DOES EXTREME OBESITY AFFECT THYROID HORMONE METABOLISM?


SUMMARY

BACKGROUND

These authors previously reported that euthyroid but severely obese subjects have higher levels of triiodothyronine (T₃), thyroxine (T₄) and thyrotropin (TSH) than normal controls, and suggested that the morbidly obese have reset their "central thyrostat" (1).

METHODS

The authors assessed the kinetics of serum T₃ and T₄ after giving 600 µg of levothyroxine (L-T₄) as an oral solution to 16 men and 22 women who were apparently euthyroid but severely obese (mean ±SD body-mass index [BMI; the weight in kilograms divided by the square of the height in meters] 48.6±8.3) and to 24 age-matched controls (mean BMI, 23.3±1.7). None of the study participants was taking any medication, had positive anti-thyroid peroxidase antibodies or any thyroid disease, or had other co-morbidities. There was no mention of smoking status. The mean basal serum TSH was 2.3±1.0 µIU/ml and the mean total T₄ was 8.7±1.3 µg/dl in the obese subjects, as compared with 1.3±0.9 and 7.5±1.3 in the controls (both P<0.001). After a 12-hour fast, the subjects were given 600 of µg L-T₄ in the morning, and blood was sampled for the next 4 hours.

RESULTS

Administering L-T₄ caused the mean serum T₃ to fall 7% in the morbidly obese subjects (from 137±16 to 128±14) at 2 hours, whereas it rose 17% (from 133±19 to 155±21) in the controls (P<0.001). The serum T₄ level rose in both groups, but it peaked later in the obese group (2.5±0.9 vs. 1.9±0.1 hr; P<0.01). Based on estimated plasma volume and the assumption that giving exogenous L-T₄ did not suppress the release of endogenous T₄ and TSH and that the endogenous production of T₄ remained constant during the study period, the calculated area under the curve was lower for obese subjects (13.5±7.4 vs. 19.1±5.4 P< 0.01), as was the maximum concentration of T₄ (5.1±2.3 vs. 6.4±1.8, P<0.05) as compared with controls.

CONCLUSIONS

The authors concluded that severely obese individuals may require higher doses of L-T₄ than normal and that impaired L-T₄ pharmacokinetics such as delayed gastrointestinal absorption might be involved. The reason for the small decrease in serum T₃ was not clear.

COMMENTARY

In view of reports of accelerated gastric emptying in morbidly obese patients, it would have been helpful if there was some other evidence of jejunoileal malabsorption to support the authors’ suggestion that delayed L-T₄ absorption was involved. Knowing the smoking history of the subjects would have been helpful, in view of the strong correlation between current smoking, BMI, and TSH levels in Norwegian men and women (2). That study also found a strong correlation between BMI and “subclinical hypothyroidism” in current smokers, as well as in never-smokers (2).

Many studies have found a direct correlation between BMI and TSH levels in apparently healthy individuals whose thyroid hormone and TSH levels are in the normal range. There is controversy concerning whether some of these individuals have “subclinical hypothyroidism,” however. It has been suggested that elevated antithyroid antibodies need to be present before entertaining the diagnosis in such cases (3).

The L-T₄ dose required to maintain euthyroidism in thyroidectomized subjects has been reported to be directly related to circulating interleukin (IL)-6 levels (4), and cells in adipose tissue from obese subjects continued on next page
are known to release more IL-6. A recent study on a variety of human cells reported that IL-6 blocks their conversion of T₄ to T₃ while increasing their inactivation of both T₃ and T₄, apparently by depletion of an intracellular thiol co-factor (5). Could the higher levels of IL-6 in severely obese individuals affect the way such individuals metabolize L-T₄?

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References


