Controlling Adverse Drug Reactions Through Improved Monitoring

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The annual cost of drug-related morbidity and mortality in the United States has been estimated at more than $136 billion.[1] Adverse drug reactions (ADRs) contribute significantly to these costs.[2] Epidemiological studies indicate that ADRs occur in 5% to 20% of all hospitalized patients,[3,4] and that 3% to 28% of all hospital admissions may be drug related.[5-10]

Adverse drug reactions and therapeutic failures can be considered subsets of adverse drug outcomes. When medication errors cause adverse drug outcomes, the focus tends to be on errors of commission (ie, mistakes in prescribing, dispensing, and/or administration of drugs). For example, dispensing errors occur when drugs have similar names (spelled or pronounced alike), or when a misplaced decimal point results in the wrong dosage. Medication errors, however, also can be errors of omission. Errors of omission leading to ADRs or therapeutic failures have been reported to include[11]:

- Drugs considered to be inappropriate for the patient's condition (ie, because of contraindications, comorbid disease states, or dose adjustments for renal insufficiency).
- Dosage or frequency of administration considered inappropriate for the patient's condition.
- Previous history of an allergy or adverse reaction to the drug.
- Drug interactions.
- Poor patient compliance.
- Incomplete or inadequate monitoring of drug therapy.

An ADR or therapeutic drug failure involving 1 of the above factors is considered to be preventable (ie, a medical error). The adverse outcome could have been avoided if optimal medical care and monitoring had been provided.

The article by Raebel et al focuses on 1 of the leading causes of preventable adverse drug outcomes—lack of therapeutic drug monitoring. In this epidemiological, retrospective review, Raebel et al report on a cohort of ambulatory patients whose therapy included drugs with narrow therapeutic indices. Due to a direct concentration-effect relationship, these drugs provide therapeutic benefits within a narrow range of concentrations. Below that range, therapeutic failure can occur. Above that range, serious ADRs can occur. Therapeutic drug monitoring, especially with patients who seem to be more at risk, may prevent adverse drug outcomes on both ends of the drug-concentration relationship.

As a pharmacist educator and clinician focusing on the identification, preventability, and analysis of ADRs, I create an annual "top 10" list of drugs that lead to hospital admissions at my practice site. It is always interesting to see that just 10 drugs cause 40% to 60% of all ADRs. Drugs on these lists (eg, warfarin, digoxin, phenytoin) often have narrow therapeutic indices. Such drugs require laboratory tests to determine the direct concentration-effect relationship. In nearly every case of hospitalization, patients taking these drugs had toxic blood levels. Had more adequate therapeutic drug monitoring been performed, many of these hospitalizations might have been avoided.

Raebel et al report a lack of therapeutic drug monitoring involving certain drugs and certain patient populations (eg, elderly, children). Fifty percent or more of patients receiving drugs such as digoxin, theophylline, procainamide, quinidine, or primidone did not have therapeutic drug monitoring tests that would indicate the plasma concentrations of these agents. Although clinical implications (ie, hospitalizations, emergency department and/or physician visits) were not evaluated, this study does show that inadequate monitoring of drugs with narrow therapeutic indices is a substantial problem. This report may increase awareness among physicians, pharmacists, and other clini-

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cians, and encourage them to be more vigilant in monitoring patients who take these agents as part of their drug therapy.

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