Available online at www.sciencedirect.com

SCIENCE DIRECT®

Metabolism Clinical and Experimental 54 (2005) 559–560

Metabolism
Clinical and Experimental

www.elsevier.com/locate/metabol

Letter to the Editor

Emerging cardiovascular risk factors in subclinical hypothyroidism: lack of change after restoration of euthyroidism

To the Editor,

In the November 2004 issue, Perez et al postulated that the clinical use of emerging cardiovascular risk factors in the clinical management of subclinical hypothyroidism (SH) is unwarranted [1].

If and when L-T4 treatment should be initiated in patients with SH still remains controversial. Most authorities in the field would agree that such treatment should be reserved for older patients with TSH greater than 10 or 12 μU/mL as well as patients with concomitant diseases, such as depression, infertility, and overt hyperlipidemia [2]. Some studies have associated subtle changes in thyroid function with increased risk of coronary artery disease [3]. Lipid abnormalities would offer the most obvious explanation for this phenomenon, but several studies have shown conflicting results concerning not only the degree of lipid changes in SH but also the effect of L-T4 substitution therapy [3].

Our research team keeps a special interest in SH. In our cohort, subjects with SH (n = 66) exhibited significantly higher levels of total cholesterol (TC), LDL cholesterol (LDL-C), apolipoprotein (Apo) B, and lipoprotein(a) [Lp(a)], thus displaying a more atherogenic lipid profile when compared with healthy individuals. L-T4 resulted in a nonsignificant reduction in total, LDL-C, and ApoB levels [4]. However, in 14 SH patients whose pretreatment total cholesterol levels exceeded 240 mg/day, L-T4 substitution resulted in a significant fall in TC, LDL-C, and ApoB levels [4].

In a subsequent study, we found that SH patients exhibited higher median values of Lp(a) compared with the control group (10.6 vs 6.0 mg/dL; P = .003) [5]. No significant differences in the frequencies of Apo(a) phenotypes were detected between patients with SH and the control group, thus emphasizing that raised Lp(a) values in patients with SH are not due to a genetic predisposition. Restoration of a euthyroid state via L-T4 treatment had a favorable effect on Lp(a) levels in the whole group of patients (median values 10.6 mg/dL pretreatment vs 8.9 mg/dL posttreatment; P = .008) [5]. Although initial Lp(a) concentrations decreased after treatment, posttreatment Lp(a) levels were higher compared with controls. Notably, a significant reduction in Lp(a) was evident in patients with low-molecular-weight Apo(a) isoforms associated with high pretreatment Lp(a) levels (median values 26.9 vs 23.2 mg/dL pre- and posttreatment, respectively; P = .03) [5]. In contrast, this beneficial effect of L-thyroxine was not observed in patients with low to moderate Lp(a) values [associated with high-molecular-weight Apo(a) isoforms]. We suggest that the 10% reduction in Lp(a) in this group of patients was very small, thus leaving the question of whether this could represent any clinical benefit with regard to atherosclerotic disease an unanswered question.

All things considered, in line with the findings of Perez et al [1], it appears that monitoring and targeted treatment of emerging cardiovascular risk factors in SH cannot at this time be justified.

References

[1] Perez A, Cubero JM, Sucunza N, Ortega E, et al. Emerging cardiovascular risk factors in subclinical hypothyroidism: lack of change after restoration of euthyroidism. Metabolism 2004;53:1512-5.
[2] Cooper DS. Subclinical thyroid disease: A clinician's perspective. Ann Intern Med 1998;129:135-8.
[3] Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism. Thyroid 2000;10:665-79.
[4] Efstathiadou Z, Bitsis S, Milionis HJ, et al. Lipid profile in subclinical hypothyroidism: is L-thyroxine substitution beneficial? Eur J Endocrinol 2001;145:705-10.
[5] Milionis HJ, Efstathiadou Z, Tselepis AD, et al. Lipoprotein(a) levels and apolipoprotein(a) isoform size in patients with subclinical hypothyroidism: effect of treatment with Levothyroxine. Thyroid 2003;13:365-9.

Haralampos J. Milionis
Alexandros D. Tselepis
Agathocles Tsatsoulis
Moses S. Elisaf
Department of Internal Medicine
Medical School
University of Ioannina
GR 451 10 Ioannina, Greece
E-mail address: hmilioni@cc.uoi.gr

0026-0495/$ - see front matter
doi:10.1016/j.metabol.2005.01.001