Drug Interactions in Cancer Patients Receiving Antidepressants Are Common, Researchers Report

Lincy Lal, PharmD, PhD, and colleagues at The University of Texas MD Anderson Cancer Center (MDACC) in Houston, Texas, found that potential drug interactions in patients treated with antidepressants were frequent and were associated with increased resource utilization (Support Care Cancer [published online ahead of print April 26, 2011] doi: 10.1007/s00520-011-1170-4). Appropriate treatment of depression in cancer patients can be difficult because antidepressants often have drug interactions, and according to the authors, the epidemiology of major drug interactions in cancer patients has been addressed by few studies.

“A significant proportion of cancer patients are taking 10 or more medications, and the number of potential drug interactions is large and ever present,” says Michael Fisch, MD, MPH, chair of general oncology at MDACC and a study coauthor.

Study Findings

The study population included 297 patients who were consistently treated at MDACC and who received at least 3 prescriptions for antidepressants for a continuous 6-month period. Antidepressants were coded into 3 categories: tricyclics, serotonin reuptake inhibitors (SSRIs), and “others,” which included some of the newer drugs such as bupropion, venlafaxine, and combination products. Occurrence and severity of potential drug interactions were evaluated by cross-checking each participant’s outpatient prescription profile with 2 drug interaction checking software programs.

Fifty patients (17%) received a tricyclic as their first prescription, 119 patients (40%) received an SSRI, and 128 patients (43%) received one of the agents listed as “other.” Overall, 145 patients (49%) were taking a drug combination that could have caused a major drug interaction with any of the antidepressants included in the study, and 99 patients (33%) had no potential for a drug interaction. A total of 118 patients (40%) had a potential interaction that could lead to serotonin syndrome and 59 patients (20%) had potential major interactions with anticoagulants. The major potential drug interactions in the study population were:

- Sertraline and heparin (bleeding risk)
- Escitalopram oxalate and heparin (bleeding risk)
- Escitalopram oxalate and oxycodone (serotonin syndrome)
- Sertraline and oxycodone (serotonin syndrome)
- Venlafaxine and heparin (bleeding risk)
- Mirtazapine and olanzapine (serotonin syndrome)
- Venlafaxine and haloperidol (cardiotoxicity)
- Venlafaxine and amoxicillin with potassium clavulanate (serotonin syndrome)
- Bupropion and dexamethasone (lower seizure threshold)
- Duloxetine and tramadol (serotonin syndrome)
- Paroxetine and heparin (bleeding risk)

There were 2.5 mean emergency room (ER) visits or hospitalizations in the 145 patients with a potential major interaction versus 1.6 in the remaining 152 patients. In a subgroup analysis, there were 2.3 mean ER visits or hospitalizations in patients receiving drugs capable of causing serotonin syndrome and 3.5 in those patients receiving concurrent anticoagulants. Multivariate analysis showed that the presence of a potential major drug interaction with antidepressants was associated with an increased number of hospital and ER visits (odds ratio [OR], 2.37),
concurrent use of potential serotonin syndrome-inducing drugs (OR, 2.28), and concurrent use of anticoagulants (OR, 3.66). Of 363 admissions, 25 were directly coded as being related to a drug interaction.

Although potential drug interactions with anticancer agents were not examined in this study, Dr. Fisch says it is an important issue. “There are numerous potential interactions between chemotherapy and antidepressants, mostly via the cytochrome P450 system,” he says. “The actual clinical significance of these interactions is not known. The most widely discussed and explored issue is the interaction between tamoxifen and antidepressants (like paroxetine and fluoxetine) metabolized by the cytochrome P450 2D6 enzyme. It remains controversial if this interaction is clinically significant, but clinicians often steer towards other antidepressants when tamoxifen is coprescribed.”

According to Dr. Fisch, more research is needed on this subject and in general, more attention to health services research in oncology is needed.

Limitations
Although the study shows an association between the presence of a potential major drug interaction and increased use of health care resources, its retrospective design precludes conclusions regarding causality. One limitation is that researchers could not obtain information on patients’ stage of disease, which may affect antidepressant use. Another limitation is the study’s reliance on admission coding, which may miss a significant number of adverse events, as there are a limited number of codes for each admission and adverse events may be lower on the coding priority list. In addition, sometimes a condition that may have been a drug interaction is only coded as the condition.

William Breitbart, MD, chief of the psychiatry service at Memorial Sloan-Kettering Cancer Center in New York City, agrees that the study does not establish causality of the ER visits to drug interactions. He is concerned that overlooking this point could lead to conclusions that may have a negative impact on treating depression in cancer patients, which is very prevalent and already undertreated.

“I am constantly being asked to consult on patients for drug interaction problems where the patient is on many drugs, yet the focus of the oncology team is the antidepressant,” he says. “They often want to stop the antidepressant due to a bias that it is not really needed.” Dr. Breitbart says he fears this article may contribute to an erroneous and amplified concern of the adverse effects of antidepressants.

Clinical Applications
Multivariate analysis showed that having a potential major drug interaction was a risk factor for increased ER visits and hospitalization. Thus, this study identifies an area where intervention may help reduce costs and lessen the occurrence of adverse events to improve patient outcomes. Interventions such as the identification of and proactive monitoring of patients at high risk for drug interactions may benefit the individual patient as well as resource utilization.

According to Dr. Fisch, the take-home message is that patients need goal-oriented prescribing with appropriate assessment to determine whether newly prescribed agents are being tolerated and whether they are achieving the intended clinical goals. “Provider-patient communication is probably the key factor for safe prescribing. Nonadherence and overadherence to prescribed medications are major issues, and nonadherence may be due, in part, to concerns about drug interactions that the patients and family may have,” he says.

Dr. Breitbart says the main point is that while this study singles out antidepressants, potential drug interactions exist ubiquitously for all drugs. “It is important for the clinician to be aware of potential drug interactions and use their clinical judgment as to the risks versus benefits,” he says. “It is always best to think of drug interactions when prescribing and try to select agents that have less potential for drug interaction. There may never be a situation in which no interaction at all exists, and clinical judgment and monitoring for clinically significant interactions is essential.”

Note: The name of this section has been changed from “News & Views” to “Perspectives: Research in Context.” It continues to provide the context for major developments in cancer prevention, detection, and treatment.