T3 Therapy Called Not Ready for Prime Time

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VANCOUVER — Triiodothyronine therapy is most definitely not a treatment whose time has come, a panel of experts agreed at a satellite symposium held in conjunction with the annual meeting of the American Thyroid Association.

Despite more than 3 decades of psychiatric interest in using T3 in the treatment of depression and more recent enthusiasm for T3 in treating primary hypothyroidism and the euthyroid sick syndrome, none of these applications is supported by reasonable clinical data—and in the case of euthyroid sick syndrome, there is a distinct potential for harm, the panelists said.

Public and physician interest in such therapy grew after a 1999 study reported superior outcomes in terms of cognition, mood, and physical symptoms in hypothyroid patients treated with a more physiologic combination of thyroxine and T3, compared with the traditional T4 replacement alone (N. Engl. J. Med. 1999; 340:424-9). Today many patients with complaints of chronic malaise or fatigue approach their physician seeking T3 therapy.

Yet none of the handful of well-designed randomized controlled trials done since the 1999 study have confirmed the initial report of superior outcomes, E. Chester Ridgway, M.D., said at the symposium, sponsored by Monarch Pharmaceuticals Inc. and Jones Pharma Inc.

"In my mind, what we have right now is a series of valid, valiant attempts to show that T3 is having benefit in patients treated for hypothyroidism. Most of the end points are mood and cognitive abilities, which in some sense are very sensitive, although they're maybe not what we're used to dealing with. But we've not been able to reproduce the initial benefits in the New England Journal paper," said Dr. Ridgway, the Frederic C. Hamilton Professor of Medicine, University of Colorado, Denver.

Elaine M. Kaptein, M.D., added that there is no role for T3 in the treatment of the euthyroid sick syndrome, either. The low serum total T3 and/or total T4 concentrations often noted in patients with prolonged severe nonthyroidal illnesses do not appear to be maladaptive. Physiologic doses of T3 have been used in many small, often uncontrolled studies in severely ill patients with a variety of such illnesses, including acute and chronic renal failure, heart failure, severe burns, and in individuals undergoing coronary artery bypass surgery. No hastening of recovery or improved survival has been seen.

None of the handful of well-designed randomized controlled trials done with T3 confirmed the initial report of superior outcomes.

There is some evidence to suggest pharmacologic doses of T3 may have a positive inotropic effect in severely ill patients without hypothalamic, pituitary, or thyroid failure. "We give dopamine without dopamine deficiency for its pressor effects. T3 could be used the same—but don't call it physiologic replacement," said Dr. Kaptein, professor of medicine at the University of Southern California, Los Angeles.

In the absence of large double-blind randomized trials, she recommended against giving T3 or T4 to patients with severe nonthyroidal illness. Concern exists that supraphysiologic doses of T3 in this setting could interfere with protein and fat metabolism and interact synergistically with catecholamines to increase myocardial oxygen demand, with resultant increased arrhythmia, MI, heart failure, and death.

James V. Hennessey, M.D., said two uses for T3 in depressed patients have been explored since the 1960s. One uses small doses of T3 to accelerate response to tricyclic antidepressants or selective serotonin reuptake inhibitors. The other uses T3 to augment antidepressant therapy to convert nonresponders to responders.

Although many psychiatrists continue to use T3 for these purposes, the clinical trials to date provide "inconsistent and noncompelling evidence" for T3 having an antidepressant-acceleration effect, and the only randomized trial of T3 augmentation of SSRI therapy failed to show a benefit and doesn't support the use of T3 in euthyroid-depressed patients, said Dr. Hennessey, an endocrinologist at Brown University, Providence, R.I. ■

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