Titrating Up May Not Be Needed for Hypothyroid

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Initiating a full starting dose of levothyroxine is safe for hypothyroid patients, and is more convenient and cost effective than working up from a lower dose, according to a prospective study.

Annemieke Roos, M.D., of the Medical Centre Rijnmond-Zuid in Rotterdam, the Netherlands, and colleagues, observed that "high doses of levothyroxine have been given to patients with myxedema coma, a patient group in whom a high prevalence of cardiac ischemia would be expected, without untoward effects," except when levothyroxine is combined with T_3.

In their study, the investigators questioned what they called the "dogma of 'start low and go slow' irrespective of age or patient," a concept they said was based on the association of hypothyroidism with ischemic heart disease (Arch. Intern. Med. 2005;165:1714-20).

Participants in the blinded study included 50 patients aged 22-86 years with first-diagnosed, untreated, primary autoimmune hypothyroidism. None of the patients had asymptomatic cardiac ischemia as demonstrated by dobutamine stress echocardiography or bicycle ergometry.

Study participants were randomized into two equal cohorts, and were started on either a high-dose regimen of oral levothyroxine (1.6 mcg/kg) or a low-dose (25 mcg) regimen that was initially adjusted with increments of 25 mcg every 4 weeks. Then, from 24 weeks onward, the dose was adjusted every 12 weeks according to serum thyrotropin and free thyroxine (FT_4) levels within the normal reference range (euthyroidism) as a target of treatment.

"At 4 weeks, median serum thyrotropin level[s] had normalized in the full-dose group… whereas in the low-dose group, the median thyrotropin level normalized only at 16 weeks," the researchers said. "A similar significant difference between the full-dose and low-dose groups with regard to the normalization of the mean FT_4 and T_3 plasma levels was observed."

There were no statistically significant differences in lipid or serum creatine kinase levels between the two groups.

"Starting healthy, adult patients aged 65 or older, or those older than 65 years with hypothyroidism but no history of ischemic heart disease, on a full dose of levothyroxine is supported by this study," Dr. Roos and associates said. They noted that no cardiac events were observed in the study participants.

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Dr. Roos and colleagues said that they believe their findings suggest that the prevalence of asymptomatic coronary artery disease in patients with untreated primary hypothyroidism is very low. They added that because patients with cardiac histories were excluded, "the findings … are possibly not applicable to patients with coronary artery disease."

In an accompanying editorial, Leonard Wartofsky, M.D., of Washington Hospital Center, argued that there are still no compelling reasons to "go fast" (Arch. Intern. Med. 2005;165:1683-4).

"Myxedema coma still has a high mortality rate, and we cannot be certain whether a given patient's death might not have been due to aggressive levothyroxine therapy," he said.

Dr. Wartofsky pointed out that the experimental protocol that Dr. Roos and colleagues used for the slow-titration group doesn't reflect what would be done in actual practice.

"Most cases of hypothyroidism are due to underlying Hashimoto disease, and a significant percentage of these patients have associated diabetes mellitus," he said. "Given the high prevalence of coronary artery disease in patients with diabetes, I do not think that it is sufficient to rely on a history of 'no known ischemic heart disease' in such patients as validating the initiation of full-replacement dosage."

Dr. Wartofsky also questioned the value of excluding patients with asymptomatic cardiac ischemia on the basis of dobutamine stress echocardiography. ■