

A Patient's Guide to the Diagnosis and Treatment of Hypothyroidism

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This article seeks to briefly review recent evidence related to the diagnosis and treatment of hypothyroidism and highlight the need for more reliable and effective standards of care to address the pervasive dissatisfaction among thyroid patients.

Introduction

In 2021 the American Thyroid Association estimated that 12% of the U.S. population would develop a thyroid condition during their lifetime, and that up to 60% would be unaware of their condition (1). The purpose of this brief commentary is to provide to doctors and patients who suspect inadequate diagnosis or treatment of hypothyroidism a contemporary update and a better understanding of effective diagnosis and treatment options they can pursue.

Background

Historically, hypothyroidism was diagnosed clinically using symptoms (2). If diagnosed, the standard treatment was natural desiccated porcine thyroid (NDT) which contains the thyroid hormones T4 *and* T3. The dose was adjusted as needed to relieve symptoms. After a sensitive test became available in 1985 for the pituitary hormone TSH (thyroid stimulating hormone) (3), a remarkable shift in diagnosis was made from clinical evaluation to biochemical testing (2, 4). This is based on American Association of Clinical Endocrinologists (AACE)/American thyroid Association (ATA) Guidelines for Hypothyroidism (2, 4) that defined hypothyroidism as an underactive thyroid gland and assumed that:

- a) "A subnormal assessment of free T4 (FT4) serves to establish a diagnosis of hypothyroidism." Also, TSH is exquisitely sensitive to minor changes in FT4, leading to the adoption of TSH as "the single best screening test for primary thyroid dysfunction for the vast majority of outpatient clinical situations" (2, 4).
- b) T4 is converted to T3 as needed, leading to treatment being changed to levothyroxine (T4) only (2, 4), and
- c) TSH within its reference range represents euthyroidism (normal), leading to the treatment dosage of T4 being adjusted to return TSH within its normal range (2, 4).

All three assumptions, which are fundamental to the Guidelines, have now been refuted by extensive scientific evidence (5-9). Due to the numerous variables in the total thyroid process, TSH shows only a weak correlation with thyroid hormone levels, and a much

weaker correlation with clinical symptoms which reflect patients' concerns (5-9). TSH is a reliable diagnostic only at very high levels indicative of overt primary hypothyroidism (or very low levels indicative of hyperthyroidism); at more moderately raised or lowered levels, however, it is an unreliable diagnostic indicator of other thyroid concerns (1, 6, 9). Treatment with levothyroxine, with TSH based dose adjustments, has been shown to frequently result in levels of FT4 and Free T3 (FT3) that are insufficient to achieve symptom relief and metabolic normality (5, 9). Symptomatic change correlates best with serum thyroid hormone levels, not TSH (6, 10).

Numerous recent studies have raised serious concerns over the continued use of TSH testing as the predominant means of diagnosing the thyroid status of a patient or determining adequacy of treatment (5-9). Recent mathematical modeling has also challenged the rationale for making TSH the predominant thyroid function test (8). TSH has instead a corrective role in FT3 homeostasis whereby the FT3 level is either robustly preserved or altered by the hypothalamic-pituitary-thyroid control system in an attempt to enable the body to adapt to new circumstances (8). This is consistent with the vital role of FT3 as the biologically active thyroid hormone that essentially regulates metabolic activity in cells. This is also reflected in an earlier, more comprehensive and effective definition for hypothyroidism: insufficient T3 genomic effect in tissue throughout the body due to inadequate supply of, or response to, thyroid hormones (8, 11). FT3 levels are highly dependent on availability of the prohormone FT4 together with the extent of its conversion to FT3. Conversion does not always occur as needed, since it is affected by a number of variables including TSH (5). Yet FT3 is seldom recommended to be tested and basically ignored in both diagnosis and treatment (2, 4, 8,12).

The Guidelines encouraged “medical professionals to use the information in conjunction with their best clinical judgment”, and warned that the Guidelines did not establish a standard of care (SOC) (2). However, both statements have been essentially ignored for the expediency of an unwarranted SOC predominantly based on TSH (2, 4) which has been adopted world-wide. The result is a large and vocal population of potentially undiagnosed hypothyroid patients with typical thyroid symptoms (12). Also, from their 2018 survey of 14,126 hypothyroid patients the ATA reported “prominent dissatisfaction” with the standard levothyroxine treatment. Patients' average rating of both their treatment and their doctors' knowledge about treatment was only 5 out of 10. Patients also expressed a strong need for newer forms of treatment (12). Such complaints need to be taken seriously because undiagnosed or inadequately treated hypothyroidism causes an extensive array of unresolved symptoms and may develop into more serious medical conditions such a high cholesterol, cardiac issues, obesity, joint and muscle pain, gradual hearing loss, reproductive system disorders, depression, periodontal problems, carpal tunnel syndrome, sleep issues and diabetes (1).

Conclusions

Recent scientific evidence has refuted major assumptions on which the AACE/ATA Guidelines for Hypothyroidism are based (5-9). The associated de facto SOC based predominantly on TSH (2, 4) should be reconsidered and amended as it is unwarranted

and clearly ineffective for many patients. The following suggestions will more effectively address the needs of both patients and doctors:

1. Diagnosis must always include a patient's full medical history.
2. Diagnosis must include an evaluation of symptoms, which reflect tissue thyroid responses, and the patient's well-being.
3. Where symptoms indicative of thyroid disease are present, an ultrasound of the thyroid is advisable.
4. Symptomatic testing and case finding should include TSH, FT4 and FT3, arguably Reverse T3, TPO ab, TG ab (only if TPO is negative and TSH is high).
5. To avoid false test results (4), thyroid hormone medication should not be taken until after blood is drawn
6. Multiple symptoms typical of hypothyroidism, accompanied by low FT4 and FT3 levels, are strongly indicative of hypothyroidism (5). Both FT4 and FT3 levels should be individually monitored and increased as needed to relieve symptoms of hypothyroidism, without creating symptoms of hyperthyroidism.
7. Cortisol, Vitamin D, B12 and ferritin should be considered and also optimized for symptom relief (5, 9).

DISCLAIMER:

This is a perspective commentary not a systematic review. This information does not constitute medical advice nor is it meant to provide specific medical recommendations.

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