Not All Unipolar Depressions Necessarily Chronic

BY BARBARA RUTLEDGE
Contributing Writer

Mendoza, Argentina — The use of antidepressants may not be effective for long-term treatment of unipolar depression, and may actually be harmful, Dr. Ulrik Malt reported at the 6th World Congress of Depressive Disorders.

"There are no good arguments for treating all unipolar depressions as a chronic disorder," said Dr. Malt, professor of psychiatry at the University of Oslo. "There are no good reasons for long-term antidepressant treatment of all unipolar depressions."

In the absence of drug treatment, about 70% of patients go into remission within 6 months after a major depressive episode, and they may remain in remission for several years, with no or clinically insignificant symptoms of depression.

Support for the use of antidepressant drugs for treating unipolar depression comes from clinical studies, but study results can be misleading

In many cases, according to Dr. Malt, the study population includes patients with other depressive disorders, rather than true unipolar depression, which he defined as a depressive episode without evidence of past hypomania or past symptoms of melancholia.

Published studies often include patients whose depression stems from bipolar spectrum disorders, which are neurobiologically distinct from unipolar depression.

Several studies have demonstrated that careful rediagnosis of patients given a diagnosis of major depressive disorder reveals a high incidence of patients with bipolar II disorder. These patients are more likely to respond to drug treatment than are patients with major depressive disorder.

Dr. Malt also questioned the data supporting long-term use of antidepressants for prevention of relapses, arguing that

In Kids, Response To Sertraline Varies With Age

Children with major depressive disorder aged 6-11 years have a significantly faster first response to both sertraline and a placebo, compared with adolescents aged 12-17 years, Dr. Craig L. Donnelly of Dartmouth-Hitchcock Medical Center in Lebanon, N.H., and his colleagues report.

The study, funded by Pfizer Inc. , is the first known to examine the differences in time to first response and time to first persistent response in children and adolescents with major depressive disorder (MDD).

The investigators looked at 226 youths with MDD. The 10-week double-blind, placebo-controlled trial was followed by a 24-week open-label trial of sertraline (J. Am. Acad. Child Adolesc. Psychiatry 2006;45:1162-70). All of the patients who received sertraline started with a 25-mg/day dose for 3 days, followed by 50 mg/day through the end of 2 weeks. The dosage was then adjusted to a maximum of 200 mg/day based on the patient's clinical response and the occurrence of side effects.

The estimated median time to first response was 15 days for children and 22 days for adolescents who took sertraline, compared with 21 days for children and 23 days for adolescents who took a placebo The time to first persistent response was significantly shorter in adolescents, but not in younger children, when compared with the placebo.

The estimated median time to first persistent response was 28 days for children and 32 days for adolescents who took sertraline, compared with 28 days for children and 32 days for adolescents who took a placebo. Patients in both age groups showed similar long-term improvements in MDD symptoms by the end of 34 weeks of treatment, and sertraline was generally well tolerated. Significantly more children than adolescents discontinued the study because of adverse events (15% vs. 4%).

Suicide-related events were reported in five patients in the sertraline group (three children, two adolescents) vs. two incidents in the placebo group (one adolescent attempted suicide twice). Those who reported suicide events were taking at least 100 mg of sertraline at the time of the events, but there was no link between the suicide events and any recent increase in the sertraline dose, the autors noted.

—Heidi Splete

studies on the long-term effects of antidepressants are biased in patient selection. Long-term studies are usually conducted as an extension of a short-term study. Placebo-responders are excluded from the short-term study, and nonresponders discontinue treatment after the short-term study is concluded. Thus, data on the efficacy of long-term use of antidepressants are obtained from a skewed patient sample, in which patients who respond favorably to drug treatment are overrepresented.

The disadvantages of long-term antidepressant treatment for unipolar depression are underrecognized or even minimized, according to Dr. Malt. Reported side effects of antidepressants include metabolic syndrome and bruxism, as well as sexual side effects, such as impaired sexual desire, impotence, and anorgasmia. Long-term use of antidepressants may lead to decreased fertility in men, with possible deleterious effects on sperm viability and motility.

In addition, with long-term antidepressant therapy, drug resistance may develop, leading to reduced efficacy in subsequent treatments in patients who initially responded to the drug but eventually discontinued its use. However, even with continuous treatment, loss of efficacy (tachyphylaxis) can occur over time. Long-term use of antidepressants can also result in discontinuation syndromes or dependence.

By treating these patients, we may be increasing the likelihood of future depressive episodes.

DR. MALT

Treatment with antidepressants, especially selective serotonin reuptake inhibitors (SSRIs), can have long-term effects on brain receptors. In a study of patients in remission from major depression, those with prior SSRI treatment were significantly more likely to experience mood worsening after tryptophan depletion than were those who been treated only with cognitive therapy (Biol. Psychiatry 2004;55:957-9).

"By treating these patients, we may actually be making them more vulnerable in the long term and increasing the likelihood of future depressive episodes," Dr. Malt said. ■