

Avoiding Drug Interactions in Hospitalized Patients

While medications are the foundation of therapy for many illnesses, they can occasionally cause unintended injury. Adverse drug events (or ADEs) vary in predictability and severity, and though some are simply unavoidable, interactions between drugs are among the most preventable. A recent study conducted in Ontario found that avoidable drug interactions increased the risk for hospital admission for drug toxicity up to twenty fold.

Drug-drug interactions (DDIs)

A DDI occurs when one medication increases or decreases the effect of another. DDIs often involve prescription medications, but even over-the-counter (OTC) drugs and complementary and alternative medications (CAMs) can play a role.

Implications of DDIs

Awareness of DDIs is vital for two key reasons. Most important, they can result in serious harm or even death, as illustrated by the highly-publicized death in 1984 of Libby Zion, an 18-year-old woman who died in a Manhattan hospital within hours of receiving meperidine (Demerol®) in addition to the antidepressant phenelzine (Nardil®), a drug usually used to treat depression. Even minor DDIs can have serious consequences. For example, an older hospitalized patient taking certain allergy medications might experience excessive sedation when given a mild sedative, which could contribute to a fall from bed.

It is also important to emphasize that DDIs can often be predicted, and, in theory, avoided by using knowledge from published reports and general pharmacologic principles. For example, the discovery that patients could develop heart irregularities when taking terfenadine (Seldane®) with the antibiotic erythromycin prompted speculation that other medications that similarly influence the liver's processing ability might also cause heart problems when taken with terfenadine. Consequently, terfenadine and related medications were removed from widespread use.

How often do DDIs cause harm?

This question cannot be fully answered, because it is very difficult to study the consequences of DDIs in the ambulatory setting. However, up to half of patients presenting in hospital emergency departments have been found to have potential DDIs, and in up to 1.5% of adverse drug events among hospitalized patients DDIs are implicated.

Reducing the likelihood of a DDI

Many of the strategies used to minimize DDIs in outpatients also apply to inpatients (see Table 1), and some call for particular emphasis. For example, avoidance of DDIs in hospitalized patients is theoretically easier, because clinicians

Table 1. Eight strategies to minimize drug-drug interactions in hospitalized patients

1. Encourage meticulous documentation of pre-admission medication use, including nonprescription and complementary medications. This may necessitate patients, or their families, bringing up-to-date medication lists and/or bottles to hospital.
2. Maintain regularly updated DDI detection software on pharmacy computer systems.
3. Discourage patient use of medications not dispensed by the hospital pharmacy, as in-hospital computerized DDI checking would not search for and detect potential adverse interactions involving these drugs.
4. Encourage physicians and pharmacists to use palmtop drug references and bookmark other online DDI resources on ward computers (Table 2).
5. Pharmacies should have at least two current editions of various drug interaction compendia (Table 2) and periodicals such as the *Medical Letter*.
6. When feasible, promote the participation of pharmacists on ward-based rounds.
7. In the physicians' writing area, post a DDI reference poster (available from most pharmacies) or, at minimum, a short-list of high-alert drugs especially prone to clinically important DDIs (Table 3).
8. At the time of discharge, encourage patients to fill prescriptions at one pharmacy only.

have greater control over medication use and dosing, which is generally tracked electronically by the pharmacy. On the other hand, well-intentioned patients or their families sometimes bring additional medications to the hospital, especially those that are not listed on the hospital's formulary. To reduce this dangerous practice, patients should be encouraged to disclose all of their medications to the nurses and physicians caring for them.

Another important matter is that no clinician can memorize the tens of thousands of reported DDIs and the potential consequences of each, so reliance on information technology is essential. Pharmacy software, while not able to detect all DDIs, certainly helps avert many, and it is critical that it be updated several times each year. In addition, physicians, pharmacists and nurses should have access to multiple electronic and print reference resources (Table 2), a modest investment in light of the potential costs of even one serious DDI.

The bottom line is that DDIs are often preventable. Hospitals can assist physicians and pharmacists in their efforts to minimize DDIs using simple and relatively inexpensive strategies. Prevention of even one serious DDI may recoup the cost of these measures several times over and, ultimately, go a long way to enhance patient safety.

Table 2. Resources for prevention of DDIs

RESOURCE	EXAMPLES	ENQUIRIES/CONTACTS
Handheld (PDA)	ePocrates Rx	www.epocrates.com (800-227-1700)
	Mosby's Drug Consult	www.mosbysdrugconsult.com (800-545-2522)
	LexiDrugs	www.skyscape.com (978-562-5555)
	Medical Letter Adverse Drug Interaction Program	www.medletter.com (800-211-2759)
	iFacts (Drug Interaction Facts)	www.factsandcomparisons.com (800-223-0554)
Internet	www.drugs.com	
	www.medicine.iupui.edu/flockhart (CYP 450 interactions)	
	www.powernetdesign.com/grapefruit (grapefruit juice interactions)	
Pocketbooks	<i>The Top 100 Drug Interactions: A Guide to Patient Management</i> (Hansten and Horn), 2003	www.hanstenandhorn/books_all.htm (800 223 0554)
	<i>The Medical Letter Handbook of Drug Interactions</i> , 2003	www.medletter.com (800 211 2759)
Bound Textbooks	Evaluation of Drug Interactions, 2003	www.firstdatabank.com/reference_products/edi/ (800 633 3453)
	<i>Drug Interaction Facts</i> , 2003	www.factsandcomparisons.com (800-223-0554)
	<i>Managing Clinically Important Drug Interactions</i> (Hansten and Horn), 2003	www.hanstenandhorn/books_all.htm (800 223 0554)

Table 3. High alert medications for DDIs*

Cardiac medications

- Digoxin
- Calcium channel blockers – e.g., verapamil, diltiazem, nifedipine

Oral anticoagulants

- Warfarin

Theophylline derivatives

Endocrine therapies

- Oral hypoglycemic agents (e.g., glyburide, pioglitazone, others)
- Lipid-lowering agents, particularly statins (e.g., atorvastatin, simvastatin)

Immunosuppressants

- Cyclosporine

Psychiatric medications

- Lithium
- Serotonin-specific reuptake inhibitors (SSRIs) – e.g., fluvoxamine, paroxetine
- Monoamine oxidase inhibitors (MAOIs) – e.g., phenelzine, tranylcypromine

Anticonvulsants

- Phenytoin, carbamazepine, phenobarbital

Antimicrobials

- Macrolide antibiotics – e.g., erythromycin and clarithromycin
- Quinolone antibiotics – e.g. ciprofloxacin
- Antiretrovirals – e.g., indinavir, ritonavir, saquinavir
- Oral antifungals – e.g., ketoconazole, itraconazole, terbinafine

*List is not exhaustive. A more formal reference should be consulted for specific drug combinations.

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