LEVOTHYROXINE INGESTION IN THE EVENING RESULTS IN BETTER ABSORPTION THAN INGESTION BEFORE BREAKFAST

Bolk N, Visser TJ, Nijman J, Jongste IJ, Tijssen JG, Berghout A. **Effects of evening vs morning levothyroxine intake: a randomized double-blind crossover trial.** Arch Intern Med 2010;170:1996-2003.

SUMMARY

BACKGROUND

Levothyroxine is usually taken in the morning on an empty stomach because food may interfere with its absorption. The purpose of this study was to determine whether taking levothyroxine at bedtime results in better absorption and improved clinical outcome than taking it before breakfast.

METHODS

This was a randomized double-blind crossover trial in which patients took a capsule of levothyroxine or placebo 30 minutes before breakfast or before sleep on an empty stomach. The patients were all on stable doses of levothyroxine for at least 6 months. Patients with thyroid cancer, gastrointestinal disorders that could alter thyroxine absorption, and medicines that could interfere with thyroxine absorption were excluded. The capsules were formulated from commercial levothyroxine sodium using lactose monohydrate as the excipient. Blood samples for measurement of thyrotropin (TSH), free thyroxine (T_4), total triiodothyronine (T_3), and lipids were obtained at baseline and every 6 weeks Patients were crossed over to the other time of ingestion at 12 weeks. The thyroid parameters were compared at the 12- and 24-week intervals for each mode of administration. Patients also completed questionnaires concerning general health, fatigue, and symptoms of thyroid dysfunction at baseline and at 12 and 24 weeks.

RESULTS

Of the 105 patients who entered the study, 90 completed it. The mean age was 48 years, the duration of hypothyroidism varied from 0.5 to 25 years, and the dose of levothyroxine varied from 50 to 250 µg with the median being 100 or 125 µg. Bedtime levothyroxine intake resulted in a decrease in TSH of 1.25 mIU/L (95% confidence interval [CI], 0.60 to 1.89; P_=0.001) relative to morning levothyroxine intake, an increase in free T_4 of 0.07 ng/dl (95% CI, 0.02 to 0.13; P = 0.01), and an increase in T_3 level of 6.5 ng/dl (95% CI, 9.0 to 12.10; P = 0.02). There were no differences between the two dosing regimens in quality of life, symptoms of fatigue, thyroid symptoms, or lipid levels. At 1 year after completion of the trial, a majority of the patients preferred the evening dose.

CONCLUSION

Ingestion of levothyroxine at bedtime resulted in better absorption than ingestion 30 minutes before breakfast.

COMMENTARY

The results of this study are consistent with anecdotal reports showing that absorption of levothyroxine is better, indicated by a lower TSH and higher free T_4 on the same dose, when the pill is taken at bedtime rather than before breakfast. However, another carefully performed study came up with the opposite result (1). In that study, breakfast was delayed for at least 60 minute before the ingestion of levothyroxine. Perhaps the interval of 30 minutes used in the study under discussion was too short to prevent food ingestion from interfering with levothyroxine absorption. However, there were differences in the study populations, such as inclusion of thyroid cancer patients in the study by Bach-Huynh et al (1).

In a number of my patients who had otherwise unexplained fluctuating serum TSH levels on the same dose of levothyroxine when they took it before breakfast, I found that changing the dose to bedtime resulted in a more reliable serum TSH level. As someone who eats breakfast as soon as possible after arising, I can sympathize with patients who do not want to wait 1 hour before eating breakfast. Let me hear from you about your experience in regard to the optimal time for taking levothyroxine.

— Jerome M. Hershman, MD

Reference

1. Bach-Huynh TG, Nayak B, Loh J, Soldin S, Jonklaas J. Timing of levothyroxine administration affects serum thyrotropin concentration. J Clin Endocrinol Metab 2009;94:3905-12.