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Improving Levothyroxine Adherence and Thyroid-Stimulating Hormone Control via Structured Clinical Pharmacist-Led Education in Patients with Hypothyroidism

ABSTRACT

Objective: Hypothyroidism requires lifelong levothyroxine (LT4) therapy, yet achieving target thyroid-stimulating hormone (TSH) levels is often hindered by complex drug–food interactions and poor adherence. This study evaluated the impact of clinical pharmacist-led education on LT4 adherence and treatment effectiveness.

Methods: This uncontrolled pre–post interventional study was conducted between November 2024 and April 2025 in an endocrinology outpatient clinic. Patients diagnosed with hypothyroidism initiating LT4 therapy were included. Baseline sociodemographic data and medication habits were recorded, and adherence was assessed using the Turkish-validated Medication Adherence Report Scale-5 (MARS-5). Participants received a 10-min structured verbal education session and an informative brochure. After 3 months, a follow-up was conducted via telephone to re-administer MARS-5 and retrieve serum TSH and free thyroxine (fT4) values from hospital records.

Results: Among 152 participants (median age 51; 86.2% female), the median MARS-5 score significantly increased from 24.0 (interquartile range (IQR) 22.0-25.0) to 25.0 (IQR 24.0-25.0; $P < .001$). Median TSH levels significantly decreased from 2.04 (0.80-3.95) to 1.17 (0.39-3.16) mIU/L ($P = .002$), while fT4 levels remained stable. Notably, the proportion of patients taking LT4 at least 30 min before breakfast improved from 45.7% to 96.7% ($P < .001$).

Conclusion: A brief, structured clinical pharmacist-led intervention significantly improved LT4 adherence and biochemical treatment outcomes. These findings underscore the clinical value of integrating pharmacist-led education and follow-up services into routine outpatient care to optimize long-term management of hypothyroidism.

Keywords: Clinical pharmacist, hypothyroidism, levothyroxine, medication adherence, patient education

Introduction

Hypothyroidism is a chronic condition in which the thyroid gland cannot produce sufficient amounts of thyroid hormone and is therefore unable to meet the body's metabolic needs.[1,2] It is known that hypothyroidism affects 1-2% of the population in areas without iodine deficiency.[3,4] According to the goiter prevalence study conducted in Trabzon province by Kocak et al., subclinical hypothyroidism was found in 3.3% and clinical hypothyroidism in 0.2% of the population.[5]

The first-line treatment for hypothyroidism is levothyroxine (LT4) replacement therapy, a synthetic hormone. During treatment, the dosage is determined based on the patient's lean body mass and adjusted according to the patient's specific needs. As treatment generally continues throughout the patient's lifetime, the physiological changes affect the maintenance dose required for LT4. Therefore, the primary aim of LT4 treatment is to maintain thyroid-stimulating hormone (TSH) levels within the reference range. LT4 should be taken regularly every day to maintain normal thyroid hormone levels. However, it is known that 31.6% of hypothyroidism patients do not take their LT4 medication regularly during the first year of treatment.[6-9]

According to the literature, it is known that many patients receive excessive or insufficient LT4 treatment in clinical practice. The underlying reasons for this outcome may include drug interactions, malabsorption syndromes, autoimmune gastritis, and poor treatment adherence.

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Sena Ustaömer[1,2]
Mefküre Durmuş[2]
Özge Üçüncü[3]
Mustafa Koçak[3]

[1]*Department of Clinical Pharmacy, Marmara University Faculty of Health Sciences, İstanbul, Türkiye*
[2]*Department of Clinical Pharmacy, Karadeniz Technical University Faculty of Pharmacy, Trabzon, Türkiye*
[3]*Department of Endocrinology and Metabolism, Karadeniz Technical University Faculty of Medicine, Trabzon, Türkiye*

Corresponding author:
Sena Ustaömer,
✉ ustaomersena@gmail.com,
senaustaomer@ktu.edu.tr

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Certain medications, such as preparations containing iron, calcium, and magnesium; sucralfate; aluminum-containing antacids; bile acid sequestrants; phosphate binders; and proton pump inhibitors (PPIs), inhibit the absorption of LT4.[10-12]

According to the World Health Organization (WHO), the concept of "medication adherence" is defined as "the extent to which a person's behavior is consistent with the healthcare provider's recommendations" regarding the dosage, frequency, and timing of prescribed medication. Several important factors can lead to patients being nonadherent to treatment, including access to care services, stress levels related to healthcare visits, psychological factors concerning the patient, side effects of medications, treatment duration, and socio-economic conditions.[2,13,14]

Although hypothyroidism is a common disorder and its treatment is well known, many patients have low compliance with levothyroxine, and their TSH levels are not within reference ranges. Understanding the barriers and determinants of treatment adherence will help improve treatment success. This study aimed to evaluate treatment adherence and effectiveness in patients diagnosed with hypothyroidism who are currently receiving LT4 therapy and to improve treatment adherence through verbal and written information.

Materials and Methods

Study Design and Participants

This uncontrolled pre-post study was conducted among patients with hypothyroidism who attended the endocrinology and metabolism outpatient clinic of Karadeniz Technical University hospital in Trabzon, Türkiye, between November 11, 2024, and April 11, 2025. Patients with hypothyroidism aged 18 years and older who visited the Karadeniz Technical University endocrinology and metabolism clinic, provided written consent, and had been using levothyroxine for at least 1 month were included in the study. Figure 1 illustrates the study design and participant flow. The study excluded pregnant and breastfeeding women, patients with communication difficulties, individuals under the age of 18, and those who did not provide written consent. The study received ethical approval from the Karadeniz Technical University Faculty of Medicine Scientific Research Ethics Committee (Decision No: 12.2024.225, Date: December 13, 2024). All procedures in this study adhered to the ethical standards set by the institutional research committee and followed the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments. All participants provided written informed consent before participation.

Sample Size

The literature indicates that groups of hypothyroid patients receiving pharmacist-led training could increase their attitude scores from an average of 14.70 (standard deviation [SD] 1.54) to 15.35 (SD 1.12) (Vanderpump, 2011). Calculations were performed at a significance level of 0.05 and a power value of 90%, and it was determined that at least 51 patients were required. Considering a 30% loss rate, a minimum of 73 patients should be included in the study.

Outcome Measures

The primary outcomes of the study were to determine patient compliance with LT4 treatment, maintain patient TSH levels within the reference range as a result of the patient education service provided, and increase treatment compliance. By systematically evaluating patients with these measurements, this study aims to provide valuable information about the effectiveness of clinical pharmacists' interventions in improving patient care and treatment outcomes.

Data Collection

Sociodemographic characteristics, concomitant medications, timing of LT4 administration (with meals and whether taken on an empty or full stomach), the interval between medication intake and meals, and the intervals between LT4 and potentially interacting drugs (e.g., proton pump inhibitors, calcium, magnesium, iron, etc.) were recorded using a patient profile form developed before the study for participants who met the inclusion criteria and were receiving LT4 therapy. Baseline serum TSH and free thyroxine (fT4) levels from the participants" initial visits were obtained and recorded using the hospital information system. To assess treatment adherence, the Medication Adherence Report Scale-5 (MARS-5), adapted and validated in Turkish, consisting of a 5-point Likert scale, was administered to all participants.[2,3] The scores obtained were documented in the patient profile form. Contact telephone numbers were recorded, and at the end of the third month following the educational intervention, participants were contacted by telephone for a follow-up MARS-5 assessment. During these calls, adherence scores and responses to questions regarding LT4 use were recorded, and patients were reminded about correct medication practices. At the end of the third month, serum TSH and fT4 levels from the second visit were retrieved from the hospital information system.

Evaluation of Laboratory Findings and Adherence to Levothyroxine Treatment

All TSH, fT4, and fT3 values evaluated in the study were obtained from blood samples taken in the morning after an 8-h fast before LT4 administration. In assessing thyroid function, the reference ranges for TSH were 0.41-6.8 mIU/mL, for fT3 2.97-4.46 mIU/mL, and for fT4 0.57-1.24 mIU/mL. Those below the reported reference ranges are considered "low," those above the reference range are considered "high," and those within the reference range are considered "normal."

The MARS-5 used in the compatibility assessment consists of 5 questions and is evaluated using a 5-point Likert scale, where 5 = never, 4 = rarely, 3 = sometimes, 2 = often, and 1 = always. The total scores

MAIN POINTS

- Structured clinical pharmacist-led education significantly improves medication adherence scores in patients with hypothyroidism.
- The intervention leads to a significant decrease in serum thyroid-stimulating hormone levels, indicating improved biochemical treatment outcomes.
- Patient behaviors regarding the correct timing of levothyroxine administration and drug-food interactions show marked improvement following clinical pharmacist intervention.
- Age is an independent predictor of post-education adherence, with older patients showing a higher likelihood of achieving full compliance.
- Integrating clinical pharmacist-led education into routine outpatient care is a valuable strategy for optimizing long-term hypothyroidism management.

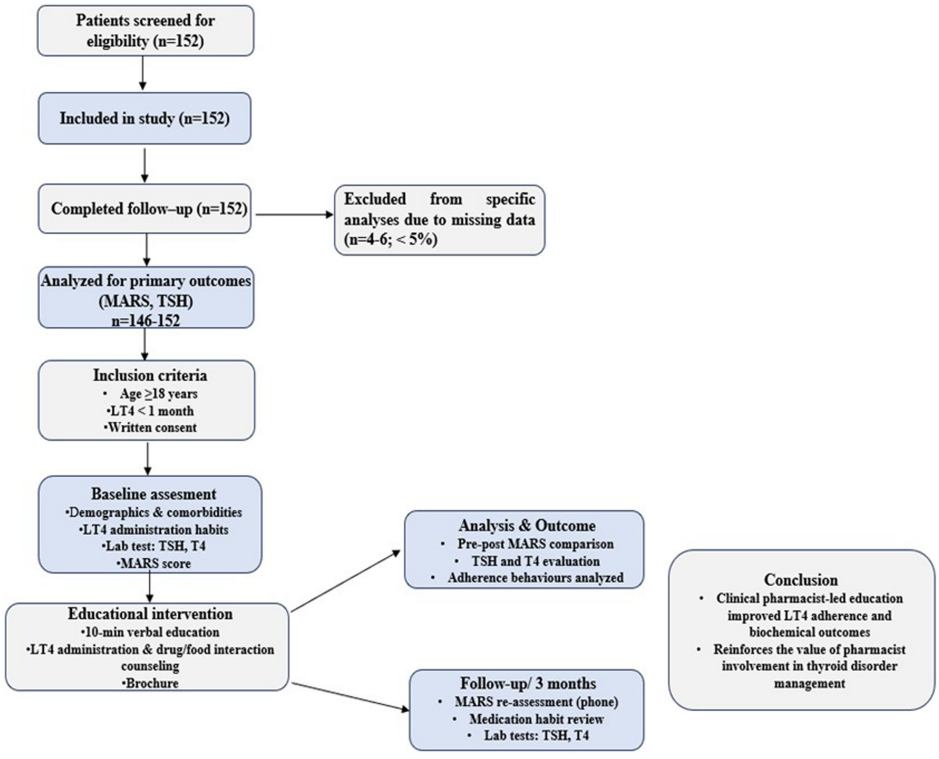

Figure 1. Study flow diagram.

obtained on the scale ranged from 5 to 25. An increase in the scores indicates compatibility, while a decrease indicates incompatibility. Although the original MARS-5 scale does not define a cut-off, for practical purposes, a score ≥ 20 was considered indicative of high adherence based on Turkish adaptation literature and the dataset distribution.[15,16]

Patient Education Service by a Clinical Pharmacist

At the initial assessment, the MARS-5 was administered, after which participants received approximately 10 min of verbal education on hypothyroidism and the appropriate use of LT4 sodium. An information brochure summarizing the educational content was also provided. The education included the principles of LT4 administration, potential drug–drug interactions (pDDIs), drug–food interactions, and treatment-related precautions. The UpToDate® Lexidrug™ database (Wolters Kluwer Health Inc.) was used to analyze pDDIs and drug–food interactions, which were then classified into risk categories A, B, C, D, and X.

In line with the Turkish Endocrinology and Metabolism Association guideline,[4] patients were instructed to take LT4 sodium on an empty stomach, preferably 1 h before breakfast. They were advised to maintain a minimum 4-h interval between LT4 sodium and concomitant use of iron supplements, antacids containing Al^{3+}, Mg^{2+}, or Ca^{2+}, proton pump inhibitors, sucralfate, bile acid sequestrants, or phosphate binders. Patients were also advised to consult their physicians in case of body weight changes exceeding 5% or regarding thyroid function testing.

Follow-up consultations were conducted via telephone, during which the MARS-5 was re-administered, and LT4 sodium use was reassessed. Patients who were using LT4 sodium incorrectly or incompletely were re-instructed on proper administration.

Statistical Analysis

IBM SPSS Statistics V 23.0 (IBM, Armonk, New York, USA) was used for analyses. Data distribution was checked using the Kolmogorov–Smirnov test. Continuous variables were presented as median (interquartile range [IQR]), while ordinal and nominal values were presented as n (%). Comparisons between dependent groups (pre-treatment and post-treatment) utilized the Wilcoxon signed-rank test, depending on data distribution. The overall goodness-of-fit of the binary logistic regression model was evaluated using the Omnibus Tests of Model Coefficients, and the proportion of variance explained by the independent variables was assessed using the Nagelkerke R-square statistic. Due to the severe ceiling effect and highly skewed distribution of the post-education MARS-5 scores, binary logistic regression was preferred over linear regression, with the dependent variable dichotomized into "Full Adherence" (MARS-5 score = 25) versus "Non-Full Adherence" (MARS-5 score < 25).

Missing Data Management

Some variables in the dataset contained missing values (particularly "education level" and " cause of hypothyroidism" with < 2%, and laboratory data with < 5%). Missing data were examined before analysis, and Little's MCAR (Missing Completely at Random) test indicated that the missingness was completely at random ($P > .05$). Given the low proportion of missing data, multiple imputation was not performed; all analyses were conducted using the available-case (complete-case) approach. The number of observations used in each table (n) is reported in the table headings.

Results

The study included 152 patients with hypothyroidism. The median age was 51 years (IQR 40-59), and the majority were female (86.2%) and aged 18-65 years (88.8%). Almost half of the participants were

primary school graduates. Regarding comorbidities, 64.7% of the patients had no additional chronic diseases, with an overall median number of 0 (IQR 0-1) accompanying conditions. The median number of medications used was 2 (IQR 1-4). The median daily LT4 dose was 100 µg (IQR 78.6-107.1), and the median duration of use was 9 years (IQR 2-13). Overall, 37.5% of patients had at least 1 comorbidity, most commonly hypertension and diabetes mellitus (Table 1).

Some variables had missing data (e.g., n = 150 for "education level", n = 150 for " cause of hypothyroidism", and n = 146 -148 for laboratory parameters). Since the proportion of missing data was less than 5%, analyses were conducted using the available data.

Table 1 Baseline Demographic and Clinical Characteristics of Patients

Variable	Frequency	Percentage
Gender		
Female	131	86.2
Male	21	13.8
Age Category		
18-65 years	135	88.8
Above 65 years	17	11.2
Education Level		
Uneducated	12	7.9
Primary school	69	45.4
Secondary school	13	8.6
High school	41	27
University degree	13	8.6
Postgraduate degree	4	2.6
Smoker		
Yes	21	13.8
No	127	83.6
Former smoker	4	2.6
Alcohol		
Yes	4	2.6
No	148	97.4
Co-morbidities		
Hypertension	57	37.5
Diabetes mellitus	28	18.4
Cardiovascular diseases	23	15.1
Hyperlipidemia	21	13.8
Depression	15	9.9
Asthma	5	3.5
COPD	2	1.3
Rheumatic diseases	2	1.3
Transient ischemic attack	1	0.6
Restless leg syndrome	1	0.6
The cause of hypothyroidism		
Thyroidectomi	97	64.6
Autoimmune	51	34
Congenital hypothyroidism	1	0.7
Thyroiditis	1	0.7
Total (n = 152)	—	100

*n: The total number of patients analyzed was 152. The number may vary slightly by variable due to missing data (< 5%).
COPD, chronic obstructive pulmonary disease.

Following the educational intervention, medication adherence improved significantly, as reflected by an increase in the median MARS-5 score (from 24.00 [IQR 22.00-25.00] to 25.00 [IQR 24.00-25.00], $P < .001$). Serum TSH levels decreased significantly (2.04 [0.80-3.95] vs. 1.17 [0.39-3.16], $P = .002$), while serum fT4 levels remained unchanged (0.87 [0.76-1.00] vs. 0.87 [0.76-0.99], $P = .626$) (Table 2, Figure 2).

Analysis of individual MARS-5 items demonstrated significant reductions in non-adherence behaviors. Improvements were observed for "I forget to take it" ($P < .001$), "I stop taking them for a while" ($P < .001$), "I skip one of the medicines" ($P < .001$), and "I take less than instructed" ($P = .008$), while "I alter the dose of my medicines" did not change significantly ($P = .096$) (Table 3).

Patient habits regarding LT4 administration also improved. After education, nearly all patients reported taking LT4 in the morning at least 30 min before breakfast, compared with 45.7% before education ($P < .001$). The proportion of patients maintaining adequate intervals between LT4 and other medications affecting absorption also increased, indicating improved understanding of proper administration (Supplementary Table S1).

Linear regression analysis was initially considered; however, due to the severe ceiling effect and highly skewed distribution of the post-education MARS-5 scores (with most participants scoring the maximum value of 25), a Binary Logistic Regression analysis was performed to ensure statistical validity. In this revised model, the dependent variable was dichotomized into "Full Adherence" (MARS-5 score = 25) versus "Non-Full Adherence" (MARS-5 score < 25). This binary approach allowed us to identify factors that specifically predict the likelihood of achieving perfect compliance, rather than assessing a continuous shift in an already saturated score.

The overall logistic regression model did not reach overall statistical significance according to the Omnibus Tests ($chi^2 = 10.950$, df = 10, $P = .361$), indicating that the combination of demographic and baseline clinical variables has a limited predictive capacity for post-education

Table 2. Comparison of MARS-5 Scores and Thyroid Function Test Before and After Patient Education

	Before Patient Education	After Patient Education	Z	P
MARS-5 score, median (IQR)	24.00 (22.00-25.00)	25.00 (24.00-25.00)	−7,792	< .001*
Serum TSH level, median (IQR)	2.04 (0.80-3.95)	1.17 (0.39-3.16)	−3,086	.002*
Serum fT4 level, median (IQR)	0.87 (0.76-1.00)	0.87 (0.76-0.99)	−,487	.626

MARS-5 n = 152, TSH n = 148, fT4 n = 146. Missing laboratory data < 5%.
MARS-5, medication adherence report scale-5; TSH, thyroid-stimulating hormone.
Wilcoxon signed ranks test.

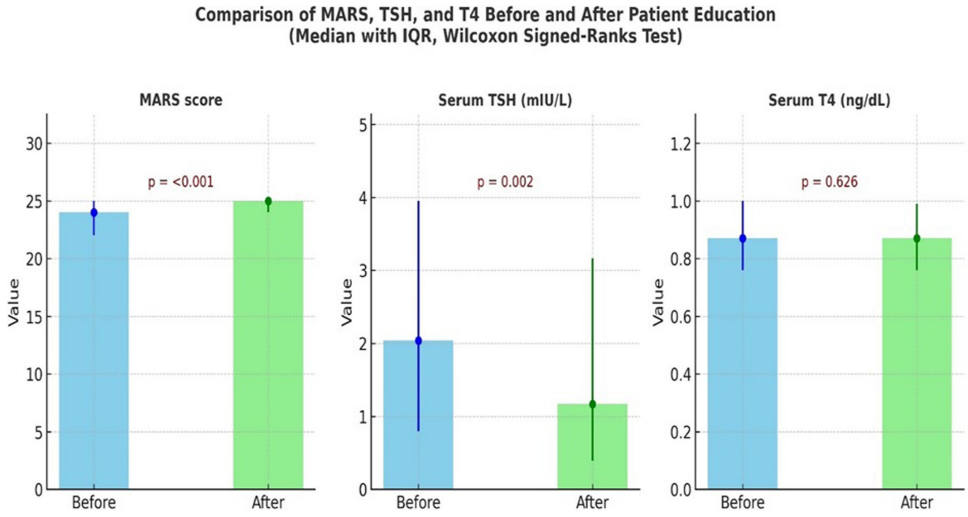

Figure 2. Change in Medication Adherence Report Scale-5, thyroid-stimulating hormone, and fT4 levels before and after education.

adherence classification. The model explained approximately 10.2% of the variance in achieving full adherence (Nagelkerke R2 = 0.102).

Nevertheless, when evaluating individual predictors within the equation, age emerged as the only significant independent factor associated with achieving full medication adherence after the educational intervention (B = 0.044, Wald = 5.984, *P* = .014, {Odds Ratio [OR]} = 1.045, 95% C.I. 1.009-1.082; Table 4). The obtained Odds Ratio indicates that with each 1-year increase in patient age, the likelihood (odds) of achieving a perfect adherence score of 25 after education significantly increases by approximately 4.5% (Table 4).

Potential drug–drug interactions with LT4 were identified in 44 patients (28.9%), most commonly with proton pump inhibitors (PPIs, n = 31), magnesium (n = 14), and calcium supplements (n = 13). Most interactions were classified as category B or D according to Lexicomp®. Magnesium, calcium, and iron supplements may reduce LT4 absorption and require a ≥ 4-h separation, whereas PPIs were considered moderate interactions requiring no additional clinical action (Supplementary Table S2).

Discussion

This study evaluated the impact of a pharmacist-led educational intervention on treatment adherence and thyroid function among patients with hypothyroidism receiving LT4. The findings demonstrate that a short-term, structured education program significantly improved medication adherence, optimized TSH levels, and reduced common medication errors. The median MARS-5 score increased from 24.0 (IQR 22.0-25.0) to 25.0 (IQR 24.0-25.0; *P* < .001), while median serum TSH levels decreased from 2.04 mIU/L (IQR 0.80-3.95) to 1.17 mIU/L (IQR 0.39-3.16; *P* = .002). These results confirm that even brief, focused educational interventions can yield measurable biochemical and behavioral improvements in a chronic condition that requires lifelong management.

Although TSH levels improved significantly, serum fT4 levels remained stable. This finding is physiologically consistent, as TSH is a more sensitive and dynamic marker of treatment response, reflecting early changes in hormone bioavailability, whereas fT4 levels remain relatively constant once within the reference range. Most participants already had adequate baseline fT4 concentrations; therefore, a substantial rise was not anticipated. Similar outcomes were reported by Cappelli et al.[17] and Shakya et al.[18] who observed that structured educational interventions improved TSH control without significant alterations in fT4 levels. Collectively, these results suggest that enhanced adherence primarily normalizes the hypothalamic–pituitary–thyroid axis rather than increasing circulating hormone concentrations.

Beyond biochemical improvements, enhanced adherence behaviors following education likely reflect increased patient awareness of correct LT4 administration practices. After the intervention, the proportion of patients who forgot to take LT4 decreased markedly (from 27.5% to 2.0%), while those taking LT4 at least 1 h before meals increased from 35.3% to 56.9% (*P* < .001). These behavioral changes are clinically meaningful, as the timing of LT4 ingestion and avoidance of drug–food interactions critically affect absorption. Education probably improved patients' perceived benefits and self-efficacy, consistent with the Health Belief Model, which posits that patients' beliefs about treatment consequences shape adherence behaviors.

Patient education produced significant improvements across multiple aspects of medication-taking behavior. The proportion of patients reporting that they "forget to take LT4" decreased from 27.5% to 2.0%, and those who "never forget" increased from 31.4% to 62.7% (*P* < .001). Likewise, the frequency of patients who "stop taking LT4 for a while" declined from 29.4% to 15.7% (*P* < .001), and those who "skip one of the medicines" decreased from 21.6% to 5.9% (*P* < .001). The time interval between LT4 administration and meals also improved substantially, with 56.9% of patients taking LT4 1 h before meals after education, compared with 35.3% at baseline (*P* < .001).

Although the educational counseling heavily emphasized taking LT4 strictly on an empty stomach in the morning, it is well established that LT4 possesses a remarkably long elimination half-life (t1/2 ~7 days). Clinical guidelines note that steady-state plasma concentrations of the hormone depend on the cumulative weekly dose rather than minor instantaneous timing shifts. Therefore, if patients inadvertently miss their morning dose, they can safely take it later in the day on an empty stomach to maintain the steady state. While completely skipping a dose leads to subtherapeutic levels and subsequent TSH

Table 3. Changes in Medication Adherence Behaviors Before and After Patient Education

	Before Patient Education (n = 152)*	After Patient Education (n = 147)* n (%)	Z	*P*
"I forget to take it."			−6.716	< .001*
Always	1 (0.7)	0 (0)		
Often	7 (4.6)	0 (0)		
Sometimes	30 (19.7)	2 (1.4)		
Rarely	46 (30.3)	35 (23.8)		
Never	68 (44.7)	110 (74.8)		
"I alter the dose of my medicines."			−1.667	.096
Always	0 (0)	0 (0)		
Often	1 (0.7)	0 (0)		
Sometimes	0 (0)	0 (0)		
Rarely	6 (3.9)	2 (1.4)		
Never	145 (95.4)	145 (98.6)		
"I stop taking them for a while."			−3.686	< .001*
Always	0 (0)	0 (0)		
Often	1 (0.7)	0 (0)		
Sometimes	12 (7.9)	2 (1.4)		
Rarely	14 (9.2)	8 (5.4)		
Never	125 (82.2)	137 (93.2)		
"I skip one of the medicines."			−5.714	< .001*
Always	0 (0)	0 (0)		
Often	5 (3.3)	0 (0)		
Sometimes	17 (11.2)	3 (2.0)		
Rarely	31 (20.4)	16 (10.9)		
Never	99 (65.1)	128 (87.1)		
"I take less than instructed."			−2.636	.008*
Always	0 (0)	0 (0)		
Often	1 (0.7)	0 (0)		
Sometimes	1 (0.7)	0 (0)		
Rarely	6 (3.9)	0 (0)		
Never	144 (94.7)	147 (100.0)		

*Data are presented as frequencies (n) and percentages (%). All MARS-5 items were fully answered by 152 participants at baseline and 147 participants at the 3-month post-education follow-up (5 patients were lost to follow-up). Wilcoxon signed-rank test was used for comparison.

Table 4. Binary Logistic Regression Analysis for Predictors of Full Medication Adherence (MARS-5 = 25) After Education

Variable	B	Standard Error	Wald	P
Gender	−0.141	0.627	0.051	.822
Age	0.044	0.018	5.984	.014*
Education level			0.851	.974
Education Level (1)	−0.699	1.412	0.245	
Education Level (2)	−0.696	1.273	0.299	
Education Level (3)	−1.139	1.368	0.693	
Education Level (4)	−0.634	1.261	0.253	
Education Level (5)	−0.608	1.342	0.205	
Duration of LT4 use	−0.008	0.025	0.095	.758
Baseline TSH level	0	0	0.11	.74
LT4 dose	0.006	0.006	1.024	.312

*Note: Dependent variable is binary coded as 0: Partial adherence (MARS-5 < 25,n = 45) and 1: Full adherence (MARS-5 = 25,n = 100). Model Omnibus Test *P* = .361, Nagelkerke R2 = 0.102.
B, unstandardized regression coefficient; CI, confidence interval; df, degrees of freedom; LT4, levothyroxine; MARS-5, Medication Adherence Report Scale-5; TSH, thyroid stimulating hormone.
P < .05 is considered statistically significant.

fluctuations, explaining this compensation window to patients during counseling provides a practical advantage. Educating patients to compensate for a missed dose within the same day rather than abandoning it entirely can make the regimen more flexible and further enhance long-term treatment compliance.

Potential drug interactions with LT4 were also evaluated. Proton pump inhibitors, magnesium, and calcium preparations were the most frequent interacting agents, with magnesium salts used by 9.2% of patients, calcium salts by 8.6%, and PPIs by 20.4%. Most of these interactions were classified as moderate or D-level, consistent with evidence that LT4 absorption is reduced when co-administered with mineral supplements.

The updated binary logistic regression analysis revealed that age was significantly associated with the odds of achieving full adherence post-education (OR = 1.045, *P* = .014). However, this finding should be interpreted with caution as it largely reflects a statistical artifact stemming from the severe ceiling effect and high clustering of MARS-5 scores at the maximum threshold of 25 post-intervention. From a clinical perspective, the educational intervention yielded high success across both younger and older patient populations throughout the entire cohort. Therefore, this age-related association does not necessarily imply that the education was inherently more effective in 1 group over another; rather, it reflects the mathematical distribution and clustering at the ceiling score level.

While standard chronic disease literature often suggests that advanced age may challenge treatment compliance due to polypharmacy or cognitive decline, the structured, multi-modal intervention—combining a 10-min verbal presentation with a physical brochure—successfully neutralized these potential barriers. It ensured that mature patients, who often maintain more predictable daily routines that accommodate the fast-and-wait restrictions of levothyroxine, could seamlessly lock into full adherence. Consequently, the findings support the broad feasibility and inclusive success of clinical pharmacist-led counseling, demonstrating that all age groups benefit substantially from structured follow-up once ceiling-effect dynamics are accounted for.

Other demographic and clinical variables, including gender, educational status, income, comorbidities, and LT4 dose, did not significantly influence adherence outcomes. This finding indicates that structured educational programs can enhance adherence regardless of sociodemographic differences, highlighting their broad applicability in endocrine practice.

The median LT4 dose was 100 µg, and the mean treatment duration was approximately 9 years, emphasizing that hypothyroidism management requires long-term follow-up and sustained patient engagement. Comorbidities were present in 62.5% of patients, with hypertension (37.5%), diabetes mellitus (18.4%), cardiovascular disease (15%), and hyperlipidemia (13.8%) being the most common, illustrating the complexity of managing this population. Shakya et al.[18] similarly reported that most patients remain on LT4 therapy for years and often require ongoing dose adjustments. Chronic disease literature consistently shows that only about 50% of patients adhere to long-term medication regimens. For example, a Lebanese study reported high adherence in only 14.5% of participants, while 54.9% demonstrated low adherence. A study from South India found overall compliance rates of 34.6% and 40.4% on 2 different scales[19-24]. In contrast, the present study demonstrated marked behavioral improvement following clinical pharmacist education, illustrating the importance of pharmacist involvement in chronic care.

At baseline, 94% of patients already exhibited high adherence (MARS-5 > 20), while 6% had low adherence. After the educational intervention, all participants demonstrated high adherence (100%). Even among those who were already highly adherent, the intervention further increased MARS-5 scores, with median values rising from 24 to 25, indicating an overall enhancement in adherence behaviors throughout the cohort.

Taken together, these findings align with national and international evidence demonstrating that educational and counseling-based interventions improve patient knowledge, medication adherence, and clinical outcomes. Nonetheless, age-related barriers may persist and warrant targeted strategies. Integrating pharmacist-led education into endocrine outpatient services could represent a cost-effective and scalable approach to improving chronic disease management.

Strengths and Limitations

This study has several strengths, including the assessment of baseline adherence scores, a 3-month post-education follow-up conducted via telephone interview, and the combined evaluation of LT4-related behaviors and laboratory parameters. However, certain limitations should be acknowledged. The sample size was relatively small, the follow-up duration was short, and adherence was self-reported rather than objectively measured. Additionally, the study's uncontrolled pre–post interventional design is a major limitation, making it difficult to definitively isolate the specific efficacy of the educational program. The observed improvements in TSH levels and adherence scores may have been influenced by factors other than the education itself, such as the patients' increased awareness from knowing they were participating in a study (the Hawthorne effect), the professional motivation provided by periodic telephone follow-ups, or the practice effect of re-administering the same questionnaire.

Furthermore, the median duration of LT4 use among the cohort was 9 years, which likely contributed to the high baseline adherence scores and created a potential ceiling effect. This high initial adherence may obscure the full potential impact of the intervention. A minor limitation was also the small proportion of missing data for certain variables (e.g., education level, thyroid function tests); however, given that missingness was minimal (< 5%), analyses using available data are unlikely to have influenced the overall results.

Future studies should utilize randomized controlled trials (RCTs) with larger cohorts and longer follow-up durations to clearly separate the intervention's effects from background follow-up factors and to assess the lasting impact of education. Including newly diagnosed patients who are initiating therapy would be highly beneficial to demonstrate the net effect of the education on lower baseline compliance rates. Finally, using objective adherence measures, digital tracking tools, and evaluating the integration of pharmacist-led education into multidisciplinary endocrine care could clarify its long-term feasibility and clinical impact.

This study points out the importance of structured patient education in the management of hypothyroidism. Providing both verbal and written guidance significantly improved levothyroxine adherence, optimized medication timing, and minimized the risk of interactions. Incorporating pharmacist-led educational programs into routine endocrine practice may enhance long-term outcomes and support optimal thyroid control, particularly among older adults.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Artificial Intelligence Usage Statement: The authors declared that Gemini was used for language editing and grammar improvement. No other Artificial Intelligence Tool was used in the preparation of the manuscript.

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