FPIN's Clinical Inquiries

Morning vs. Evening Administration of Levothyroxine

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Clinical Question

Does taking levothyroxine in the evening vs. morning reduce its effectiveness for reducing thyroid-stimulating hormone (TSH) levels?

Evidence-Based Answer

The effectiveness of levothyroxine for reducing TSH levels is most dependent on the timing of meals in relation to drug administration. (Strength of Recommendation: C, disease-oriented outcome.) There is conflicting evidence. In two studies, levothyroxine taken at least two hours after eating in the evening maintained or improved TSH levels compared with morning administration. However, another study found that evening administration was less effective than administration at least 60 minutes before breakfast.

Evidence Summary

A 2010 randomized, double-blind, placebo-controlled, crossover study of 90 adults with primary hypothyroidism compared whether taking levothyroxine 30 minutes before breakfast vs. at bedtime affected TSH levels.[1] Patients had been receiving a stable levothyroxine dosage for at least six months before the study, and those with thyroid carcinoma were excluded. Patients received each regimen for three months, and reported not eating for several hours before bedtime administration. Bedtime administration significantly decreased TSH levels by 1.25 mIU per L compared with morning administration (95% confidence interval, 0.60 to 1.89). In a 24-week period, patients missed a mean of 1.3 capsules in the morning and 1.9 capsules in the evening ($P = .54$).

A 2009 randomized crossover study compared the effects of administering levothyroxine in the morning at least one hour before breakfast, within 20 minutes of breakfast, and at bedtime (at least two hours after eating).[2] TSH levels were measured in 65 adults with primary hypothyroidism who had been on stable levothyroxine dosages for at least six months. All patients received each levothyroxine regimen for eight weeks. Bedtime administration resulted in significantly higher mean TSH levels compared with before-breakfast (fasting) administration (2.19 mIU per L vs. 1.06 mIU per L; $P < .001$), but significantly lower mean TSH levels compared with breakfast (nonfasting) administration (2.19 mIU per L vs. 2.93 mIU per L; $P = .026$). Changes to meal timing, medication compliance, or levothyroxine timing occurred at a rate of 1.2%.

A 2015 randomized, double-blind, placebo-controlled, crossover study compared the effects of morning (30 minutes before breakfast) vs. evening (60 minutes before dinner) administration ▶

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of levothyroxine in 50 adults with hypothyroidism.[3] A therapeutic TSH level was required for inclusion. Patients received each regimen for 60 days, and TSH levels were measured at the end of each phase. Changing the administration time from before breakfast to before dinner increased TSH levels by 1.47 mIU per L ($P = .001$). Medication compliance was not monitored.

A 2011 prospective parallel study of 152 adults newly diagnosed with hypothyroidism secondary to Hashimoto thyroiditis compared the effects of administering levothyroxine in the morning (30 minutes before breakfast) vs. evening (at least two hours after dinner).[4] Levothyroxine was initiated at a dosage of 1.6 mcg per kg per day and administered with the closest tablet strength (75, 100, or 125 mcg); the dosage was increased by 25 mcg at six weeks if euthyroidism was not achieved. At 12 weeks, there was no significant difference in mean TSH levels between the morning and evening dosing groups (5.13 mIU per L vs. 3.27 mIU per L; $P = .31$). Medication compliance was not reported.

Recommendations from Others

The American Thyroid Association recommends that levothyroxine be consistently taken 60 minutes before breakfast or at bedtime, at least three hours after dinner.[5]

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