When mixing drugs makes malpractice

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Amitriptyline toxicity kills patient

Unknown North Carolina venue

A 26-year-old woman with diabetes saw a psychiatrist to manage her depression. The psychiatrist increased her amitriptyline dosage to 300 mg nightly and over 10 months added:

- alprazolam (unknown dosage, nightly)
- quetiapine (400 mg bid)
- extended-release venlafaxine (225 mg bid)
- and promethazine (100 mg bid).

The patient also took insulin for diabetes.

Several weeks later, the woman was found dead in her home. An autopsy revealed amitriptyline toxicity as the cause of death. The medical examiner noted "a much larger concentration of the metabolite nortriptyline in the liver versus the parent drug," suggesting a metabolism problem, rather than an overdose, caused the toxic build-up.

The patient's estate claimed that amitriptyline was cardiotoxic at the prescribed dosage and combined with the other medications used and that the patient was not properly monitored.

• A $2.3 million settlement was reached.

Fatal cardiac arrest after 2 concomitant antidepressants

Gwinnett County (GA) Superior Court

A 40-year-old woman was under a psychiatrist's care for anxiety and depression. The psychiatrist continued sertraline, which the woman had been taking, and added nortriptyline. Several weeks after the patient began taking the medications together, she had a fatal cardiac arrest.

The patient's estate argued that:

- toxic levels of the antidepressants caused her death
- sertraline and nortriptyline should not be taken concurrently because one drug inhibits clearance of the other
- the psychiatrist should have monitored the patient to make sure sertraline and nortriptyline levels remained normal.

The psychiatrist argued that coronary artery disease caused the patient's death—not the combination of medications.

The medical examiner was unable to say which condition more likely led to the patient's death.

• The defendant was awarded $3 million. A statutory capitation reduced the award to $1.65 million.

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Dr. Grant's observations

As these cases demonstrate, lawsuits against psychiatrists commonly include allegations of preventable prescribing missteps and drug-drug interactions[1] (*Box*).[2-4] Negligent use of medications may be alleged for:

- failure to use appropriate medication
- excessive dosing
- failure to monitor serum levels.

Failure to use appropriate medication is often claimed when complications result from off-label prescribing. To protect yourself from such a claim, carefully document:

- the rationale for using off-label medication
- reasons that FDA-approved medications were not selected
- the fact that you informed the patient about the off-label medication's side effects, risks, and benefits (see "*Off-label prescribing: 7 steps for safer, more effective treatment*," *page 14*).

When a patient is taking multiple medications, interactions can inhibit drug metabolism and render normal doses excessive.[5] When prescribing drugs known to have adverse effects with excessive dosing, such as tricyclic antidepressants and lithium, failing to monitor serum levels could be considered malpractice. In fact, the courts view actions such as prescribing doses that exceed FDA recommendations or failing to monitor levels as prima facie evidence of negligence, requiring the psychiatrist to prove otherwise.

Amitriptyline and nortriptyline have shown cardiac toxicity in overdose,[6] and their serum levels increase when used with other antidepressants.[7,8] Standard of care dictates serum level monitoring particularly when you use tricyclics:

- in doses higher than recommended by the FDA (300 mg/d for amitriptyline, 150 mg/d for nortriptyline)
- with other drugs that affect their metabolism.[9]

You cannot rely on pharmacy computer programs to catch potentially important drug-drug interactions. One study found that even among pharmacies with such programs, one-third of pharmacists filled prescriptions for a dangerous medication combination.[10]

How to prevent fatal errors. Don't shy away from using medications that require serum level monitoring. Anticipating and monitoring drug-drug interactions becomes second nature once you've used these medications frequently. Plus, patients benefit from a greater array of safe and effective treatment options.

The following strategies can help you avoid mistakes and malpractice claims.[1,11]

Clinical practice. Obtain a comprehensive patient history and necessary examinations

Box

Adverse event incidence: Numbers tell a troubling story

More than twice as many Americans died from medication errors in 1993 than in 1983, according to a comparative review of U.S. death certificates from that period.[2]

Between 1985 and 1999, more than 10,000 medication error claims were closed. Patients received payment in 36% of claims, totaling more than $461 million, the Physician Insurers Association of America reported.[3]

47% of 424 randomly selected visits to a hospital emergency department led to added medication, an analysis found. In 10% of those visits, the new medication added potential for an adverse interaction.[2]

8% of 1,520 significant adverse drug events were caused by drug-drug interactions, three studies of events occurring between 1976 and 1997 found. Serum levels that could be monitored were done so only 17% of the time. Lawsuits resulted in 13% of the cases with settlements/judgments averaging $3.1 million.[4]

before prescribing medications. See patients at clinically appropriate intervals.

Ask the patient about other medications he or she is taking, including over-the-counter medications, herbal remedies, and dietary supplements. Remind the patient to report changes in medications or new medications prescribed by another physician.

Put in place a process to obtain appropriate baseline laboratory testing and to ensure that follow-up testing is completed and reviewed. Monitoring lab results becomes particularly important in cases—such as these two—when escalating levels of certain medications can cause adverse effects.

Communicate with the patient's other physicians about all the medications that are being prescribed to him and about signs, symptoms, and responses to the medications.

Educate yourself by participating in continuing education programs, discussions with colleagues, and through relevant literature. Review drug manufacturer alerts.

Patient education. Educate patients about medication instructions, including the dosage and frequency, ways to identify side effects, and what to do in the event of side effects or a bad reaction. Get informed consent.

Be aware of and inform the patient about potentially lethal side effects of misusing or abusing certain medications. Address the use of street drugs and how they interact with prescription medications; make appropriate treatment assessments and referrals for addiction and dependence issues.

Documentation. Keep thorough records of medications prescribed: dosage, amount, directions for taking them, and other instructions to the patient. Document results of laboratory testing and any decisions you make based on medication serum levels.

When using polypharmacy that increases the risk of adverse interactions, document a clear rationale in patients' charts.

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