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Case Report

Validity of rapid free T4 testing to distinguish levothyroxine non-compliance from malabsorption: a case report

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ABSTRACT

Refractory hypothyroidism is characterised by persistently elevated thyroid-stimulating hormone (TSH) despite adequate or high-dose levothyroxine therapy. It presents a common clinical challenge, often requiring evaluation for causes such as poor adherence, drug interactions, or gastrointestinal malabsorption. Pseudomalabsorption due to inconsistent medication intake is the most frequent and reversible cause. Differentiating this from true malabsorption is crucial, as the latter may necessitate investigation for conditions like celiac disease, inflammatory bowel disease, or post-surgical states. The levothyroxine absorption test (LT4AT) is commonly used for this purpose, but conventional protocols are lengthy, costly, and inconvenient. Recently, simplified approaches using a single high oral dose with early measurement of serum free thyroxine (FT4) have been proposed. A rise in FT4 within a few hours indicates adequate intestinal absorption. We report a 54-year-old woman with refractory hypothyroidism in whom a short-duration LT4AT confirmed adequate absorption, suggesting pseudomalabsorption.

Keywords: Hypothyroidism, Levothyroxine, Medication adherence, Drug absorption

INTRODUCTION

Levothyroxine is the main treatment for hypothyroidism, yet many patients do not reach target TSH levels despite apparently adequate dosing, a situation termed "refractory hypothyroidism".[1] This requires careful evaluation to distinguish true physiological malabsorption from non-compliance, as malabsorption calls for alternative therapies, whereas non-compliance requires education and adherence support.[2,3] Standard methods like the LT4AT involve long observation and multiple blood draws, burdening patients and healthcare systems.[4] Rapid free T4 testing may offer a less invasive, more efficient way to determine the cause of persistent hypothyroidism, especially when adherence is uncertain.[5,6] This case study describes a case where rapid free T4 testing was used to supervise levothyroxine dosing to differentiate malabsorption from non-compliance and streamline diagnosis.

CASE REPORT

A 54-year-old woman with primary hypothyroidism presented for evaluation of persistently elevated TSH levels. She had been receiving oral levothyroxine therapy for several years. The dose increased gradually from 100 µg/day to 300 µg/day during follow-up because laboratory tests continued to show biochemical hypothyroidism. The patient reported regular medication intake and denied missed doses. Medication history did not include calcium supplements, iron preparations, proton pump inhibitors, or other agents known to reduce levothyroxine absorption. General exam showed stable vital signs without features of severe hypothyroidism/gastrointestinal disease. Continued elevation of TSH while receiving high-dose levothyroxine raised suspicion of impaired intestinal absorption. A LT4AT was performed after an overnight fast. Baseline serum FT4 measured 0.6 ng/dl (reference range 0.8-2.0 ng/dl). The patient received 1000 µg oral levothyroxine

under supervision. Serial FT4 measurements were obtained at hourly intervals. FT4 levels measured 0.6 ng/dl at 1 hour, 0.7 ng/dl at 2 hours, 0.9 ng/dl at 3 hours, and 1.1 ng/dl at 4 hours. Interpretation criteria include an FT4 increment greater than 0.4 ng/dl or a 2.5-fold rise within 2-3 hours. The increase in FT4 from 0.6 ng/dl to 1.1 ng/dl represented a rise of 0.5 ng/dl, indicating adequate gastrointestinal absorption of levothyroxine. The biochemical response supported pseudomalabsorption related to inconsistent medication intake.

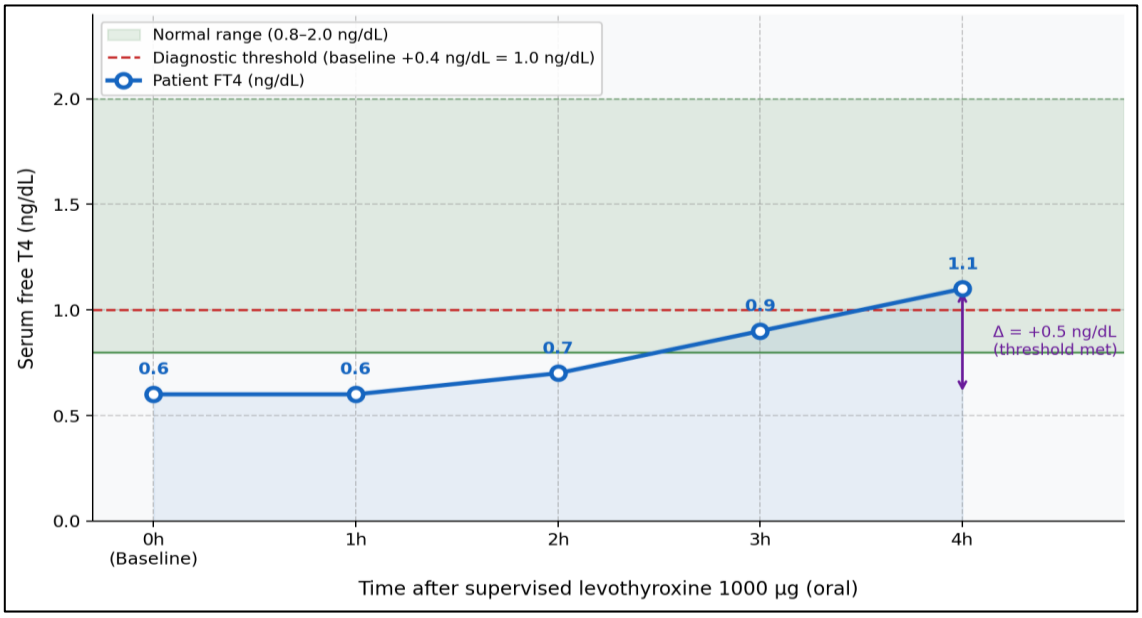

Figure 1: Serial FT4 measurements after supervised LT4 1000 µg.

DISCUSSION

Refractory hypothyroidism refers to persistent elevation of TSH in patients receiving apparently adequate doses of levothyroxine and represents a frequent diagnostic problem in endocrine practice.[1] Several factors contribute to this condition, including inconsistent medication intake, drug interactions, and impaired gastrointestinal absorption of levothyroxine.[2] Determining the underlying cause is essential because the clinical approach differs between pseudomalabsorption related to irregular drug intake and true malabsorption caused by gastrointestinal disorders.[2,3]

Patients who require unusually high daily doses of levothyroxine often undergo assessment for impaired intestinal absorption, particularly when medication adherence remains uncertain.[2] The LT4AT has been used to differentiate true malabsorption from pseudomalabsorption in such situations.[3] Conventional protocols require prolonged observation and repeated laboratory measurements over several hours or days, which increases patient inconvenience and resource use in routine practice.[4] Simplified protocols using early measurement of FT4 after administration of a supervised high oral dose have therefore been proposed as an alternative strategy.[4,5]

Clinical studies evaluating abbreviated absorption tests report that measurement of FT4 after a large oral levothyroxine dose provides useful information on intestinal uptake of the drug.[5] An increase in FT4 greater than 0.40 ng/dl or a rise within the first few hours after administration indicates adequate absorption and supports pseudomalabsorption related to irregular medication use.[5,6] Minimal change in FT4 concentrations suggests impaired gastrointestinal absorption and warrants further evaluation for intestinal disorders affecting drug uptake.[6]

The present case demonstrates the practical application of this approach in a patient with biochemical hypothyroidism while receiving high-dose levothyroxine therapy. The patient was taking 300 µg of levothyroxine daily and reported regular medication intake without exposure to drugs known to interfere with levothyroxine absorption. Persistent elevation of TSH led to a LT4AT after an overnight fast using a supervised oral dose of 1000 µg levothyroxine. Serial FT4 measurements increased from 0.6 ng/dl at baseline to 1.1 ng/dl at four hours, corresponding to an increment of 0.5 ng/dl. This increase exceeded the commonly used diagnostic threshold of 0.4 ng/dL and indicated adequate gastrointestinal absorption of levothyroxine.[5,6]

The biochemical response supported pseudomalabsorption rather than true intestinal malabsorption as the cause of uncontrolled thyroid function. Similar observations appear in previous reports where early FT4 measurement after supervised levothyroxine administration allowed differentiation between poor adherence and impaired intestinal uptake.[4,5] Identification of adequate absorption directs attention toward medication adherence and prevents unnecessary investigation for gastrointestinal

disease. Short-duration FT4-based absorption testing offers practical advantages. The procedure can be completed within a few hours and requires a limited number of blood samples, which reduces patient burden and avoids prolonged supervised therapy or extensive gastrointestinal investigations.[4] The findings in this case support the use of supervised levothyroxine administration with serial FT4 measurement as a practical method for evaluating refractory hypothyroidism and identifying patients who require adherence-focused management rather than evaluation for malabsorption.

CONCLUSION

Evaluation of patients with persistently elevated thyroid-stimulating hormone while receiving high-dose levothyroxine should include assessment of drug absorption. In this case, supervised levothyroxine administration with serial FT4 measurement confirmed normal intestinal absorption. Identification of pseudomalabsorption helps clinicians focus on improving medication adherence and prevents unnecessary investigations for gastrointestinal causes of uncontrolled hypothyroidism.

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REFERENCES

1. Quiroz-Aldave JE, Concepción-Zavaleta MJ, Durand-Vásquez MDC, Concepción-Urteaga LA, Gamarra-Osorio ER, Suárez-Rojas J, et al. Refractory hypothyroidism: Unraveling the complexities of diagnosis and management. Endocr Pract. 2023;29(12):1007-16.
2. Santos Monteiro S, Santos TS, Lopes AM, Oliveira JC, Freitas C, Couto Carvalho A. Levothyroxine malabsorption or pseudomalabsorption? A question in the management of refractory hypothyroidism. Endocr Connect. 2022;11(12):e220355.
3. Caron P, Tudor C, Grunenwald S. Levothyroxine absorption test with the daily levothyroxine dose in patients with “refractory hypothyroidism. J Endocr Soc. 2025;9(4):1-6.
4. Amiyangoda G, Antonypillai CN, Gunatilake SSC, Weerathunge TT, Ediriweera D, Kosgallana SGPD, et al. Rapid supervised levothyroxine absorption test in refractory hypothyroidism: suggestion for assessing absorption using two blood samples in low-resource settings. Endocr Connect. 2024;13(10):e240277.
5. Alhassan AA, Alidrisi HA, Mansour AA. Validity of the rapid thyroxine absorption test for the differentiation between levothyroxine non-compliance and malabsorption in thyroid-stimulating hormone refractory hypothyroidism. Cureus. 2023;15(4):e37776.
6. Oueslati I, Terzi A, Yazidi M, Kamoun E, Feki M, Chihaoui M. Levothyroxine absorption test in patients with refractory hypothyroidism: how to interpret patient’s response to the test? Endocrine. 2025;90(1):166-71.

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