



## Patients with Hypothyroidism Taking Desiccated Thyroid Extract Lost Weight As Compared with an Equivalent Dose of Levothyroxine

The patients were treated with either DTE (Armour) or L-T<sub>4</sub> (Synthroid) in coded identical capsules. After 6 weeks taking the preparation, serum TSH was checked and the dose adjusted, if necessary, to achieve a target level of 0.5 to 3.0 mU/L. When this was achieved, the patients continued on the dose for at least 12 more weeks. Then they were crossed over to the other preparation for 16 weeks.

At the start of the study, and after each period on the thyroid preparation, the patients had biochemical and psychometric evaluations. The biochemical tests included TSH, free T<sub>4</sub>, total T<sub>3</sub>, sex hormone-binding globulin (SHBG), T<sub>3</sub> resin uptake, and reverse T<sub>3</sub>.

The primary outcomes were four psychometric tests, including memory testing using the Wechsler memory scale, Beck Depression Inventory, a thyroid symptom questionnaire, and a quality-of-life general health questionnaire. At the completion of the study, each patient was asked whether he or she preferred the first or the second treatment.

In the statistical analysis, P values <0.05 were considered significant, and there was no adjustment for multiple comparisons.

### Results

A total of 70 patients completed the study (53 women and 17 men; mean age, 51 years [range, 23 to 65]). With regard to the primary outcome, the patients showed no significant difference in symptom scores, answers on general health questionnaires, or neuropsychological testing between the two thyroid replacements. There

was a decrease of 2.86 lb in the weight of patients during DTE therapy as compared with L-T<sub>4</sub> therapy (P<0.001). With regard to drug preference, 34 patients (49%) preferred DTE, 13 (19%) preferred L-T<sub>4</sub>, and 23 (33%) had no preference; the preference for DTE over L-T<sub>4</sub> was statistically significant (P<0.002).

In subgroup analysis, patients preferring DTE had an average of 4-lb weight loss during the DTE treatment as compared with the L-T<sub>4</sub> treatment (P<0.001), and their subjective symptoms—such as concentration, memory, sleep, happiness, and energy level—were significantly better while taking DTE; some tests of memory were objective psychometric parameters that improved significantly during the DTE treatment period, but similar improvements in memory were seen in those who preferred L-T<sub>4</sub> as compared with baseline.

Based on the amounts of each preparation to maintain a normal serum TSH, the mean (±SD) L-T<sub>4</sub> dose during the study was 119.2±38.9 µg/day (range, 75 to 225); and the DTE dose during the study was 80.6±30.0 mg/day (range, 43 to 172). Therefore, 1 mg of DTE would be approximately equivalent to 1.47 µg of L-T<sub>4</sub>.

During the DTE therapy, the serum T<sub>3</sub> and TSH were significantly higher, and the T<sub>4</sub> and FT<sub>4</sub> were significantly lower than during the L-T<sub>4</sub> therapy.

### Conclusions

Desiccated thyroid extract therapy did not result in a significant improvement in quality of life as compared with L-T<sub>4</sub> therapy. DTE caused modest weight loss, and nearly half of the study patients preferred it over L-T<sub>4</sub>.

## ANALYSIS AND COMMENTARY ● ● ● ● ●

In recent years, there have been many studies comparing combinations of L-T<sub>4</sub> and T<sub>3</sub> with L-T<sub>4</sub> alone. In general, these studies have not shown the improvement in psychometric parameters reported in a highly cited study written 14 years ago (3). This has led most clinicians to avoid combination therapies.

In addition, supranormal T<sub>3</sub> levels occurring several hours after ingestion of T<sub>3</sub> will sometimes trigger tachycardia in susceptible patients. In the current study, the mean serum TSH was in the normal range, and indeed the level while taking DTE was very slightly, but significantly, higher than the level during L-T<sub>4</sub> therapy. This indicated that a higher dose was

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not the cause of the weight loss during DTE therapy. Perhaps the elevated serum  $T_3$ , compared with that during  $L-T_4$  therapy, has a greater effect on the thyroid-hormone alpha-receptor that is mainly responsible for caloric expenditure. Celi et al. have reported that subjects with hypothyroidism who are taking  $T_3$  alone in a dose equivalent to that of  $L-T_4$ , based on serum TSH, had reduced weight (4).

Should the present study be used as a basis for more prescriptions for DTE in patients who demand it? DTE is now standardized by its  $L-T_4$  and  $L-T_3$  content. The ratio of potency (micrograms of  $L-T_4$  per milligram of DTE = 1.47) found in this study is smaller than the 1.67 ratio cited in USP drug information (5), but considerably higher than the value of 1  $\mu\text{g}/\text{mg}$  calculated based on TSH suppression to 5 mU/L and to suppression of TRH-induced TSH reported in a study in 1978 (6). This could have been due to different potency or bioavailability of each preparation at that time. Based on the currently stated  $T_4$  and  $T_3$  content of Armour thyroid, 38  $\mu\text{g}$  of  $T_4$  and 9 of  $\mu\text{g}$   $T_3$  per 65 mg of DTE, that is equivalent to about 69.5  $\mu\text{g}$  of  $T_4$ , if one assumes that  $T_3$  is 3.5 times more potent than  $T_4$  when given orally. The ratio of  $L-T_4$  to DTE in micrograms per milligram

(69.5/65 = 1.07), is closer to the 1  $\mu\text{g}/\text{mg}$  proposed in 1978 than the 1.47  $\mu\text{g}/\text{mg}$  found in this study. It requires considerable variability in absorption of the two preparations to arrive at the conclusion that 1 mg of DTE is equivalent to 1.47  $\mu\text{g}$  of  $L-T_4$ . However, the comparison of potency in fact shows large individual variability, so that switching from one preparation to the other requires careful titration in each individual.

Many endocrinologists refuse to prescribe DTE under any circumstances, even telling the patient to find another doctor who may do it. I think that the present study shows that the switch is not so dangerous, as long as the serum TSH remains in the normal range with careful titration of the DTE dose. The many years of satisfactory therapy with synthetic levothyroxine make it the vastly preferred substitution therapy, but for the patient who insists on continuing or trying DTE, I think that it is no more dangerous than adding some additional  $L-T_3$  in the hope that it will improve persistent "hypothyroid" symptoms in the patient taking  $L-T_4$ .

I am interested in receiving comments about this point of view from our readers.

### References

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