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Title: Combined therapy with levothyroxine and liothyronine in two ratios, compared with levothyroxine monotherapy in primary hypothyroidism: a double-blind, randomized, controlled clinical trial.

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Source: The Journal Of Clinical Endocrinology And Metabolism [J Clin Endocrinol Metab] 2005 May; Vol. 90 (5), pp. 2666-74. *Date of Electronic Publication:* 2005 Feb 10.

Publication Type: Clinical Trial; Comparative Study; Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't

Language: English

Journal Info: *Publisher:* Oxford University Press *Country of Publication:* United States *NLM ID:* 0375362 *Publication Model:* Print-Electronic *Cited Medium:* Print *ISSN:* 0021-972X (Print) *Linking ISSN:* 0021972X *NLM ISO Abbreviation:* J. Clin. Endocrinol. Metab. *Subsets:* Core Clinical (AIM); MEDLINE

Imprint Name(s): *Publication*: 2017- : New York : Oxford University Press
Original Publication: Springfield, Ill. : Charles C. Thomas

MeSH Terms: Hypothyroidism/*drug therapy
Thyroxine/*administration & dosage
Thyroxine/*therapeutic use
Triiodothyronine/*administration & dosage
Adolescent ; Adult ; Aged ; Cognition/drug effects ; Double-Blind Method ; Drug Therapy, Combination ; Female ; Humans ; Male ; Middle Aged ; Thyrotropin/blood

Abstract: Controversy remains about the value of combined treatment with levothyroxine (LT4) and liothyronine (LT3), compared with LT4 alone in primary hypothyroidism. We compared combined treatment with LT4 and LT3 in a ratio of 5:1 or 10:1 with LT4 monotherapy. We conducted a double-blind, randomized, controlled trial in 141 patients (18-70 yr old) with primary autoimmune hypothyroidism, recruited via general practitioners. Inclusion criteria included: LT4 treatment for 6 months or more, a stable dose for 6 wk or more, and serum TSH levels between 0.11 and 4.0 microU/ml (mU/liter). Randomization groups were: 1)

continuation of LT4 (n = 48); 2) LT4/LT3, ratio 10:1 (n = 46); and 3) LT4/LT3, ratio 5:1 (n = 47). Subjective preference of study medication after 15 wk, compared with usual LT4, was the primary outcome measure. Secondary outcomes included scores on questionnaires on mood, fatigue, psychological symptoms, and a substantial set of neurocognitive tests. Study medication was preferred to usual treatment by 29.2, 41.3, and 52.2% in the LT4, 10:1 ratio, and 5:1 ratio groups, respectively (chi2 test for trend, P = 0.024). This linear trend was not substantiated by results on any of the secondary outcome measures: scores on questionnaires and neurocognitive tests consistently ameliorated, but the amelioration was not different among the treatment groups. Median end point serum TSH was 0.64 microU/ml (mU/liter), 0.35 microU/ml (mU/liter), and 0.07 microU/ml (mU/liter), respectively [ANOVA on ln(TSH) for linear trend, P < 0.01]. Mean body weight change was +0.1, -0.5, and -1.7 kg, respectively (ANOVA for trend, P = 0.01). Decrease in weight, but not decrease in serum TSH was correlated with increased satisfaction with study medication. Of the patients who preferred combined LT4/LT3 therapy, 44% had serum TSH less than 0.11 microU/ml (mU/liter). Patients preferred combined LT4/LT3 therapy to usual LT4 therapy, but changes in mood, fatigue, well-being, and neurocognitive functions could not satisfactorily explain why the primary outcome was in favor of LT4/LT3 combination therapy. Decrease in body weight was associated with satisfaction with study medication.

Substance Nomenclature: 06LU7C9H1V (Triiodothyronine)
9002-71-5 (Thyrotropin)
Q51BO43MG4 (Thyroxine)

Entry Date(s): *Date Created:* 20050212 *Date Completed:* 20050609 *Latest Revision:* 20131121

Update Code: 20181210

PMID: 15705921

Database: MEDLINE Complete