Triiodothyronine Enhances Response to Sertraline

BY JANE SALODOF MACNEIL
Southwest Bureau

PARIS — Triiodothyronine supplementation significantly increased the antidepressant effects of sertraline in a randomized placebo-controlled clinical trial presented by Dr. Bernard Lerer in a breaking news session at the annual congress of the European College of Neuropsychopharmacology.

Israeli patients treated with sertraline (Zoloft) and triiodothyronine (T_3) were nearly three times more likely to respond (odds ratio 2.93), compared with a cohort given sertraline and a placebo. Some 69.8% (37/53 patients) had at least a 50% reduction in their Hamilton Rating Scale for Depression (HAM-D) scores on the active drug combination vs. 50% (25/50 patients) in the control group.

The sertraline-T_3 cohort also was much more likely (odds ratio 2.69) to go into remission by the sixth week of treatment. At that point, 58.5% (31/53) of the T_3-augmented patients but only 38% (19/50) of the placebo group was in remission.

"Results of the current controlled study support the efficacy of T_3 as an enhancer of antidepressant action," said Dr. Lerer, director of the Hadassah Biological Psychiatry Laboratory and a professor of psychiatry at the Hadassah-Hebrew University Medical Center in Jerusalem.

Both groups of patients started on 50 mg per day of sertraline for 1 week, followed by 100 mg per day for 7 weeks. The T_3 dose also was titrated up from 20-25 mcg per day the first week to 40-50 mcg per day for the rest of the trial.

T_3's effects in the trial appeared to be related to the hormone's effect on thyroid function, according to Dr. Lerer. He said patients who responded to the active-drug combination tended to have lower baseline levels of T_3 than those who did not. Patients who remitted on T_3 and sertraline also had greater reductions in thyroid-stimulating hormone (TSH) than those who did not go into remission. Neither effect was seen in the sertraline-placebo group.

"The precise clinical role of T_3 needs to be further defined, and predictors of response need to be identified," Dr. Lerer said in his conclusion.

In September, an antidepressant trial in the United States reported that T_3 augmentation resulted in more remissions and fewer adverse events than lithium augmentation in treatment-resistant patients (Am. J. Psychiatry 2006;163:1519-30). Reviewing this and previous studies of T_3 and antidepressants, Dr. Lerer said researchers suspect patients with thyroid dysfunction are less able to respond to antidepressants. Prevalence of depression is higher in patients with hypothyroidism, he noted, whereas thyroid dysfunction is also more prevalent in patients with depression.

Though some studies have shown T_3 to elicit responses more often in women than in men and also to speed response to antidepressants, Dr. Lerer said neither effect was seen in the new trial. He also reported no difference in adverse events with T_3, compared with placebo.

Sertraline was chosen for the study because it is little used in Israel, Dr. Lerer said, and therefore, the trial was better able to enroll patients. Patients with clinical hyper- or hypothyroidism or other thyroid disorders, including subclinical hypothyroidism were excluded from the study.

Investigators randomized 124 patients (60 augmented with placebo and 64 with T_3). Only 103 patients (50 given placebo and 53 augmented with T_3) were included in the intent-to-treat analysis, as investigators did not count 21 patients who dropped out without completing one clinical visit.

Baseline characteristics were similar between both arms of the trial. Each had 29 female patients. The average age was 41-45 years.

Laboratory values also were comparable at baseline, but significantly different post treatment. Almost no change was seen in the placebo group. Both TSH and thyroxine fell during the trial and T_3 increased, however, in the group augmented with T_3.

Despite good results with T_3 augmentation, Dr. Lerer said no patients were kept on treatment for more than 3 months post study. He urged caution until long-term effects are better understood.

The study received support from the Stanley Medical Research Institute in Chevy Chase, Md. Investigators from Beer Yaakov Mental Health Center in Israel and Global Medical Institutes in Princeton, N.J., also participated in the trial, which was coordinated by Dr. Lerer's group. ■