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Review Article

Medication Adherence Among Patients with Hypothyroidism Receiving Levothyroxine: A Review

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ABSTRACT

Hypothyroidism is a prevalent endocrine disorder resulting from insufficient production of thyroid hormones, particularly thyroxine (T4) and triiodothyronine (T3), which play critical roles in metabolic regulation and overall physiological function. Levothyroxine (LT4), a synthetic T4 replacement, is the standard treatment to restore euthyroidism. Despite its efficacy, achieving optimal therapeutic outcomes heavily depends on consistent patient adherence to prescribed therapy. Non-adherence remains a widespread challenge, influenced by various factors such as forgetfulness, lack of awareness, complex dosing regimens, cost, and coexisting conditions. Barriers to adherence include both unintentional factors like cognitive decline or misunderstanding instructions, and intentional ones such as perceived lack of efficacy or concerns about side effects. Inadequate adherence can lead to persistent symptoms, altered biochemical parameters, and increased risk of complications. Identifying and addressing these barriers is crucial in managing hypothyroid patients effectively. Methods to evaluate adherence include patient self-reports, pill counts, pharmacy refill records, and validated adherence scales. Strategies to improve adherence range from patient education and medication reminders to simplifying regimens and enhancing doctor–patient communication. This review emphasizes the importance of early diagnosis, regular monitoring, and a patient-centred approach to therapy. Tailoring interventions to individual patient needs can improve adherence, optimize treatment outcomes, and enhance quality of life for individuals with hypothyroidism.

INTRODUCTION

Hypothyroidism, a chronic endocrine condition marked by insufficient thyroid hormone production primarily thyroxine (T4) and triiodothyronine (T3) [1,2]. These hormones play avital role in regulating metabolism, energy production, and overall physiological balance. The

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most frequent causes of hypothyroidism are autoimmune thyroiditis (Hashimoto's thyroiditis), iodine deficiency, certain medications, thyroid surgery or radiation therapy to the neck [3,4]. General symptoms of hypothyroidism are fatigue, weight gain, cold intolerance, constipation, dry skin. Other symptoms include neurological, psychological, reproductive and cosmetic symptoms like depression, poor memory, hoarseness, slowed heart rate, fertility problems, irregular menstrual periods, coarse hair, brittle nails, swelling in the neck, puffy hands etc. [3,5,6]. Opinion is made through blood test showing elevated Thyroid Stimulating Hormone (TSH) and low situations of free T4 level [7]. Effective management primarily involves lifelong administration of levothyroxine (LT4), a synthetic hormone that compensates for this deficiency [8]. As the treatment is lifelong, consistent medication adherence is essential for effective disease management and it is crucial for maintaining optimal thyroid function, also preventing associated complications like dementia, depression etc [9,10,11,12]. However, ensuring adherence presents challenges influenced by diverse factors including education, access, physiological health, and health system interactions [13].

Prevalence of Hypothyroidism and Its Adherence to Levothyroxine

The global prevalence of hypothyroidism is estimated to be 1% and 2%, with higher rates in older adults and women [1,3]. Subclinical hypothyroidism can affect as numerous as 10% of the older adults. In iodine deficient areas, the rate is significantly higher. [1,14] In India it affects approximately 11% of the population. Inland regions like Kolkata, Delhi, Ahmedabad, Bangalore, and Hyderabad about 11.7% are affected as compared to coastal areas like Mumbai, Goa, and Chennai that is about 9.5% [15,16]. Adherence to Levothyroxine (LT4) therapy is less than optimal; studies report that around 17% of patients are poorly adherent and 39% were highly adherent, impacting treatment outcomes. Despite the availability of LT4 in various formulations, non-adherence persists due to misconceptions, inconvenience, or lack of symptom relief. [16,17]

DIAGNOSIS

Diagnosing hypothyroidism involves measuring serum thyroid-stimulating hormone levels (TSH) and free thyroxine (FT4) levels. Primary hypothyroidism typically shows elevated TSH and low FT4, whereas subclinical cases exhibit high TSH with normal FT4. Autoimmune screening for anti-thyroid peroxidase antibodies is also useful, especially in Hashimoto's thyroiditis. Diagnosis is confirmed with repeated testing to rule out transient abnormalities and guide long-term treatment decisions [18,19].

MANAGEMENT

Hypothyroidism

is managed by restoring acceptable situations of thyroid hormones in the body, primarily through hormone relief remedy. The most commonly prescribed medication is levothyroxine, a synthetic version of thyroxine (T4), which helps normalize thyroid hormone levels [20,21]. The available doses of levothyroxine are 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, 200 mcg etc [22]. The treatment is personalized based on factors like the patients age, weight, cardiovascular health, and the degree of hormone deficiency. Patients typically start with a calculated dose, adjustments to the dose are usually made every 6 to 8 weeks until stable hormone levels are attained [21,22,24]. For optimal absorption, levothyroxine should be taken on an empty stomach, generally 30-60 minutes before a

meal [25]. Substances like calcium, iron, and certain foods can interfere with its absorption and should be spaced apart from the medication [9,26,27]. Patient education plays a key role in achieving long-term treatment success. Understanding the importance of consistent medication use and regular follow-up helps prevent complications and supports overall well-being [28].

Encouraging Adherence to Levothyroxine In Patients With Hypothyroidism

Adherence to levothyroxine therapy is essential for effective management of hypothyroidism [23,29]. Inconsistent or incorrect use of the medication can lead to persistent symptoms, metabolic imbalance, and reduced quality of life. Therefore, promoting adherence is a vital aspect of long-term treatment [30,31,32]. Studies across various regions indicate significant variations in adherence levels. Research from Spain shows a high adherence rate of approximately 86%, while countries like Nepal report about 51.3% adherence among patients. In contrast, lower adherence rates are observed in several Middle Eastern countries, including Lebanon and Saudi Arabia, where non-adherence exceeds 50% in many cases. In the United States, data suggests that around 40-52% of patients discontinue or inconsistently take their medication within 6-12 months of initiation [33,34,35]. Patient education is a cornerstone of adherence. Individuals should be clearly informed about the importance of regular, lifelong treatment, how levothyroxine works, and the consequences of nonadherence [14,36,37]. Proper timing and method of intake also influence therapeutic success. Patients should be advised to take levothyroxine on an empty stomach, at the same time each day, and to avoid certain foods, calcium, or iron supplements around dosing time, as these can impair absorption [23,25]. In patients with forgetfulness or busy schedules, reminder tools like phone alarms or pill organizers can support regular use [38]. Regular follow-ups help reinforce adherence by assessing symptoms, adjusting dosages, and re-emphasizing the importance of treatment. Healthcare providers play a crucial role in building rapport and tailoring communication to the patient's literacy level and cultural background, which significantly improves medication-taking behaviour [39].

Barriers To Adherence

Despite the effectiveness of levothyroxine in managing hypothyroidism, several factors can hinder patients from taking their medication consistently and correctly. These barriers can be personal, social, or systemic.

1. **Lack of Awareness and Knowledge**: Many patients are unaware that hypothyroidism is a chronic condition requiring lifelong therapy. Misconceptions about levothyroxine, such as fears of dependency or weight gain, may lead to intentional non-adherence.

2. **Complex Dosing Instructions:** Levothyroxine must be taken on an empty stomach, at least 30–60 minutes before breakfast or other medications. This strict schedule can be inconvenient and lead to skipped or mistimed doses.

3. **Forgetfulness and Routine Disruption:** Busy lifestyles, travel, or changes in daily routine may result in missed doses. Older adults, especially those with cognitive impairment, are more prone to forgetting medications.

4. **Side Effects or Perceived Ineffectiveness:** Some patients experience symptoms such as palpitations or anxiety when over-treated, or they may feel no improvement in symptoms,

leading them to stop the medication prematurely.

5. **Mental Health Issues:** Depression, anxiety, and other psychological disorders can reduce motivation and attention to self-care, including medication adherence.

6. **Cost and Access to Medication:** In some regions, limited access to healthcare, high medication costs, or inconsistent supply can interfere with regular medication use.

7. **Poor Patient-Provider Communication:** When patients feel rushed or misunderstood by their healthcare provider, they may hesitate to ask questions or express concerns, which can undermine adherence [13,21,29,36].

Factors Associated with Adherence and Non-Adherence

Adherence to levothyroxine therapy is crucial for maintaining euthyroid status in patients with hypothyroidism [40]. Various patient-related, therapy-related, and healthcare system-related factors influence both adherence and non-adherence [41].

Factors Promoting Adherence

- **Patient education and awareness**: Those who understand the importance of levothyroxine and the consequences of poor control are more likely to adhere.

- **Simple dosing regimen:** Once-daily oral dosing makes levothyroxine easier to incorporate into a routine.

- **Symptom relief and improved quality of life:** When patients experience benefits from treatment, they are more motivated to remain compliant.

- **Effective patient-provider communication:** A supporting relationship with healthcare professionals fosters trust and improves adherence [42].

Factors Contributing to Non-Adherence

- **Misconceptions about therapy**: Some patients discontinue treatment when symptoms resolve, believing ongoing therapy is unnecessary [31].

- **Complex or disrupted routines**: Variations in lifestyle, travel, or irregular schedules can cause missed doses [31].

- **Adverse effects or slow symptom improvement**: Patients may become discouraged if they don't feel better quickly or experience minor side effects.

- **Absorption issues and interactions**: Taking levothyroxine with food, calcium, or iron can reduce its effectiveness, leading to confusion or intentional discontinuation.

- **Mental health issues:** Depression, forgetfulness, or cognitive disorders may impair consistent medication use [24].

Identifying these factors through patient interviews and follow-ups allows healthcare providers to offer targeted interventions to improve adherence.

Tactics to Measure Adherence

Measuring patient adherence to medication is essential to ensure the effective management. Several direct and indirect methods are used in clinical practice and research to evaluate how well patients follow their prescribed regimen [43,44]. Different methods to measure adherence in patients with hypothyroidism includes;

1. **Self-Reported Questionnaires:** Patient Self-Reports among the most commonly used methods due to their simplicity and low cost. Tools such as the Morisky Medication Adherence Scale (MMAS), Medication Adherence Report Scale (MARS), Brief Medication Questionnaire (BMQ) etc., can provide insight into medication-taking behaviour [33,45].

MMAS exists two interpretations; a 4-item (MMAS-4) and an 8-item (MMAS-8) questionnaire. It assesses behaviours such as forgetting doses, carelessness, stopping drug when feeling better, and stopping when feeling worse. Each item is scored, and total scores categorize adherence as low, medium or high [45,46]. MARS is a self-reported scale typically includes 5-10 items evaluating both international non-adherences, such as deciding not to take medicine or forgetting. Respondents rate statements on a Likert Scale, with higher scores reflecting better adherence [47].

2. **Pill Counts:** This method involves counting the number of remaining pills during follow-up visits and comparing then with the expected count based on the prescription. While objective, it assumes the patient took the pills rather than discarding them or taking multiple doses incorrectly [39].

3. **Pharmacy Refill Records:** Tracking prescription refills provides a reliable and objective measure of adherence over time. Metrics like the Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC) help quantify how consistently a patient fills prescription [48,49,50].

4. **Electronic Monitoring devices:** Devices like smart pill bottles or medication dispensers record each time the container is opened. These tools provide highly accurate data but may be costly and not always feasible in routine practice.

5. **Biochemical Markers:** Thyroid function test, especially serum TSH and free T4 levels, can indirectly suggest adherence. Unexpected results, such as elevated TSH despite a prescribed dose, may indicate non-adherence or issues with absorption [28].

Each method has advantage and limitations, and combining multiple approaches often provides a more accurate picture of adherence [51].

CONCLUSION

As hypothyroidism is a lifelong condition that can be effectively managed with levothyroxine therapy when taken consistently and correctly. The benefits of treatment are closely tied to how well patient's adherence to their prescribed regimen. Poor adherence can lead to persistent symptoms, biochemical imbalances, and reduced quality of life. To ensure successful outcomes, a comprehensive and patient-centred approach is crucial. This includes educating patients about the importance of daily medication, potential consequences of missed doses, and how to correctly take levothyroxine. Physiological support should also be considered, especially for patients experiencing depression, anxiety, or cognitive challenges that may affect adherence. Additionally, health systems need to reduce barriers such as medication costs, limited access to healthcare, and complex dosing routines. Promoting consistent levothyroxine use through education, support, and accessible healthcare can ultimately transform the management of hypothyroidism.

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