CV Risk Not Caused by Radioiodine Therapy

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VANCOUVER, B.C. — The increased risk of vascular death seen in a recent study of hyperthyroid patients treated with radioiodine was confined to the period before they became hypothyroid and went on thyroxine replacement therapy, Jayne A. Franklyn, M.D., said at the annual meeting of the American Thyroid Association.

"We can speculate that the increased risk of vascular deaths was seen only in patients before they became hypothyroid because developing an underactive thyroid is an indicator of the complete cure of hyperthyroidism," said Dr. Franklyn, professor of medicine at the University of Birmingham (England).

In an earlier population-based study of 7,209 hyperthyroid Birmingham-area patients treated with radioiodine between 1950 and 1989 with 105,000 person-years of follow-up, all-cause mortality was 13% greater than in the age- and gender-matched general U.K. population. Mortality rates due to cardiovascular and cerebrovascular disease, thyroid disease, and fracture of the femur were all significantly increased, which raised the possibility that the increased mortality might be due to an adverse effect of radioiodine. However, Dr. Franklyn and her coinvestigators noted that the excess mortality was greatest in the first year following radioiodine therapy and might be a result of the hyperthyroidism, which was often most severe around the time of radioiodine therapy, they said (N. Engl. J. Med. 1998;338:712-8).

In her latest study, Dr. Franklyn reported on 2,668 Birmingham-area patients over age 40 who received radioiodine for hyperthyroidism in 1984-2002. During nearly 16,000 person-years of follow-up, all-cause mortality rose by 14% vs. that in a matched U.K. general population, while vascular mortality was increased by 19%.

The key finding was that the mortality increase was confined to the 1,456 patients who had not received thyroxine after radioiodine therapy, typically because their hyperthyroidism had not been completely cured. Patients who had not received T4 had a 26% greater all-cause and 32% greater vascular mortality, compared with the matched general population. In contrast, patients on T4 replacement had nonsignificant 8%-10% reductions in mortality relative to the general population. ■

Food Interferes With Rapid-Release L-T4

VANCOUVER, B.C. — Bioavailability of even the newer rapid-release formulation of levothyroxine known as Levoxyl is reduced 40% by taking the tablets close to a meal, Michael J. Lamson, Ph.D., said at the annual meeting of the American Thyroid Association.

The hope was that Levoxyl's rapid release might permit a new flexibility in dosing, allowing patients to take the drug in proximity to meals instead of on an empty stomach, as recommended for L-T4 therapy. But that wasn't the case in the first large study to assess the effects of a meal on oral absorption of L-T4 using the Food and Drug Administration's formal bioequivalence methodology, said Dr. Lamson of King Pharmaceuticals R&D in Cary, N.C.

He reported on 48 healthy participants in a randomized, three-way crossover trial. They took two 300-mcg tablets of Levoxyl on three occasions, each separated by a 35-day washout. One dose was taken under fasting conditions. The second dose was taken 10 minutes before eating a meal and the third dose was taken just after a meal.

Bioavailability of L-T4 was reduced by 40% regardless of whether subjects took the drug shortly before or immediately after the meal. This is a clinically significant finding, because it is well established that even small changes in L-T4 bioavailability can have a profound impact upon the success of oral replacement therapy.

In clinical terms, this means that taking rapid-release L-T4 in proximity to a meal or a medication known to interfere with L-T4 renders a 100-mcg dose of Levoxyl equivalent to a 60-mcg dose, Dr. Lamson said. Patients who have been taking their L-T4 with meals may require a dose correction of up to 40%.

—Bruce Jancin