Thyroid Therapy or Dysfunction in Athletes: Is it Time to Revisit the Clinical Practice Guidelines?

Krista G. Austin, PhD;[1] and Steven Petak, MD, JD, MACE, FACP[2]

Abstract
Recent media have highlighted the controversy surrounding treatment of elite athletes for hypothyroidism. The World Anti-Doping Agency denied a request by the United States Anti-Doping Agency to ban the use of thyroid medication. At present, there is no scientific evidence that thyroid medication has the potential to enhance performance. Clinical practice guidelines are not definitive in regard to what classifies a patient as having hypothyroidism. Thyroid-stimulating hormone and free T4 are recommended to screen for thyroid disease; however, the thyrotropin-releasing hormone stimulation test is still advocated by some for detecting the earliest stages of hypothyroidism. Hypothyroidism has been demonstrated to reduce cardiopulmonary function and result in musculoskeletal symptoms, such as fatigue and muscle stiffness. Symptoms of hypothyroidism, including depression, fatigue, and impaired sleep, are similar to those reported in overtraining. These patients may have hypothalamic-pituitary dysfunction that may complicate interpretation of basal thyroid-stimulating hormone and free T4. To date, no association has been identified between training state and hypothyroidism. Research to more clearly define hypothyroidism using provocative testing, evaluate the potential for thyroid medication to enhance performance, and examine whether training may induce hypothyroidism in athletes is desirable.

Introduction

Over the past several years, the use of thyroid medication by elite athletes has come under scrutiny by the media and significant doubt has been cast over the diagnosis of thyroid disease in this population (1). Overtraining has been proposed as the reason for the hypothyroidism reported by elite athletes, and as a result, the United States Anti-Doping Agency (USADA) requested the World Anti-Doping Agency (WADA) ban the use of thyroid medication (2). Based on consensus from experts, USADA's request was denied by WADA given the scientific evidence available did not support overtraining induced hypothyroidism or the ability of thyroid medication to enhance performance. Furthermore, the use of thyroid medication did not meet the additional criteria set forth by WADA, posing a risk to health or violating the spirit of sport, to be considered a medication that should be placed on the list of prohibited medications. The use of thyroid medication by athletes remains a controversial issue with only a paucity of research available and limited understanding of potential hypothyroidism in this population. This commentary is intended to highlight the current clinical practice guidelines (CPG), the state of knowledge regarding exercise and hypothyroidism, and identify future directions for research aimed at elucidating causes of hypothyroidism in the athlete population.

Diagnosing Hypothyroidism

The American Association of Clinical Endocrinology (AACE) developed CPG to assist medical providers in the diagnosis and treatment of hypothyroidism (3). Since the early 1990s, the development of third generation assays for thyroid-stimulating hormone (TSH) lead to the almost near extinction of the previously established gold standard method for assessment of thyroid function, the thyrotropin-releasing hormone (TRH) stimulation test. TRH has subsequently become unavailable commercially, further limiting additional work on thyroid evaluation in select populations. In agreement with most professional organizations, AACE recommends the use of TSH to screen for thyroid disease (3). The adequacy of utilizing basal TSH alone to screen for the earliest stages of hypothyroidism has been questioned given it cannot reliably identify and diagnose subtle abnormalities of the hypothalamic-pituitary-thyroid axis (4,5).

According to the CPG, normative upper-limit TSH reference criterion for initiation of treatment for hypothyroidism is 4.5 $mIU{\cdot}L^{-1}$ based on epidemiological data from the National Health and Nutrition Examination Survey (NHANES) III.[3] However, the CPG highlights an argument for 2.5 or 3.0 $mIU{\cdot}L^{-1}$ as the upper limit, and a more recent analysis of NHANES III supports 1.5 and 2.0 $mIU{\cdot}L^{-1}$ in women and men, respectively (6). During pregnancy, the upper limit for TSH is 2.0,

[1]Performance and Nutrition Coaching, LLC, Solana Beach, CA; and [2]Division of Endocrinology, Houston Methodist Hospital, Houston, TX

Address for correspondence: Krista G. Austin, PhD, Performance and Nutrition Coaching, LLC, Solana Beach, CA 92075; E-mail: krista.g.austin@gmail.com.

1537-890X/1812/474–476
Current Sports Medicine Reports

3.0, and 3.5 $mIU \cdot L^{-1}$ in the first, second, and third trimesters, respectively (3). Criterion for diagnosis of hypothyroidism utilizing the TRH stimulation test also is varied and ranges from 12.5 to 25 $mIU \cdot L^{-1}$ or a 20-$mIU \cdot L^{-1}$ change from baseline (7,8). To date, robust longitudinal data or clinical trials have not been conducted to provide definitive criterion for diagnosis of hypothyroidism utilizing base TSH or the TRH stimulation test. Given the evidence for variation in the upper limit of TSH and limitations in the scientific evidence available to support a definitive criterion for hypothyroidism, AACE reminds practitioners to take into account individual patient circumstances when providing medical care. Furthermore, the CPG clearly states that it is not intended to serve as standard of care or replace a medical professional's independent judgment regarding treatment (3).

Exercise and Thyroid Function

Hypothyroidism has been demonstrated to reduce exercise capacity and endurance performance (9). Thyroid therapy has the potential to improve musculoskeletal complaints, such as cramps and fatigue. Cardiac function including left ventricular ejection fraction and peak filling rate also may show improvement (9). However, improvements in maximal power output, strength, and oxygen-carrying capacity (as a function of hormone replacement and without a training program) predominately only occur in overt hypothyroidism (9). Despite thyroid therapy, some patients with overt or subclinical hypothyroidism are unable to improve exercise tolerance due to ongoing symptoms (9).

Thyroid function has been shown to be relatively stable in asymptomatic euthyroid athletes (10–15). In euthyroid athletes, measurements of TSH, free T4, and free T3 before and after exercise show a decrease or no change in TSH and an increase or no change in free T3 or T4 (14). Studies of strength athletes ranging from 24 wk to 1 year report variations in free T4 based on intensity and volume; however, no systematic changes of clinical significance are observed over the training cycle (11,12). Rowers monitored over a 20-wk period of endurance training showed either a positive or negative thyroid hormone response. A negative response was indicated by decreases in TSH and free T3; however, athletes with a negative response returned toward baseline values by the end of the study period (13). In a survey of nonelite female runners, training intensity nor duration were associated with a diagnosis of thyroid dysfunction (16). Research examining root cause dysfunction in athletes presenting with symptoms of hypothyroidism has not previously been published and leaves a significant gap in the research literature. Furthermore, the potential for hypothyroidism or other forms of endocrine dysfunction has not been explored in overtrained athletes despite the similarities in symptomology (*e.g.*, fatigue, depression, anxiety, poor sleep, under performance, etc.).

Thyroid Medication for Health Versus Performance Enhancement

Use of L-thyroxine therapy in euthyroid individuals has been demonstrated to improve health through lowering total cholesterol and low-density lipoproteins (17), as well as, improving mood in patients with depression (18,19) and affective disorder (20). Treatment with L-thyroxine also has been associated with positive outcomes in infertility treatment (8) and is recommended early on in pregnancy to prevent adverse medical issues when TSH is outside the recommended ranges for each trimester (3). To date, the short- or long-term use of L-thyroxine or combinations with L-triiodothyronine to enhance athletic performance has not been explored. This can be attributed to the research literature surrounding hyperthyroidism and the detrimental effects it has shown on the cardiovascular, respiratory, and musculoskeletal system, many of which are equivocal impairments to that experienced as a result of hypothyroidism (9,15). Research examining whether thyroid medication could enhance performance would first need to identify a definitive criterion for hypothyroidism and then account for critical factors, such as rate of adaptation to training, modulation of the training load, energy availability, sport specificity, influence of other medications, and individual pharmacokinetics of thyroid hormone.

Conclusions

Collaboration between clinical physiologists and endocrinologists is needed to develop robust, scientific criterion for when patients should be medically treated for hypothyroidism. Furthermore, the TRH stimulation test should be evaluated to determine whether it should be used in better defining thyroid dysfunction in special patient populations, such as elite athletes. In addition, a better understanding for the role of training load, energy availability, and the potential for the overtraining syndrome to contribute to the development of hypothyroidism is warranted. Exploration of the speculation that short- or long-term use of thyroid hormone to enhance performance in euthyroid athletes is needed to clarify the concern raised by USADA.

Key Points

- Special populations, such as elite athletes, may not fall into the typical general population addressed by clinical guidelines.
- Hypothalamic-pituitary-thyroid function may be better assessed in such populations by provocative studies, such as the TRH test.
- A paucity of data makes further studies of these populations important in furthering our understanding of physiology in addition to providing guidance in clinical interventions.
- Performance optimization may be possible with this better understanding and concerns with "enhanced" performance can be addressed.

The authors declare no conflict of interest and do not have any financial disclosures.

References

1. Longman J. U.S. antidoping agency seeks to depose doctor who treated top track athletes. 2016. [cited 2018 December 29]. Available from: https://www.nytimes.com/2016/06/29/sports/usada-track-and-field-doping-jeffrey-brown-investigation.html.
2. Germano S. In rebuff to USADA, WADA declines to ban thyroid medication. 2015. [cited 2018 December 29]. Available from: https://www.wsj.com/articles/in-rebuff-to-usada-wada-declines-to-ban-thyroid-medication-1443568862.
3. Garber JR, Cobin RH, Gharib H, *et al*; American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr. Pract.* 2012; 18:988–1028.
4. Sheth JJ, Thakore PB, Trivedi BB, *et al*. Sub-biochemical hypothyroidism: an exaggerated thyroid stimulating hormone response to thyrotrophin releasing hormone. *J. Assoc. Physicians India.* 1999; 47:275–9.

5. Ylli D, Wartofsky L. Can we link thyroid status, energy expenditure, and body composition to management of subclinical thyroid dysfunction? *J. Clin. Endocrinol. Metab*. 2018; 104:209–12.
6. Spencer CA, Hollowell JG, Kazarosyan M, *et al*. National Health and nutrition examination survey III thyroid-stimulating hormone (TSH)-thyroperoxidase antibody relationships demonstrate that TSH upper reference limits may be skewed by occult thyroid dysfunction. *J. Clin. Endocrinol. Metab*. 2007; 92:4236–40.
7. Spencer CA, Schwarzbein D, Guttler RB, *et al*. Thyrotropin (TSH)-releasing hormone stimulation test responses employing third and fourth generation TSH assays. *J. Clin. Endocrinol. Metab*. 1993; 76:494–8.
8. Raber W, Vierhapper H. The usefulness of thyrotropin-releasing hormone stimulation test in subfertile female patients. *Gynecol. Endocrinol*. 2008; 24:359–60.
9. Lankhaar JA, de Vries WR, Jansen JA, *et al*. Impact of overt and subclinical hypothyroidism on exercise tolerance: a systematic review. *Res. Q. Exerc. Sport*. 2014; 85:365–89.
10. Hoffman JR, Epstein S, Yarom Y, *et al*. Hormonal and biochemical changes in elite basketball players during a 4-week training camp. *J. Strength Cond. Res*. 1999; 13:280–5.
11. Alen M, Pakarinen A, Häkkinen K. Effects of prolonged training on serum thyrotropin and thyroid hormones in elite strength athletes. *J. Sports Sci*. 1993; 11:493–7.
12. Pakarinen A, Alén M, Häkkinen K, Komi P. Serum thyroid hormones, thyrotropin and thyroxine binding globulin during prolonged strength training. *Eur. J. Appl. Physiol. Occup. Physiol*. 1988; 57:394–8.
13. Baylor LS, Hackney AC. Resting thyroid and leptin hormone changes in women following intense, prolonged exercise training. *Eur. J. Appl. Physiol*. 2003; 88:480–4.
14. Schmid P, Wolf W, Pilger E, *et al*. TSH, T3, rT3 and fT4 in maximal and submaximal physical exercise. *Eur. J. Appl. Physiol. Occup. Physiol*. 1982; 48:31–9.
15. Pakarinen A, Häkkinen K, Alen M. Serum thyroid hormones, thyrotropin and thyroxine binding globulin in elite athletes during very intense strength training of one week. *J. Sports Med. Phys. Fitness*. 1991; 31:142–6.
16. Matsumura ME, Bucciarelli M, Perilli G. Relationship between training intensity and volume and hypothyroidism among female runners. *Clin. J. Sport Med*. 2015; 25:551–3.
17. Sjouke B, Elbers LPB, van Zaane B, *et al*. Effects of supra-physiological levothyroxine dosages on liver parameters, lipids and lipoproteins in healthy volunteers: a randomized controlled crossover study. *Sci. Rep*. 2017; 7:14174.
18. Gold MS, Pottash AL, Extein I. Hypothyroidism and depression. Evidence from complete thyroid function evaluation. *JAMA*. 1981; 245:1919–22.
19. Bauer M, London ED, Rasgon N, *et al*. Supraphysiological doses of levothyroxine alter regional cerebral metabolism and improve mood in bipolar depression. *Mol. Psychiatry*. 2005; 10:456–69.
20. Bauer M, Priebe S, Berghöfer A, *et al*. Subjective response to and tolerability of long-term supraphysiological doses of levothyroxine in refractory mood disorders. *J. Affect. Disord*. 2001; 64:35–42.