

**REPLACEMENT THERAPY OF PRIMARY HYPOTHYROIDISM:
MONOTHERAPY WITH L-THYROXINE AND COMBINATION THERAPY OF L-THYROXINE AND TRIIODOTHYRONINE**

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ABSTRACT: The prevalence of overt hypothyroidism in the general population is 0.2 - 2%, but in certain groups of the population, in particular, among the elderly, it reaches 15%, so hypothyroidism is one of the most common endocrine diseases. Overt hypothyroidism is an absolute indication for replacement therapy with thyroid hormones. Currently, L-thyroxine monotherapy is mainly used for replacement therapy of hypothyroidism, although studies that would directly compare it with L-T4 + LT3 combination therapy have been virtually non-existent to date. In recent years, reports have begun to appear in the literature on some advantages of L-T3 + L-T4 combination therapy for hypothyroidism. A number of studies indicate positive dynamics of psychological indicators against the background of L-T4 + L-T3 combination therapy compared to L-T4 monotherapy. On the other hand, some studies have not confirmed the advantages of combination therapy compared to L-T4 monotherapy. Thus, to date, there is no clear data on the possible advantages and disadvantages of combination therapy L-T4 + L-T3 compared to L-T4 monotherapy. It should be noted that, despite the simplicity and convenience of L-T4 monotherapy, some patients, for various reasons, are in a state of chronic decompensation of hypothyroidism, or, despite maintaining a normal TSH level, present complaints characteristic of hypothyroidism, which to some extent may be evidence of the imperfection of this replacement therapy.

Objective and tasks

The aim of the work was to evaluate the characteristics of L-T4 replacement monotherapy compared to combination therapy with L-T4 and L-T3 in patients with primary overt hypothyroidism. To achieve this goal, the following tasks were put forward:

1. To evaluate the quality of hypothyroidism compensation in patients receiving L-T4 monotherapy and to compare the levels of TSH and thyroid hormones during L-T4 replacement monotherapy and L-T4+L-T3 combination therapy.
2. To evaluate the dynamics of lipid spectrum parameters during two replacement therapy options.
3. To evaluate and compare bone metabolism parameters and their dynamics during two replacement therapy options.

4. To evaluate the safety of using physiological doses of L-T3 from the standpoint of the possible impact on cardiovascular system performance.

Scientific novelty

1. For the first time, a comparative study of two options of replacement therapy for primary hypothyroidism was conducted: L-T4 monotherapy and L-T4+L-T3 combination therapy using physiological doses of L-T3 using a crossover design and randomization when forming groups.

2. It was shown that despite adequate L-T4 therapy, atherogenic dyslipidemia often persists in patients and positive dynamics of the lipid spectrum was demonstrated when patients were transferred to L-T4+L-T3 combination therapy.

3. The feasibility of assessing peripheral markers of thyroid hormone effects, in particular, lipid spectrum parameters for a comprehensive assessment of hypothyroidism compensation was demonstrated.

4. When assessing the dynamics of bone metabolism markers against the background of combination therapy for hypothyroidism, a more pronounced activation of bone resorption was revealed compared to bone formation.

5. The absence of a negative effect of physiological doses of L-T3 preparations on the state of the cardiovascular system during combined replacement therapy for hypothyroidism has been proven.

6. In some patients with persistent symptoms against the background of adequate L-T4 monotherapy, positive dynamics of the psychoemotional state were noted when transferred to combination therapy

CONCLUSIONS

1. L-T4 replacement monotherapy, which achieves normalization of TSH levels, is accompanied by the circulation of a non-physiologically high fT4 level, while an increase in the L-T4 dose, leading to a decrease in TSH levels to a low-normal level, does not ensure the maintenance of a GGZ level similar to that in healthy people.

2. A single dose of L-T3 preparations in the morning does not allow adequately modeling the production of triiodothyronine by the thyroid gland due to the short half-life of L-T3 preparations.

3. Against the background of L-T4 replacement monotherapy, atherogenic dyslipidemia persists in some patients with hypothyroidism, which is eliminated by prescribing combination therapy with L-T4 and L-T3 preparations. 4. Prescribing combination therapy L-T4+L-T3 is accompanied by a somewhat greater activation of bone resorption compared to L-T4 monotherapy, which may be accompanied by a decrease in bone mineral density. 5. In some patients with hypothyroidism, despite adequate L-T4 monotherapy according to

hormonal study data, a number of symptoms persist that can be relieved by switching to combination therapy L-T4+L-T3.

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