Preference, Cost Should Drive SSRI, SNRI Choice

BY DIANA MAHONEY
New England Bureau

Second-generation antidepressants are similarly effective in the treatment of major depression in adults, so drug selection should be driven by adverse event profile, cost, and patient preference, according to a clinical practice guideline issued by the American College of Physicians.

Basing their conclusions on evidence derived from 203 clinical studies involving selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and selective serotonin norepinephrine reuptake inhibitors (SSNRIs), the guideline authors wrote that "existing evidence does not justify the choice of any second-generation antidepressant over another on the basis of greater efficacy and effectiveness."

They also determined that the efficacy and effectiveness of the various agents did not differ among subgroups based on age, sex, race, or ethnicity.

Because the various agents are associated with different adverse events, "physicians and patients should discuss adverse event profiles before selecting a medication," the authors wrote (Ann. Intern. Med. 2008;149:725-33).

For example, although sexual dysfunction is a commonly reported adverse event associated with second-generation antidepressants, "bupropion is associated with a lower rate of sexual adverse events than fluoxetine or sertraline, whereas paroxetine has higher rates of sexual dysfunction than fluoxetine, fluvoxamine, nefazodone, or sertraline," they stated. "In addition, SSRIs are associated with an increased risk for suicide attempts compared with placebo."

The practice guideline also recommends that clinicians:

► Regularly assess patient status, therapeutic response, and adverse effects of antidepressant therapy beginning within 1-2 weeks of treatment initiation.

► Modify treatment if the patient does not have an adequate response within 6-8 weeks.

► Continue treatment for 4-9 months after a satisfactory response in patients with a first episode of major depressive disorder, and consider longer treatment after a satisfactory response in patients who have had two or more episodes of depression.

The authors stress the importance of monitoring patients for behavioral changes that could indicate a worsening of depression and note that the risk for suicide attempts is greater during the first 2 months of treatment than during other times. Additionally, they state that "one of the most important aspects of care is assessing the response to treatment and making necessary changes in therapy," including adding other therapeutic modalities or alternate drugs.

Acknowledging that other treatment approaches, such as cognitive-behavioral therapy and psychotherapy, can be used in the management of depression, "the scope of this guideline is limited to pharmacotherapy with second-generation antidepressants," the authors wrote.

The American College of Physicians' recommendations are in line with the current treatment guidelines of the American Psychiatric Association, according to Dr. James Jefferson of the University of Wisconsin, Madison. "In general, I agree with the [ACP] recommendations, although I am sure various pharmaceutical companies are going to be going over them with a fine-toothed comb," he said in an interview. The focus on drug therapy alone is not inappropriate, he noted, stating that the authors "had a very specific goal." ■

Paroxetine Linked to Sperm DNA Fragmentation

BY KERRI WACHTER
Senior Writer

SAN FRANCISCO — Treatment with paroxetine (Paxil) appears to put healthy men at greater risk of sperm DNA fragmentation, according to data from a small study presented at the annual meeting of the American Society for Reproductive Medicine.

In 35 healthy male volunteers, SSRI treatment was significantly correlated with increased DNA fragmentation (odds ratio 11.12, $P = .0003$) on multivariate logistic regression, after correcting for age and body mass index.

Based on these preliminary findings, it would be premature to suggest changing to an alternate therapy.

DR. TANRIKUT

"Healthy volunteers demonstrated a dramatic increase in DNA fragmentation within just a few weeks of paroxetine treatment, without an apparent impact on standard semen parameters. This negative impact on sperm DNA fragmentation may affect reproductive outcomes," even with intracytoplasmic sperm injection, study investigator Dr. Cigdem Tanrikut said in an interview.

"Certainly, one should query male patients about SSRI use. However, based on these preliminary findings, it would be premature to suggest a patient come off of SSRIs altogether or change to an alternate therapy given the lack of data regarding other newer antidepressants," said Dr. Tanrikut, director of male reproductive medicine at Massachusetts General Hospital's fertility center in Boston.

Men in the study ranged in age from 18 to 65 years. Intake assessment included physical exam, semen analysis, and the Brief Sexual Function Inventory (BSFI). Repeat semen analysis was obtained before SSRI initiation.

Paroxetine was given for 5 weeks: 10 mg daily during week 1; 20 mg daily during week 2; 30 mg daily during weeks 3-4; and 20 mg daily during week 5. Semen analysis was performed at weeks 2 and 4. One month after cessation of the SSRI, a final semen analysis was then performed. The BSFI was completed at week 4 and at the final semen collection.

Standard World Health Organization evaluation of semen parameters was performed in a certified laboratory. TUNEL (terminal dUTP nick-end labeling) assays were performed at baseline and at week 4 to evaluate the percentage of sperm DNA fragmentation. Semen parameters and TUNEL assays for each participant were compared at each time point.

Semen parameters—including volume, concentration, motility, and morphology—were not significantly altered during SSRI treatment. However, the mean DNA fragmentation TUNEL score was significantly higher with SSRI use, compared with baseline measurements (30.3% vs. 13.8%, $P = .0002$). The unadjusted odds ratio of having abnormal DNA fragmentation while on paroxetine was 9.33.

In addition, the BSFI revealed significant sexual dysfunction on paroxetine as compared with baseline. Up to 35% of men noted significant changes in erectile function, and up to 47% of subjects reported ejaculatory difficulties while on paroxetine. At least partial recovery of sexual function was noted within 1 month after stopping treatment.

The study was supported by the Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust and Brady Urology Foundation. ■

Menopause Affects Presentation of Major Depression

BY DAMIAN McNAMARA
Miami Bureau

LAKE BUENA VISTA, FLA. — Menopausal status and use of hormone therapy can influence the presentation and treatment of major depression, according to Dr. Susan G. Kornstein, professor of psychiatry and obstetrics-gynecology at Virginia Commonwealth University, Richmond.

Dr. Kornstein and her associates evaluated differences in depression by menopausal status using data from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, sponsored by the National Institute of Mental Health. "We looked at whether major depressive disorder presents differently in the pre-, peri-, and postmenopausal period," said Dr. Kornstein, also executive director of the Institute for Women's Health and the Mood Disorders Institute at VCU Medical Center.

The study included 948 premenopausal, 376 perimenopausal, and 566 postmenopausal participants. Women taking hormone therapy were excluded.

Postmenopausal women were less likely to have a family history of depression and more likely to experience an older age of depression onset and more medical comorbidity.

"Depression presenting in postmenopausal women may be more related to general medical comorbidity or hormonal factors or aging as opposed to a lifelong depressive disorder," she said.

Dr. Kornstein and her colleagues also compared 177 women taking hormone therapy with 566 women not taking hormone therapy. "Women taking hormone therapy were more likely to have recurrent depression and greater general medical comorbidity. But more interaction with health care providers may have led to more opportunities to be prescribed hormone therapy."

Participants taking hormone therapy reported better physical health and were less likely to report sympathetic arousal or melancholic features of depression. "This can point to some benefit of hormone therapy on depressive symptoms, although estrogen is not a treatment for depression in postmenopausal women," Dr. Kornstein said. "But we can say that hormone therapy does not seem to worsen depressive symptoms."

In perimenopausal women, estrogen has been shown to be an effective treatment for depression, when used either alone or in combination with antidepressants; however, risks and benefits of estrogen use must be weighed (Arch. Gen. Psychiatry 2001;58:529-34; Expert Rev. Neurother. 2007;10:1285-93). In contrast, estrogen alone has been shown to be ineffective in postmenopausal depression (Psychiatry 2004;55:406-12).

"The literature suggests psychotherapy is as effective as medication for mild to moderate depression, and the combination may be superior to either alone" (N. Engl. J. Med. 2000;342:1462-70; Psychiatr. Ann. 2002;32:465-76). Psychotherapy may also have a "long-term benefit in preventing relapse of depression," Dr. Kornstein said (Am. J. Psychiatry 2004;161:1872-6). ■