Sertraline Falls Short for Depressed HF Patients

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — Sertraline did not significantly improve depressive symptoms or cardiovascular status among depressed patients with heart failure, compared with placebo in a 12-week, randomized, double-blind study.

A second, posthoc analysis of the data indicates that patients who achieve remission of depression experience prognostic and functional improvements, including statistically fewer mean cardiovascular events during long-term follow-up, compared with nonremitters.

Dr. Wei Jiang presented results of both the primary and secondary analyses of the Sertraline Antidepressant Heart Attack Randomized Trial in Congestive Heart Failure (SADHART-CHF) at a meeting of the New Clinical Drug Evaluation Unit (NCDEU) sponsored by the National Institute of Mental Health.

She and her associates assessed depressive symptoms, cardiovascular status, and long-term mortality rates in 234 patients who were randomized to sertraline (Zoloft, Pfizer Inc.) and an additional 235 who received placebo. At the end of the 12-week trial, there were 144 patients remaining on treatment and 146 others in the placebo group.

In an intent-to-treat analysis, there was a significant reduction in Hamilton Depression Rating Scale scores in both groups, compared with baseline. However, no significant differences were found between groups in these Hamilton scores, composite cardiovascular scores, fatal or nonfatal cardiovascular events, or results of the Kansas City Cardiomyopathy Questionnaire. In addition, long-term survival did not differ significantly between groups.

The null findings might result from an effect of a nurse-facilitated supportive intervention for all participants, Dr. Jiang said. "But a placebo effect cannot be ruled out."

Dr. Jiang receives research support from the NIMH (sponsor of the study), the National Heart, Lung, and Blood Institute, and from Pfizer for an unrelated study. Pfizer's only role in SADHART-CHF was to supply the sertraline, she added.

"We spent 6 years doing the study, and now we are stuck. There is no antidepressant we can recommend to cardiologists for this population. Other than sertraline, almost all other classes of antidepressants … have cardiovascular concerns," said Dr. Jiang, who is on both the internal medicine and the psychiatry and behavioral sciences faculties at Duke University, Durham, N.C.

The search for a safe and effective treatment for depression is important and should continue, Dr. Jiang said, because depression is "highly prevalent" in patients with heart failure. A 22% prevalence of depression was found in a meta-analysis, for example (J. Am. Coll. Cardiol. 2006;48:1527-37).

This study suggested that there was an increased risk for death and secondary cardiac events in depressed versus nondepressed patients (risk ratio 2.1).

The 469 participants in the primary analysis were 45 years or older, had a New York Heart Association classification of II or higher, and a left ventricular ejection fraction of 45% or less. Mean age was 63 years in the treatment cohort and 62 years in the placebo group. Men comprised 57% and 62%, respectively, of these cohorts.

Those randomized to treatment received sertraline between 50 mg/day and 200 mg/day or matched placebo. The average sertraline dose was 69 mg/day and 75 mg/day for placebo. "That is too low," a meeting attendee said during a question-and-answer session. "That is what we thought, also," Dr. Jiang said. "I agree with you, but we felt many patients would drop out [if dosing were higher]. Remember that 41% of the sertraline arm dropped out."

The same person commented further that sertraline might have been more effective at a higher dose. "There are studies showing 50 mg is enough, so I don't know the right answer," she replied.

Dr. Jiang also presented results of a posthoc analysis of remission using Hamilton Depression scores. Remission was associated with prognostic and functional improvement in depressed heart failure patients during the 12-week intervention phase. In addition, there was a statistical difference in mean overall cardiovascular events between that favored remitters (1.11) versus nonremitters (1.66) during follow-up.

Again, there was no significant difference in long-term survival between the 208 remitters and 194 nonremitting patients (mean survival of 866 days versus 793 days). The remaining 67 patients were classified as early terminators because they dropped out of the study prior to the first treatment.

Achievement of remission should be a target for additional studies of patients with heart failure and comorbid depression, Dr. Jiang said.

In addition, more data are needed to identify factors that might indicate which heart failure patients are likely to respond to different antidepressant modalities, she said. ■

Depressed Patients May Not Follow Hypertension Regimen

BY KATE JOHNSON

MONTREAL — Hypertensive patients who have depression are less likely to stick to their therapy regimen than are those who are not depressed or are in remission from depression, according to a study of 161 patients.

"This suggests that any change in depressive symptomatology over time can affect medication adherence and may be clinically important," Sara Gallagher said at the annual meeting of the Society of Behavioral Medicine.

The finding that remission of depressive symptoms is associated with improved adherence suggests a benefit to addressing depression.

Her study was embedded in a randomized, controlled trial of the effect of motivational interviewing on medication adherence (Am. J. Hypertens. 2008;21:1137-43). The 161 hypertensive African Americans in the study were followed in primary care practice. The patients had a mean age of 54 years, and 87% of them were women. Depressive symptomatology was assessed at baseline and at 6 and 12 months using the Center for Epidemiologic Studies–Depression Scale (CES-D).

A total of 44% of the patients were classified as nondepressed, with a CES-D score of less than 16 at all time points, while 19% were considered depressed, with a score of 16 or above at all time points. The remaining 37% of the patients were classified as in remission, meaning that they progressed from depressed to nondepressed during of the study, said Ms. Gallagher, of New York (N.Y.) University.

Medication adherence was assessed at baseline and at 12 months using the self-reported Morisky scale. At baseline, 64% of the study population reported nonadherence to their medication, and this dropped to 48% at the end of the study.

A multivariate analysis revealed that depressive symptoms were associated with medication nonadherence, Ms. Gallagher reported.

Among the depressed patients, only 34% reported adherence at 12 months, compared with 66% of those in the nondepressed group and 47% of those who were in remission.

The study confirms previous findings that depressive symptoms are associated with poor medication adherence, Ms. Gallagher said. However, the finding that remission of depressive symptoms is associated with improved adherence suggests a benefit to addressing patient depression in this context, she said. ■

Depression Worsens Impact of CVD Risk Factors in Women

BY KATE JOHNSON

MONTREAL — In women with documented cardiovascular risk factors, those with comorbid depression have a greater risk of clinical events, compared with their nondepressed counterparts, according to new findings from the Women's Ischemic Syndrome Evaluation (WISE), trial sponsored by the National Heart, Lung, and Blood Institute.

"Many studies have associated depression with an increased risk of cardiovascular disease incidence, but until now, the predictive value of these risk factors has been unknown," reported Thomas Rutledge, Ph.D., of the department of psychiatry at the University of California, San Diego.

"We wanted to know whether the added presence of depression would statistically worsen the relationship between cardiac risk factors and outcome," he explained at the annual meeting of the Society of Behavioral Medicine.

Dr. Rutledge examined the association of cardiovascular disease (CVD) risk factors with actual CVD events in 153 depressed and 718 nondepressed women who were enrolled in the WISE trial. The women were a mean age of 60 years and all of them had been referred for coronary angiography because of symptoms suggestive of myocardial ischemia.

CVD risk factors were assessed, including smoking, dyslipidemia, hypertension, obesity, diabetes, and level of physical activity.

Depression was defined as self-reported current use of antidepressants to treat depression.

Over a mean follow-up period of 5.9 years, the CVD mortality rate was higher in depressed women with CVD risk factors than it was in nondepressed women with the same risk factors (11.5% vs. 9.2%, respectively). Similarly, depressed women experienced more cardiovascular events such as stroke, myocardial infarction, and heart failure (23.9% vs. 13.3%).

For four of the six individual CVD risk factors, "the combination of depression and the risk factor was associated with a significantly worse event rate, compared with the risk factor alone," said Dr. Rutledge. "The exceptions were smoking and diabetes, but these were the two risk factors for which we had the smallest sample size, so power was possibly an issue."

Excluding these exceptions, the combination of depression and risk factors was associated with an average 12%-13% increase in death and events, compared with risk factors alone, he said. ■

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