Subject: UNUSUAL ELEVATION OF SERUM TSH IN ITALY (and elsewhere?)

Title: Altered intestinal absorption of L-thyroxine caused by coffee.

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Reference: Thyroid 18: 293-301, 2008

SUMMARY

Objective: To report eight case histories, as well as in vivo and in vitro studies showing coffee's potential to impair L-thyroxine (T4) intestinal absorption.

Design: Of eight women with inappropriately high or non-suppressed thyroid-stimulating hormone (TSH) when T4 was swallowed with coffee/espresso, six consented to the evaluation of their T4 intestinal absorption. This in vivo test was also administered to 9 volunteers. In three separate tests, two 100 µg T4 tablets were swallowed with coffee, water, or water followed, 60 minutes later, by coffee. Serum T4 was assayed over the 4-hour period of the test. Two patients and two volunteers also agreed on having tested the intestinal absorption of T4 swallowed with solubilized dietary fibers. In the in vitro studies, classical recovery tests on known concentrations of T4 were performed in the presence of saline, coffee, or known T4 sequestrants (dietary fibers, aluminium hydroxide, and sucralfate).

Main Outcome: For the in vivo test, average and peak incremental rise of serum T4 (AIRST4 and PIRST4), time of maximal incremental rise of serum T4 (TMIRST4), and area under the curve (AUC) were determined. In patients and volunteers, the four outcome measures were similar in the water and water + coffee tests. In patients and volunteers, compared to water, coffee lowered AIRST4 (by 36% and 29%), PIRST4 (by 30% and 19%), and AUC (by 36% and 27%) and delayed TMIRST4 (by 38 and 43 minutes); bran was a superior interferer. In the in vitro studies, coffee was weaker than known T4 sequestrants.

Conclusions: Coffee should be added to the list of interferers of T4 intestinal absorption, and T4 to the list of compounds whose absorption is affected by coffee.

COMMENT

Several substances & pharmacological agents have been shown to interfere with thyroid hormones, and various mechanisms underlie these interferences. For instance, estrogen derivatives act on thyroid hormone (TH) binding proteins and TH metabolism. Others agents such as salicylates, heparin, carbamazepine, phenytoine & coumarine derivatives act directly on TH binding properties and metabolism. Others, such as rifampicine, act by yet unexplained mechanisms. A series of substances have also been shown to interfere directly with the gastrointestinal absorption of L-thyroxine (T4) given orally for treatment of hypothyroidism. Among these, the most frequently considered are bile acid sequestrants, calcium salts, raloxifene, sucralfate (a sucrose sulfate-aluminum complex used to treat peptic ulcers) and other aluminium or magnesium hydroxides, ferrous sulphate (forming a ferric-thyroxine complex in the gastro-
intestinal tract), inhibitors of proton pump, soy proteins and dietary fiber supplements, not to mention obviously the interferences due to malabsorptive digestive disorders (such as celiac disease, etc.) and non compliance (the first item to consider when something goes unexpectedly wrong with T4 administration).

To obviate such potential interferences, it is recommended to administer T4 in the morning on an empty stomach with 1-2 teaspoonfuls of water, and then wait for at least 15 minutes before eating breakfast. Recently, we commented on an interesting article showing improvement in T4 absorption when the medication was taken in the evening before bedtime, i.e. several hours after the last meal (see Thyroid Update 2007-II-6; article by Bolk et al.).

In the present article, our Italian colleagues discovered something quite unusual: altered T4 absorption caused by morning coffee. The data are convincing, with 8 clinical observations of elevated TSH in hypothyroid T4-treated patients who drank their ‘usual’ espresso(s) with the T4 intake and normalisation of serum TSH, using the same T4 dosage, when the espresso was replaced by … water (this is a crime for an Italian waking up). They also investigated indices of T4 absorption in an acute loading test using 200 µg of T4 in volunteers, and showed delayed absorption when taken with coffee.

Thus in conclusion, coffee should be added to the list of potential interfering substances with the absorption of oral T4. Noteworthy, all patients were women and we do not know whether the same would occur in men. However (for this reason), some of the volunteers were men. The effect of coffee was variable from one individual to another, but it seems clear that liquid coffee (freshly brewed espresso) is capable of sequestering T4 in vitro, an additional proof of its potential interfering effect in vivo. Finally, it should be noted that Italian (or for that matter Sicilian) espresso is quite strong and also that some patients had the habit of drinking 2 or 3 cups with the T4 intake. It remains to be seen whether the same phenomenon would occur with Belgian coffee (American coffee cannot seriously be called coffee) but, in the mean time, this may explain some unusual observations in some of our own patients.

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

See Example below

<table>
<thead>
<tr>
<th>Case no. (age)</th>
<th>Relevant history</th>
<th>TSH (mIU/L) when L-T4 swallowed with</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Water</td>
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<tr>
<td>1 (62 years)</td>
<td>A bank employee with primary hypothyroidism (TSH = 32 mU/L) due to Hashimoto’s thyroiditis. Treated with 100 µg/day L-T4 (1.7 µg/[kg BW·day]), which she swallowed with water 1 h prior to breakfast, TSH was normalized. Four years later, she returned to us hypothyroid (TSH = 24.7 mU/L). The same dose of L-T4 was swallowed with a double espresso, and another cup was drank 5–10 min later. Over the next 4 years, TSH was normal when she returned to swallow the same dose of L-T4 with water, 30 min prior to coffee. Finally, TSH increased again (4.7–6.9) when she swallowed L-T4 either with one cup of espresso or with water, but followed by one cup of espresso 1–5 min later.</td>
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<td>0.9–1.9</td>
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