L-thyroxine requirement in patients with autoimmune hypothyroidism and parietal cell antibodies.

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SUMMARY

Background: Hypothyroid patients on T4 therapy may require replacement doses exceeding the theoretical needs to normalize serum TSH due to low patient compliance, drugs interference, and malabsorption.

Objective: The authors examined whether autoimmune gastritis might cause increased T4 requirement in patients with autoimmune thyroiditis receiving L-thyroxine replacement.

Patients: The authors studied 391 patients with clinical or subclinical hypothyroidism from autoimmune thyroiditis who had achieved normal serum TSH concentration (0.3-3.0 µU/ml) under T4 for at least 6 months. Patients were screened for serum parietal cell antibodies (PCA) as a marker of autoimmune gastritis, and the PCA status was correlated with the T4 dose. They also studied a group of 60 patients receiving T4 replacement after total thyroidectomy.

Results: PCA-positive (155/391) and PCA-negative (236/391) patients did not differ for pre-therapy serum TSH levels and thyroid volume. The T4 requirement was significantly (P = 0.002) higher in PCA-positive (1.24 µg/kg/d) than in PCA-negative patients (1.06 µg/kg/d), and a significant positive correlation was found between T4 requirement and serum PCA levels. Among PCA-positive patients, T4 requirement was even higher in those with proven gastritis (1.52 µg/kg/d) compared with those without gastric damage (1.15 µg/kg/d) (P < 0.0001). The increased T4 requirement was confirmed also in PCA-positive thyroidectomized patients (1.81 µg/kg/day) compared with PCA-negative thyroidectomized patients (1.52 µg/kg/d). Independent variables affecting T4 requirement were PCA and serum TSH at diagnosis.

Conclusion: Autoimmune gastritis is an additional factor affecting T4 requirement in patients with autoimmune thyroiditis. Serum PCA measurement should be considered in patients with an unexplained high requirement of T4.

COMMENT

This commentator has purposely coupled present interesting article with the previous one (Thyroid Update 2008-II-10). In replacement therapy with L-thyroxine (T4) for hypothyroidism, the classical way to estimate T4 requirements is based on body weight, using the average figure of 1.6-2.0 µg/Kg body weight per day (at least, for a full replacement). Such theoretical calculation depends also, in practice, upon possible interfering factors, namely low compliance, reduced intestinal drug absorption, modified metabolism of thyroid hormones, possible interferences with other substances or medications, especially iron supplements, some statins, calcium carbonate, antacids, inhibitors of proton pump, soy proteins and high fiber.
intake. Recently, *Helicobacter pylori* infection has been indicated as an additional cause of reduced L-T4 absorption, secondary to atrophic gastritis and impaired gastric secretion.

The frequent association of autoimmune thyroiditis with parietal cells antibodies (PCA) in the context of atrophic body gastritis prompted the authors to investigate whether such an association might constitute an additional cause for increased T4 requirements in patients receiving thyroid hormone. Among 697 consecutive patients with hypothyroidism secondary to autoimmune thyroiditis and receiving T4, seen in their institution (2004 to 2006), 391 patients remained eligible for further study after applying exclusion criteria delineated in detail in the article. In these 391 patients, PCA were found in 155/391 (i.e. 40%). While patients with/without PCA did not differ by clinical criteria, they differed significantly by the mean T4 dosage required to maintain a euthyroid status: 1.24 versus 1.06 µg/kg/day, i.e. 17% higher. Seventy-three PCA positive patients benefited from gastric endoscopy: 47/73 patients were shown to have histologically proven gastric atrophy. In them, difference in daily T4 requirement was even greater: 1.52 versus 1.15 µg/kg/day, i.e. 32% higher.

The mechanism likely responsible for reducing T4 absorption in PCA-positive patients may be related to the impaired chlorhydric acid secretion as a result of the chronic damage of the gastric mucosa and particularly the reduced number and function of oxyntic glands.

The authors concluded that when hypothyroid patients have unexplained high T4 requirements, measurements of PCA (and gastric endoscopy?) should be included in the work-up of the patients.

*(Daniel Glinoer, M.D.; Ph.D.)*

See Figure