitable course of action. PT