Original Article

Parents' Adherence to Medical Advices about Administering Levothyroxine Therapy to their Hypothyroid Children

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Abstract

Background: The most frequent reason for unsatisfactory thyroid disease control is poor adherence to treatment. In order to increase adherence to treatment, health care providers should give caregivers precise instructions. **Objectives:** To evaluate parents' adherence to medical advice about administering levothyroxine to their hypothyroid children, and whether a child's age and sex, duration of disease, the presence of additional chronic diseases, and who is the caregiver have an impact on their compliance. **Materials and Methods:** A cross-sectional study was performed at pediatric endocrinology outpatient clinic in in Iraqi National Endocrine and Diabetes Center. It is a 2-part questionnaire-based study, done by face-to-face interview. First part included patients' demographic data, whereas second part questions were related to parental adherence to the medical advice about levothyroxine administration. Parents were considered compliant if they strict to all three rules (giving the medicine daily on an empty stomach and 30-60 minutes before eating). **Results:** Fifty-four hypothyroid children were recruited. 83.3% of parents never forgot to give levothyroxine to their children; 87% and 83.3% gave it always on an empty stomach and 30–60 min before eating, respectively. 74% of parents were compliant to levothyroxine administration rules. There was no significant association between parents' compliance and the patient's age and sex, duration of hypothyroidism, presence of other chronic diseases, and the caregiver. **Conclusions:** Poor parents' adherence to medical advices is still a problem, and it is not related to the patient's age and sex, disease duration, presence of other chronic disease, nor caregiver.

Keywords: Adherence, advice, children, hypothyroidism, levothyroxine, parents

Introduction

Early diagnosis and treatment of hypothyroidism are crucial due to the processes of brain development that depend on thyroid hormones in the first few years of life and successful treatment strategies appear to be particularly critical for achieving the best outcomes in terms of mental and neuromotor development. However, even with larger dosages of levothyroxine (L-T4), some hypothyroid patients might not attain normal thyroid stimulating hormone (TSH) concentrations. The most frequent reason for poor and unsatisfactory TSH control is poor adherence to treatment. In order to increase adherence to treatment, health care providers should give the caregivers precise instructions and clear recommendations.[1-3]

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L-T4 tablets are absorbed to an extent of around 70%, primarily in the duodenum and the jejunum. The ideal time to ingest L-T4 is in the morning, at least 30–60 min before breakfast, as fasting enhances its absorption.[4-6] When L-T4 is taken with food, its pharmacokinetics and therapeutic effectiveness are impaired and the peak value of L-T4 absorption reduced,[4] in addition to the drug bioavailability, by 15% to as much as 40%.[7] For this reason, it is crucial to check that L-T4 is being

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administered properly in children who do not respond to treatment and, if necessary, reassess the administration method.

The likelihood of impaired L-T4 absorption associated with gastrointestinal illnesses (celiac disease, lactose intolerance, infection with *Helicobacter pylori*, inflammatory bowel diseases, and *Giardia lamblia*),[4] or the interference of drugs or substances with its metabolism or absorption (proton-pump inhibitors, sucralfate and aluminum-containing antacids, supplements containing calcium and iron, bile acid sequestrants, phosphate binders, and infant formulas containing soy protein, iron, and calcium supplements) should also be taken into consideration.[8]

This study aimed to evaluate parents' adherence to medical advice about administering levothyroxine to their hypothyroid children, and whether a child's age and sex, duration of disease, the presence of additional chronic diseases, and who is the caregiver have an impact on their compliance.

Materials and Methods

A descriptive, cross-sectional study was conducted at pediatric endocrinology outpatient clinic in Iraqi National Endocrine and Diabetes Center, Mustansiriyah University, in Baghdad City, Iraq, which is one of the largest tertiary centers providing pediatric endocrine services. The study was conducted between 22nd of August and 28th of September, 2022. The medical research ethics committee at Mustansiriyah University approved the study with (IRB 6 on August 2022). All participants gave a signed informed consent before their involvement.

The study recruited any hypothyroid (central or primary hypothyroidism) children and adolescent of both sex who consulted pediatric endocrinology clinic for routine follow-up throughout the study period and met the inclusion and exclusion criteria. Inclusion criteria were: age 1 month to 16 years, and the diagnosis and follow-up for patients were done by the same pediatric endocrinologist in the center. Patients whose parents were unaware about the three rules of administration of L-thyroxin (giving the medicine daily on an empty stomach and 30–60 min before eating) or did not consent to the interview were excluded from this study.

The study was questionnaire-based, done by face-to-face interview by the endocrinologist involved in the management of the patients. In all of the cases, the interviewee was the mother, father or both of them.

The questionnaire contained two parts; the first part included questions about patients' demographic data: age group (<1 year, 1–12 year, >12 year), sex, duration of disease (<1 year, 1–5 year, >5 year), presence of other chronic disease such as diabetes mellitus, celiac disease, etc.) and who is the caregiver, followed by second part questions related to parental adherence to the three medical advice about L-T4 administration: How many times per week did the child miss the medicine? Was the child always taking the medicine on an empty stomach? Were they always adhered to giving the medicine 30–60 min before eating? Parents were considered compliant if strict patients were done to all three rules (giving the medicine daily on an empty stomach and 30–60 min before eating).

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, N.Y., USA) version 27. Categorical variables were presented as frequencies and percentages. The association between categorical variables was determined using the Fisher's Exact Test and Pearson chi-square. A *P* value of ≤0.05 was considered as significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' parents verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 6 on August 1, 2022.

Results

Fifty-four hypothyroid children and adolescent were included in this study; their characteristics are shown in

Table 1: Patients' characteristics

Variable	Number (%)
Patient sex	
Males	23 (42.6%)
Females	31 (57.4%)
Patient age	
<1 year	1 (1.85%)
1–12 year	34 (62.96%)
>12 year	19 (35.19%)
Disease duration	
<1 year	21 (38.9%)
1–5 year	20 (37.03%)
>5 year	13 (24.07%)
Other chronic disease	
Yes*	20 (37.03%)
No	34 (62.96%)
Caregiver	
Father	34 (62.96%)
Mother	20 (37.03%)

*2 with diabetes mellitus, 1 with coeliac disease, and 17 having variable non-autoimmune chronic conditions, such as epilepsy and congenital heart disease

Table 2: Parents' adherence to each of the three rules of thyroxin therapy and to all of them

Variables	Number = 54	Percentage %
Forget to give levothyroxine (times/week)		
0	45	83.30%
≥1	9	16.70%
Giving levothyroxine on an empty stomach		
Yes	47	87%
No	7	13%
Giving levothyroxine 30–60 min before eating		
Yes	45	83.30%
No	9	16.70%
Compliant*		
Yes	40	74%
No	14	26%

*Adherent to all 3 rules

Table 3: Association of parents' compliance (adherence to all 3 rules) with the patient's age, sex, duration of the disease, presence of other chronic disease, and the caregiver

Variable	Compliant number (%)	Non-compliant number (%)	*P* value*
Age			0.96
<1 year	1 (2.5)	0	
1–12 year	25 (62.5)	9 (64.3)	
>12 year	14 (35)	5 (35.7)	
Sex			0.52
Male	16 (40)	7 (50)	
Female	24 (60)	7 (50)	
Disease duration			0.96
<1 year	6 (15)	2 (14.3)	
1–5 year	20 (50)	7 (50)	
>5 year	14 (35)	5 (35.7)	
Other chronic disease			0.28
Yes	11 (27.5)	6 (42.9)	
No	29 (72.5)	8 (57.1)	
Caregiver			0.6
Father	26 (65)	8 (57.1)	
Mother	14 (35)	6 (42.9)	

*Pearson chi-square test. *P*-value of ≤ 0.05 was considered as significant

Table 1. Parents' adherence to L-T4 therapy is shown in Table 2. Forty parents (74%) were complaint (adherent to all 3 rules). There was no significant association between parents' compliance to L-T4 administration rules and the patient's age, sex, duration of hypothyroidism, presence of other chronic diseases, and the caregiver as shown in Table 3.

Discussion

One long-standing and well-known issue with patients who have chronic disorders is non-compliance with prescribed medications. In addition to the doctor–patient relationship, the frequency of dose, duration of treatment, and number of medications are all linked to the development of non-compliance. The lifelong daily administration of thyroxin may result in patient non-compliance.[9] To our knowledge, this is the first study done in Iraq about L-T4 treatment adherence among pediatric age group.

In the current study, most of caregiver parents were fathers (62.96%) [Table 1]; this result was different from Brito *et al.*[3] in which females were predominantly giving care to their children especially when it comes to giving medications and supervising it (94.3%).

Regarding parents' adherence to medical advice about L-T4 drug, (83.3%) of parents never forgot to give the medicine to their children [Table 2]. This is fortunately a good result because European Society for Pediatric Endocrinology Consensus recommends adherence to L-t4 treatment since it is important to achieve normal growth, puberty, and

fertility.[10] On the other hand, 16.7% of parents forgot to give L-T4 to their children once or more weekly [Table 2]. This result is lower than the result of study done in Germany by Lass and Reinehr[11] which showed that 58% of hypothyroid children treated with thyroxin missed at least 1 dose per week, this could be explained by the fact that the German study involved higher number of adolescents than the current study, reaching to their conclusions that puberty and self-administration of drugs were negative predictors of treatment adherence. Therefore, in puberty, prevention and treatment efforts should be made to optimize adherence, especially when adolescents take their drugs themselves.

In consistent with the American Thyroid Association recommendations,[6] the current study showed that in most children (87%) L-T4 was always taken on an empty stomach, and 83.3% of respondents always adhered to giving the medicine 30-60 minutes before eating [Table 2]; this result may be explained by the close follow-up and strong advice by endocrinologist who is responsible for the care of patients in this tertiary center.

Present study showed that in spite of being the majority of caregiver were adherent to all 3 rules, 26% were not [Table 2], that is, 26% of hypothyroid children and adolescents were not optimally managed (further study is required to look for this poor adherence).

In chronic diseases, like hypertension, adherence to medication was observed more in female patients and in those with higher educational level,[12] whereas another one study showed no effect for sex, educational level, and duration of disease on adherence.[13] Regarding hypothyroid children, age and sex of the patient, duration of disease, presence of other chronic disease, and who is the caregiver were not considered as risk factors for parental non-compliance [Table 3], which emphasized the need for providing all caregiver of hypothyroid children with continuous learning about the importance of adherence to advice rules and explanation of non-adherent drawback at each visit or through educational training sessions and guidebook specifically for them regardless the patient's age and sex, duration of disease, presence of other chronic disease, and caregiver. Education not only involved the daily intake of drug, but awareness of confounding factors that may affect drug absorption because early diagnosis and prompt management with adequate doses of L-T4 results in favorable neurodevelopmental outcomes in most patients with congenital hypothyroidism.

Conclusion

Poor parents' adherence to medical advices about administering L-T4 therapy to their hypothyroid children is still a problem, and it is not related to the patient's age and sex, disease duration, presence of other chronic disease, nor care giver.

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Conflicts of interest

There are no conflicts of interest.

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