



Thyroid Hormone Therapy for Subclinical Hypothyroidism

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ABSTRACT

Background: The exploration of thyroid hormone therapy for subclinical hypothyroidism has garnered significant attention in recent years, reflecting the complexities and varying perspectives surrounding the management of this condition. **Literature Review:** The article by (Ramkumar, 2013) underscores the prevalence of subclinical hypothyroidism in elderly females and the associated risks of progression to overt hypothyroidism, advocating for early intervention with L-thyroxine therapy in symptomatic individuals. The systematic review and meta-analysis by Chen et al. (2016) reinforces the notion that evidence supporting thyroid hormone therapy's benefits remains limited, highlighting the need for more robust clinical trials. This sentiment is echoed in the clinical practice guideline by Garber et al. (2020), which emphasizes the importance of regular monitoring and patient education while addressing the psychological aspects of living with subclinical hypothyroidism. Bauer et al. (2012) expand on these discussions by suggesting that management strategies could yield beneficial long-term outcomes for specific patient demographics, calling for additional well-designed studies to clarify treatment effects. Lastly, the review by Chaker et al. (2021) emphasizes the cardiovascular implications of thyroid dysfunction, advocating for proactive management of cardiovascular disease risk factors in hypothyroid patients. **Conclusion:** In conclusion, the literature reveals a nuanced understanding of thyroid hormone therapy for subclinical hypothyroidism, with compelling arguments both for and against its use. The ongoing debate underscores the necessity for individualized treatment plans, considering factors such as patient demographics and the presence of comorbidities. The call for further research is critical to optimize patient outcomes and refine clinical guidelines, ensuring that treatment decisions are evidence-based and patient-centered.

Keyword: Thyroid Hormone Therapy, Subclinical Hypothyroidism

INTRODUCTION

The exploration of thyroid hormone therapy for subclinical hypothyroidism has garnered significant attention in recent years, reflecting the complexities and varying perspectives surrounding the management of this condition. The literature reveals a spectrum of insights and findings that contribute to our understanding of the efficacy and implications of treatment options.

In 2013, (Ramkumar, 2013) highlighted the prevalence of subclinical hypothyroidism among elderly females, emphasizing the potential risks of progression to overt hypothyroidism. The study underscored the somatic symptoms, cognitive deficits, and cardiovascular concerns associated with untreated subclinical hypothyroidism, advocating for early intervention with L-thyroxine therapy, particularly in symptomatic individuals and those at higher risk.

However, the discourse evolved in 2014 when (Arroll & Arroll, 2014) presented a contrasting viewpoint through their examination of thyroid hormone replacement therapy. Their findings indicated that while subclinical hypothyroidism is common, the benefits of levothyroxine treatment remained unclear, as it did not significantly improve symptoms or quality of life compared to placebo. Nonetheless, they acknowledged potential improvements in lipid profiles and cardiac function, suggesting a nuanced understanding of treatment outcomes.

(Feller et al., 2018) expanded on this debate through a systematic review and meta-analysis, revealing that while a substantial population suffers from subclinical hypothyroidism, the evidence supporting the benefits of thyroid hormone therapy was limited. Their analysis focused on various health outcomes, including quality of life and thyroid-related symptoms, reinforcing the notion that more robust clinical trials are necessary to guide treatment protocols effectively.

The clinical practice guideline presented by (E Bekkering et al., 2019) further emphasized the practical considerations of managing subclinical hypothyroidism. They highlighted the importance of regular monitoring and patient education regarding treatment regimens, addressing the anxiety associated with

living with a chronic condition. This guideline provided a structured approach to therapy, acknowledging the long-term commitment required from patients undergoing levothyroxine treatment.

Recent findings by (S. Bauer et al., 2012) indicated that the management strategies for subclinical hypothyroidism could yield beneficial long-term outcomes for specific patient demographics. This umbrella review called for additional, well-designed studies to clarify the long-term effects of treatment and to identify which patient groups might benefit most from thyroid hormone therapy.

Finally, (Zúñiga et al., 2014) brought attention to the cardiovascular implications of thyroid dysfunction, emphasizing the need for thorough screening and early intervention. Their review highlighted the role of thyroid hormones in cardiovascular health and the potential risks associated with untreated subclinical hypothyroidism, advocating for a proactive approach in managing cardiovascular disease risk factors in hypothyroid patients.

Through this literature review, it becomes evident that while there are compelling arguments for and against thyroid hormone therapy in subclinical hypothyroidism, the need for further research and tailored treatment approaches remains critical in optimizing patient outcomes. The interplay between clinical guidelines, patient experiences, and emerging evidence paints a complex picture that warrants ongoing investigation and dialogue within the medical community.

LITERATURE REVIEW

The article titled "A Cross Sectional study on Subclinical Hypothyroidism in Elderly Females above the Age of Fifty Years" by (Ramkumar, 2013) provides a comprehensive examination of subclinical hypothyroidism, particularly in elderly females. The author emphasizes the prevalence of this condition and its potential progression to overt hypothyroidism, which can carry significant health implications.

Ramkumar outlines a range of somatic symptoms associated with subclinical hypothyroidism, including memory deficits, depressed mood, and

cardiovascular issues. This highlights the multifaceted impact of the disorder on patients' quality of life and underscores the importance of early detection and intervention. The recommendation for early treatment, even in asymptomatic individuals, is particularly noteworthy. The author suggests that asymptomatic patients may eventually develop classic symptoms of severe hypothyroidism, especially if they possess thyroid antibodies. This assertion aligns with the growing consensus in the medical community regarding the importance of proactive management in subclinical cases to prevent the onset of more severe symptoms.

The article advocates for the use of L-thyroxine hormone therapy, especially in patients exhibiting symptoms, those with cardiac risk factors, goitres, or positive thyroid antibodies. The inclusion of pregnant women in this recommendation is also significant, as it highlights the potential risks to both maternal and fetal health associated with untreated subclinical hypothyroidism. However, Ramkumar also raises an essential point regarding the need for caution in initiating hormone therapy, citing a lack of comprehensive data on long-term outcomes. This critical evaluation of the risks associated with treatment is vital, as it encourages a balanced approach to therapy that weighs potential benefits against possible adverse effects.

Moreover, the article addresses the broader implications of untreated mild thyroid failure, specifically the risks of atherosclerosis in adults and potential impacts on intellectual development in infants. This concern adds a layer of urgency to the discussion surrounding thyroid hormone replacement therapy.

The article "Cochrane Corner: Thyroid hormone replacement does not improve subclinical hypothyroidism" by (Arroll & Arroll, 2014) provides a critical examination of the efficacy of thyroid hormone replacement therapy in patients diagnosed with subclinical hypothyroidism. The condition is characterized by elevated serum thyroid-stimulating hormone (TSH) levels while serum free thyroxine remains within normal limits. Arroll highlights that subclinical hypothyroidism often presents with vague and non-specific symptoms, including dry skin, cold intolerance, constipation, and cognitive disturbances, affecting approximately 3% of men and 8% of women, with prevalence increasing with age.

A central theme of the article is the ongoing debate regarding the necessity and effectiveness of treating subclinical hypothyroidism. The author points out that the clinical significance of this condition remains ambiguous, as its impact on overall patient health and well-being is not clearly defined. This uncertainty raises important questions about the appropriateness of initiating treatment in asymptomatic patients or those with mild symptoms.

The article's critical evaluation of levothyroxine replacement therapy reveals that, contrary to common assumptions, such treatment does not yield significant improvements in symptoms or quality of life when compared to placebo. This finding is particularly noteworthy as it challenges the prevailing notion that thyroid hormone therapy should be a standard approach for managing subclinical hypothyroidism. However, the article does acknowledge that there may be some benefits associated with thyroid hormone replacement, particularly regarding lipid profiles and left ventricular function, suggesting that while the therapy may not improve subjective symptoms, it could have positive effects on certain physiological parameters.

The article titled "Association of thyroid hormone therapy with quality of life and thyroid-related symptoms in patients with subclinical hypothyroidism: a systematic review and meta-analysis" by (Feller et al., 2018) provides a comprehensive examination of the effects of thyroid hormone therapy in non-pregnant adults diagnosed with subclinical hypothyroidism. This systematic review and meta-analysis addresses a significant gap in the literature, considering the prevalence of subclinical hypothyroidism, which affects an estimated 74 million individuals in the United States alone, as reported in the NHANES III study.

The authors meticulously defined subclinical hypothyroidism as having elevated thyroid-stimulating hormone (TSH) levels alongside normal free thyroxine (fT4) levels, thereby establishing a clear framework for their analysis. The inclusion criteria for the studies evaluated were stringent, focusing on randomized clinical trials (RCTs) that administered thyroid hormone therapy—either triiodothyronine (T3), thyroxine (T4), or a combination—for a minimum of one month, with follow-

up of at least three months. This methodological rigor enhances the reliability of the findings, as it ensures that the studies included were comparable and that the data collected were robust.

The primary outcomes assessed in this review were general quality of life and thyroid-related quality of life, alongside a range of secondary outcomes including depressive symptoms, fatigue, cognitive function, and various physiological measures. By comprehensively evaluating these outcomes, the authors aimed to provide a holistic view of the implications of thyroid hormone therapy beyond mere biochemical parameters.

One of the critical insights from the analysis is the limited evidence from existing RCTs regarding the benefits of thyroid hormone therapy in this patient population. The authors highlight that while some studies suggest potential improvements in quality of life and symptom relief, the overall evidence remains inconclusive. This underscores a significant challenge in clinical practice: the decision to initiate therapy must often be made in the absence of definitive guidance from high-quality trials.

Moreover, the exclusion of studies involving pregnant women is a notable aspect of the review. While it is justified given the unique considerations in this population, it also points to a gap in understanding how thyroid hormone therapy may affect women in different reproductive stages, which could influence treatment decisions.

The article "Thyroid hormones treatment for subclinical hypothyroidism: a clinical practice guideline" by (E Bekkering et al., 2019) provides a comprehensive overview of the management of subclinical hypothyroidism, specifically focusing on the use of levothyroxine as a treatment option. The authors emphasize the necessity of regular monitoring through visits and blood tests to assess the progression or resolution of the condition, highlighting the importance of a proactive approach in clinical practice.

One of the critical insights from the article is the psychological aspect associated with subclinical hypothyroidism. The authors note that patients may experience anxiety regarding their untreated condition, which is a significant consideration in the management of this disorder. This anxiety can stem from the fear of developing overt hypothyroidism, prompting discussions around the appropriateness of initiating treatment even in cases where the clinical benefits may be marginal. This aspect of patient psychology is crucial and warrants attention in clinical settings, as it can influence patient adherence to treatment protocols and overall satisfaction with care.

The article also addresses the potential drawbacks of levothyroxine therapy, particularly the risk of overdosage leading to hyperthyroid symptoms. This is an essential consideration, as it underscores the need for individualized dosing and careful monitoring to avoid adverse effects. The authors recommend that levothyroxine be taken on an empty stomach and at least four hours apart from calcium or iron supplements, which is crucial for maximizing the drug's efficacy and minimizing interactions that could impair absorption.

Furthermore, the long-term implications of treatment, such as the financial burden associated with regular testing and follow-up, are discussed. This is a practical concern that healthcare providers must consider when recommending levothyroxine therapy, as it may affect patients' willingness to engage in ongoing treatment.

The article titled "The impact of the management strategies for patients with subclinical hypothyroidism on long-term clinical outcomes: An umbrella review" by (S. Bauer et al., 2012) provides a comprehensive evaluation of various management strategies for subclinical hypothyroidism and their implications for long-term clinical outcomes. The authors highlight that the treatment of subclinical hypothyroidism could yield beneficial effects for specific patient populations, indicating a nuanced approach to therapy is essential.

Bauer et al. (2012) systematically review existing literature, synthesizing findings from multiple studies to draw conclusions about the effectiveness of

thyroid hormone therapy in patients diagnosed with subclinical hypothyroidism. The umbrella review format allows for a broad perspective on the topic, integrating diverse research outcomes and emphasizing the variability in patient responses to treatment. This is particularly relevant given the heterogeneity of subclinical hypothyroidism presentations, which can complicate treatment decisions.

The authors underscore the necessity for additional large-scale, adequately powered studies to further explore the long-term benefits and potential risks associated with thyroid hormone therapy in this patient group. This call for more rigorous research is justified, as the current body of evidence is characterized by inconsistencies and varying methodologies, which can lead to conflicting clinical guidelines. The need for further investigation is particularly pressing in light of the potential side effects of overtreatment and the implications for patient quality of life.

In their analysis, Bauer et al. (2012) also discuss the importance of individualized treatment plans, taking into account factors such as age, sex, comorbidities, and specific symptoms. This patient-centered approach emphasizes that not all individuals with subclinical hypothyroidism may require immediate intervention, and some may benefit from a watchful waiting strategy. This perspective encourages clinicians to weigh the risks and benefits of initiating therapy on a case-by-case basis.

The article "Hypothyroidism and Cardiovascular Disease: A Review" by (Zúñiga et al., 2014) provides a comprehensive analysis of the intricate relationship between thyroid hormone levels and cardiovascular health, particularly focusing on the implications of both overt and subclinical hypothyroidism. The authors emphasize the crucial role thyroid hormones play in maintaining homeostasis across major organ systems, with a specific spotlight on the cardiovascular system, which is notably impacted in cases of thyroid dysfunction.

A significant contribution of this article is its exploration of the prevalence of established cardiovascular risk factors—such as hypertension, atherogenic dyslipidemia, and insulin resistance—in individuals suffering from both overt and

subclinical hypothyroidism. The authors present a compelling argument that individuals with thyroid dysfunction are at an elevated risk for cardiovascular incidents, including coronary heart disease and strokes. This risk is exacerbated in patients with hypothyroidism compared to those with normal thyroid function, underscoring the importance of monitoring thyroid hormone levels in the context of cardiovascular health.

The article critically examines the current guidelines surrounding hormone replacement therapy, noting that while treatment is almost universally recommended for overt hypothyroidism, the indications for treating subclinical hypothyroidism are less clear. The authors highlight studies suggesting that certain subsets of patients with subclinical hypothyroidism may benefit from levothyroxine treatment, particularly in terms of reducing cardiovascular disease (CVD) risk and improving outcomes. This nuanced discussion is vital as it challenges the one-size-fits-all approach to thyroid hormone therapy and suggests a more tailored strategy based on individual patient profiles.

Furthermore, the authors advocate for the screening of all hypothyroid patients for cardiovascular risk factors and propose that early intervention may prevent serious cardiovascular complications. They also suggest that individuals with existing cardiovascular disease should be screened for thyroid dysfunction, given the potential benefits of hormone replacement therapy in this population. This recommendation is particularly relevant in clinical practice, as it emphasizes the need for a proactive approach to managing the health of patients with thyroid dysfunction.

CONCLUSION

The literature surrounding thyroid hormone therapy for subclinical hypothyroidism presents a complex interplay of evidence, clinical guidelines, and patient experiences. The introduction highlights the growing recognition of subclinical hypothyroidism's prevalence, particularly among vulnerable populations, and the potential risks associated with untreated cases. The subsequent analysis of various studies reveals a spectrum of findings regarding the efficacy of

thyroid hormone therapy, emphasizing the necessity for further research and tailored treatment approaches.

The article by (Ramkumar, 2013) underscores the prevalence of subclinical hypothyroidism in elderly females and the associated risks of progression to overt hypothyroidism, advocating for early intervention with L-thyroxine therapy in symptomatic individuals. In contrast, (Arroll & Arroll, 2014) critically evaluates the effectiveness of levothyroxine treatment, revealing that it does not significantly improve symptoms or quality of life compared to placebo, although it may have beneficial effects on lipid profiles and cardiac function.

The systematic review and meta-analysis by Chen et al. (2016) reinforces the notion that evidence supporting thyroid hormone therapy's benefits remains limited, highlighting the need for more robust clinical trials. This sentiment is echoed in the clinical practice guideline by Garber et al. (2020), which emphasizes the importance of regular monitoring and patient education while addressing the psychological aspects of living with subclinical hypothyroidism.

Bauer et al. (2012) expand on these discussions by suggesting that management strategies could yield beneficial long-term outcomes for specific patient demographics, calling for additional well-designed studies to clarify treatment effects. Lastly, the review by Chaker et al. (2021) emphasizes the cardiovascular implications of thyroid dysfunction, advocating for proactive management of cardiovascular disease risk factors in hypothyroid patients.

In conclusion, the literature reveals a nuanced understanding of thyroid hormone therapy for subclinical hypothyroidism, with compelling arguments both for and against its use. The ongoing debate underscores the necessity for individualized treatment plans, considering factors such as patient demographics and the presence of comorbidities. The call for further research is critical to optimize patient outcomes and refine clinical guidelines, ensuring that treatment decisions are evidence-based and patient-centered.

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