

Showing That a Persistently Hypothyroid Patient Has an Increase of Free T₄ Two Hours after Ingestion of 1 mg of Levothyroxine May Overcome Nonadherence

Jerome M. Hershman

Walker JN, Pallai S, Ibbotson V, Vincent A, Karavitaki N, Weetman A, Wass JA, Allahabadia A. A thyroxine absorption test followed by weekly thyroxine administration: a method to assess non-adherence to treatment. Eur J Endocrinol 2013;168:913-7.

SUMMARY • • • • • • • • • • •

Background

Many patients taking levothyroxine (L-T₄) at a dose considered appropriate based on body weight have an elevated serum TSH, even after they have a normal serum TSH while taking the same dose of L-T₄. This may be due to ingestion of food with the dose or taking drugs that block absorption, such as iron, calcium, bile acid-sequestering resins, or phosphate binders or taking drugs that accelerate degradation of L-T₄, such as diphenylhydantoin. Patients may not absorb L-T₄ because of celiac disease, atrophic gastritis, or gastrointestinal surgery. When these causes have been eliminated, the issue of noncompliance, or nonadherence in current terminology, arises. Most patients deny this behavior. The current study used administration of a weekly dose of L-T₄ under observation to determine whether nonadherence was a probable cause of the elevated serum TSH.

Methods

At two sites in the United Kingdom, patients were identified who had a serum TSH persistently above 5.5 mU/L despite adequate daily doses of L-T₄ and no evidence of interfering drugs or diseases. The patients had baseline measurements of FT₄ and TSH; then each patient received an oral weekly dose of L-T₄ and had a measurement of FT₄ at 60, 120, 180, and 240 minutes

after ingestion of the L- T_4 . The patient continued on the same weekly dose of L- T_4 given under supervision for 4 weeks with serum TSH measurement 1 week after the final dose.

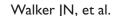
Results

Twenty-three patients participated in the study. The mean age was 45 years (range, 20 to 88) and the median weight 87 kg (range, 53 to 143). The mean (±SD) TSH before the study was 41±45 mU/L and the mean prestudy L-T₄ dose was 2.31±0.56 μg/kg/day. The mean weekly dose administered was $7 \times 1.69 \pm 0.2 \,\mu\text{g/kg}$. In 19 of the 23 patients, the maximal rise in serum FT₄ occurred by 120 minutes, with almost a doubling of FT4 at this time, increasing from 13 at baseline to 25 pmol/L at 120 minutes. The 3 patients with the most severe hypothyroidism had the lowest rise in FT₄ at 120 minutes. At the final blood test after 4 weeks of treatment, TSH was reduced in 17 of 23 patients (47±50 at baseline to 18±21 mU/L). In 6 patients, the 4-week TSH was higher than the baseline.

Conclusions

Measurement of FT_4 120 minutes after a weight-related weekly dose of L- T_4 can be used to show maximal T_4 absorption and aid in overcoming nonadherence with therapy.

continued on next page





Showing That a Persistently Hypothyroid Patient Has an Increase of Free T4 Two Hours after Ingestion of 1 mg of Levothyroxine May Overcome Nonadherence

ANALYSIS AND COMMENTARY • • •

This study addresses an important problem, namely, nonadherence with L-T₄ therapy resulting in persistent hypothyroidism, a common occurrence and a very difficult issue to deal with. The authors emphasize a principle of treatment: "adherence to medication is the key link between process and outcome in medical care and without it, the likelihood of treatment failure is high." The serum TSH provides a simple way to document nonadherence. Many years ago, my colleagues and I studied serum TSH levels in our endocrine clinic population and found that about 7% who previously had a normal TSH while taking a given dose of L-T₄ had an elevated TSH during long-term follow-up (1). When confronted with the possibility of nonadherence with the dose, less than half of the patients admitted to it. For the patients who frequently forget to take L-T₄ on a daily basis, a weekly dose can be given and is usually without side effects because of the long half-life of L-T₄ (2).

In the article reviewed here, the average patient in the study received 1030 μ g of L-T₄ as the weekly dose.

The weekly doses may have borne some relationship to the prescribed doses that were presumably not ingested by the patients with any regularity, but the reasons for the variations in dose were not clearly stated. The failure to normalize serum TSH in a high proportion of the patients in this study is most likely due to the fact that it can take serum TSH as long as 6 weeks to normalize on a given optimal dose of L-T₄; 4 weeks was too short a time for this to occur. In fact, 6 of the 23 patients had an even higher TSH at the end of the study, indicating that the estimated weekly dose was too low for these patients.

The main conclusion is that giving the nonadherent patient a 1 mg dose of L- T_4 in the office and measuring FT₄ at baseline and at 2 hours will show that the patient can absorb the dose. Whether the nonadherent patient will become adherent after demonstrating that she can absorb L- T_4 is another issue. The authors recommend a nonjudgmental discussion about adherence. In my experience, few patients admit to being nonadherent as the basis for their elevated serum TSH, but the absorption test could help if the patient agrees to do it.

References

- 1. England ML, Hershman JM. Serum TSH concentration as an aid to monitoring compliance with thyroid hormone therapy in hypothyroidism. Am J Med Sci 1986;292:264-6.
- Grebe SK, Cooke RR, Ford HC, Fagerström JN, Cordwell DP, Lever NA, Purdie GL, Feek CM. Treatment of hypothyroidism with once weekly thyroxine. J Clin Endocrinol Metab 1997;82:870-5.