

# **Desiccated Thyroid Extract Versus Synthetic LT4/T3 Combination Versus LT4 Monotherapy in the Treatment of Primary Hypothyroidism With Special Attention to the Thr92AlaD2 Polymorphism**

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**Introduction:** Before the availability of levothyroxine (LT4), patients were treated with desiccated thyroid extract (DTE). When switching from DTE to LT4, despite adequate dosing based on serum TSH levels, some patients still feel unwell with fatigue, mental foggy, weight gain etc. A recent randomized, crossed over study between DTE vs. LT4 conducted in our department showed that once-daily DTE caused modest weight loss and possible improvement in mental health scores without appreciable adverse effects; also, nearly half of the study patients preferred DTE over LT4. A few studies have shown that LT4/T3 combination had beneficial effects in improving quality of life relative to LT4 alone. Furthermore, it has been reported that patients with CC genotype in the deiodinase type 2 polymorphism responded more favorably with LT4/T3 combination than T4 monotherapy. Hypothesis: This study investigated the efficacy and effectiveness of DTE vs. LT4/T3 combination vs. LT4 monotherapy in hypothyroid patients based on genotypic differences of deiodinase type 2.

**Methodology:** This was a prospective, randomized, double-blind, crossover study. 75 subjects completed the study. There were 3 arms: DTE, LT4+T3 combination, and LT4 alone. Each subject was randomly allocated to one of these 3 arms for 12 weeks randomly. The study was powered to detect the primary outcome. The primary endpoint was post-treatment score on the 36-point thyroid symptom questionnaire. Secondary endpoints were weight, general health questionnaire, the Beck depression inventory, Wechsler Memory testing, lipid panels and thyroid function tests. Analysis was performed with a linear mixed model using subject as a random factor and group as a fixed effect.

**Results:** There was no significant difference between the 3 arms on the thyroid symptom questionnaire ( $p=.32$ ), and the secondary outcomes showed no between group differences. Auditory memory index ( $p=.008$ ), and visual working memory index ( $p=.02$ ) were higher in the Hashimoto's than non-Hashimoto's group. There was no significant primary or secondary outcome difference among various genotypes of deiodinase 2. There was no relationship between Hashimoto's vs. non-Hashimoto's based on genotypes or likelihood of carrying Thr92AlaD2 polymorphism. Though there was no statistically significant preference for any treatment, numerically more patients with Hashimoto's preferred DTE and LT4/T3 combination than LT4-monotherapy.

**Conclusions:** There was no significant difference between hypothyroid patients taking DTE vs. LT4/T3 combination vs. LT4 monotherapy. Numerically, Hashimoto's patients tended to prefer DTE and LT4/T3 combination. Also, there was no observed relationship between Hashimoto's and polymorphism. Further studies with more patients may be needed.