

## **Comorbidity of Migraine with Hypothyroidism in Uzbekistan**

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### **ABSTRACT**

The article focuses on the comorbidity of migraine and hypothyroidism, where there are several conflicting views. The aim of the study was to study the effect of levothyroxine on migraine course in the Uzbek population with migraine and subclinical hypothyroidism. The study examined 60 (100%) patients with migraine and subclinical hypothyroidism. All patients received standard treatment for migraine. Twenty-six were prescribed levothyroxine and 34 were prescribed iodine. Patients were re-examined after 3 months. The addition of levothyroxine to treatments when migraine and subclinical hypothyroidism coexisted reduced the number and extent of migraine headaches, as well as anxiety and depression. Improvement in quality of life was observed in patients. This information confirms. migraine hypothyroidism comorbidity

**Keywords:** migraine, levothyroxine, comorbidity, hypothyroidism, treatment.

### **INTRODUCTION**

The comorbidity of migraine and thyroid disease has been studied for several years (2,3,8,15). There are several conflicting views on the comorbidity of migraine and hypothyroidism. Studies have shown that hypothyroidism is one of the most common comorbid diseases of migraine, and migraine causes an increase in headache attacks [5].

Lisotto and a group of scientists examined 3,727 patients with a diagnosis of primary headache from 2005 to 2011 and found significantly more hypothyroidism in migraine than in the general population (8).

Studies show that hypothyroidism is more common after the age of 60 years observed (11). In contrast, menopause in menopausal women then a decrease in the amount of headache is observed. But some it is hypothesized that hypothyroidism has an effect on the increase in migraine headache rates even after the age of 60 years in patients (8). According to a study by Martin A. and a number of scientists, 8412 people have had a headache that has been under medical supervision for 20 years on examination, there was no history of headache hypothyroidism was detected 21 percent more than in humans (10).

An article by Rubino E and a number of scientists published in the 2019 journal Cephalalgia compared 151 patients with subclinical hypothyroidism and 150 patients in the comparison group to determine the association between migraine and hypothyroidism. Migraine has been found to be more common in subclinical hypothyroidism than in the reference group (12).

Bougea A. and several scientists have found that patients with subclinical hypothyroidism and aura-free migraine have a decrease in headache severity and the amount of headaches after levothyroxine treatment. Significant improvement in quality of life was observed after treatment (4).

In a 2017 article published in the journal *Cephalalgia*, both subclinical and overt hypothyroidism were reported after treatment with levothyroxine relief of pain was observed (9).

However, in hypothyroidism, as a result of hormonal therapy with levothyroxine, the symptoms of hypothyroidism are reduced, and it has been found that headache persists in some patients (6). Thyroid disease is a headache because the results vary the connection remains unknown.

**Purpose:** To study the effect of levothyroxine on migraine course in the Uzbek population with migraine and subclinical hypothyroidism.

## **METHODS**

The study was conducted in Tashkent, Republic of Uzbekistan. The study included 60 patients diagnosed with migraine and subclinical hypothyroidism. Diagnosis of migraine during the study was made in 2013 by the International Organization for Headaches criteria (ICHD-3). All patients underwent clinical neurological, instrumental (MRI), hormonal (TTG, TZ free, T4 free) examinations and endocrinologist examination. All patients were recommended standard migraine treatments after the initial examination. Twenty-six patients with subclinical hypothyroidism were prescribed 50 mg of levothyroxine and 34 mg of iodine 200 mg on the recommendation of an endocrinologist. All patients were monitored. Patients underwent re-neurological examination after 3 months.

### **Subject Recruitments**

The study examined patients aged 18 to 55 years with a diagnosis of migraine and subclinical hypothyroidism. Of the patients, 42 were women and 18 were men. Patients were examined in 2 groups according to endocrinologist treatment.

Group 1: 26 patients receiving levothyroxine.

Group 2: 34 patients who did not receive levothyroxine.

Pregnant and lactating women, patients with concomitant severe somatic diseases, epilepsy, mental illness, alcoholism, drug addiction, organic diseases of the brain and other diseases of the thyroid gland not taken.

### **Standardized Instruments**

Patients with subclinical hypothyroidism were diagnosed with serum TSH and T4. Normally, the amount of TSH in whey in adults is 0.4 - 4.5 mIU / l. Subclinical hypothyroidism was defined as an increase in serum TSH above 4.5 mIU / l and normal T4 (4.5-13 µg / dl) (12). The HADS scale was used to assess the level of panic and depression in patients. The HADS scale consists of 2 parts to determine the level of anxiety and depression. Answers are determined on a 4-point scale from 0 to 3 points. The highest score in each category - 21 points. 1-8 points correspond to the absence of signs of anxiety and depression; 8-10 points correspond to subclinical anxiety and depression; 11 points and above clinically expressed anxiety and depression. The intensity of the headache was assessed by scale VAS (visual analogue scale). Headache severity was assessed according to the following criteria: no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm), severe pain (75-100 mm).

A QVM (migraine quality of life) questionnaire was used to assess patients' quality of life. The

QVM scale consists of 20 questions and assesses the decline in quality of life functionally, psychologically, socially and medically. The questionnaire did not complicate the 5 questions about "how difficult your life has become in the last 3 months", but it is determined by the answers, such as average, significant and very difficult. The total score is 0 to 100 points, is the best indicator of quality of life.

### Statistical Analysis

Statistical analysis was performed using GraphPad Prism 7 software for Mac. The information collected, the database was created using Microsoft Excel for Mac. Descriptive data are presented as means, standard deviations (SD), and percentages. The statistical significance among the mean values in different groups and subgroups was determined by one and two methods of analysis of variance (ANOVA) with the subsequent publication of special tests (Tukey test). Intergroup Differences were compared using t-tests and x<sup>2</sup>-tests as appropriate. Statistical threshold \* p<0,05, \*\* p <0,01\*\*\* p <0,001 is considered statistically significant.

## RESULT

According to the study statistics, women outnumbered men. The sex and age distribution of patients are given in Table 1

Table 1

### Demographic data of patients

	<b>Migraine+Subclinical hypothyroidism</b>
	<b>N %</b>
<b>Women</b>	42 (70%)
<b>Men</b>	18 (30%)
<b>Average age</b>	35,4 ± 11,2

The monthly amount and duration of initial and post-treatment headache in patients are given in Table 2. As shown in the table, the monthly amount and duration of headache in both groups decreased after treatment compared to the initial examination. No headache was observed in 80% of patients in group 1 (21 people) and in 35% (12 people) of patients in group 2. The monthly amount and duration of headache were significantly reduced in patients receiving levothyroxine compared to patients not receiving levothyroxine (r <0.05). A month-long dose of headache in patients receiving levothyroxine did not receive levothyroxine compared with patients 4 times, the average duration decreased by 3 times.

Table 2

### Monthly amount and duration of headache in patients

	Before	Review (after 3 months)	

	treatment	Group1(with levothyroxine)	Group 2 (without levotrixin)	P
Monthly the frequency head pain(average month)	18,4 ± 4,2	1,66±2,24	6,64±2,82	p<0,05
Длительность головной боли (averagetime)	6,2± 4,6	0,68 ± 1,2	2,4±1,64	p<0,05

The intensity of the headache was determined on the VAS scale. Preliminary examination revealed severe and moderately severe headache in patients. Your average score on the scale was 78.6 + 10.2 (mm). At re-examination after 3 months, the intensity of headache in both groups of patients decreased compared to the initial examination, but the intensity of headache in patients of the first group (who received levothyroxine) was lower than in patients of the second group (who did not receive levothyroxine (56 mmHg)). ; 24.6 + 12.2 (mm) ;. On re-examination, patients receiving levothyroxine did not have severe headache after treatment, 80% of patients did not have headaches, 20% had mild to moderate headaches. In 5% of patients who did not receive levothyroxine, severe headache, and in 60% of mild to moderate headache persisted. The results of determining the intensity of headache on the VAS scale are given in the table below (Table 1).

Table1

Headache intensity according to the Vas scale:

Your scale	Before treatment I (n-60)	After treatment		P
		With levothyroxine (n-26)	Without levothyroxine (n-34)	
No pain	-	80%	35%	
Weak pain	-	15 %	45%	
Moderate pain	32%	5%	15%	
Strong pain	68%	-	5%	

Average score	78,6±10,2	56,3±16,4(MM);	24,6±12,2(MM)	p<0,05
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The level of anxiety and depression in all patients was calculated on the basis of the results obtained using the HADS scale. In migraine and hypothyroidism comorbidity, anxiety was detected in 58 (97%) patients, with an average score of 16.6 + 4.6 on the HADS scale. When re-examined after 2 months of treatment, the level of panic decreased in both groups. In 41% of patients who did not receive levothyroxine (14 people) remained alert (average 12.6 + 3.6 points), in patients who received levothyroxine this figure was 15% (4 people) (average 8.2 + 1.8 points). The level of anxiety in patients with migraine comorbidity with hypothyroidism before and after treatment is given in Table 3.

Table3

Frequency of occurrence of anxiety on the HADS scale

HADS scale		Alarm N %	Average score
Before treatment (N 60)		58 (97%)	16,6±4,6
After treatment	With livothyroxine (N 26)	4 (15%)	8,2±1,8
	Without livothyroxine (N 34)	14(41%)	12,6±3,6
P		p<0,05	

Depression was observed in 43 (72%) patients with migraine and hypothyroidism with an average score of 14.2 + 4.6 on the HADS scale. Treatment decrease in the rate of depression in patients after treatments was reported to be significantly better in patients receiving levothyroxine ( $r < 0.05$ ). In group 1, 2 (8%) (mean 9.2 + 1.4 points) and in group 2, 8 (24%) (mean 11.6 + 5.6 points) patients retained symptoms of depression. Frequency of depression in the combination of migraine with hypothyroidism and hyperthyroidism, presented in Table 4.

Таблица 4

Depression on a HADS scale

		Depression N %	Average score
Before treatment (N 60)		43 (72 %)	14,2±4,6
After treatment	With levothyroxine (N 26)	2 (8%)	9,2±1,4
	Without livothyroxine (N 34)	8 (24%)	11,6±5,6
P		p<0,05	

When considering the relationship between anxiety and depression with migraine, the

chances of relating symptoms to anxiety are higher, than for symptoms of depression (Table 3.4). Assessment of patients' quality of life according to the QVM survey

According to the results, the initial examination revealed a low quality of life in patients ( $n = 60$ )  $48.2 + 16.5$  (1-100). Patients showed improved quality of life on re-examination after 3 months. In group 1 ( $n = 26$ ) the results of the survey on the sand survey averaged  $72.5 + 12.4$  points, in group 2 ( $n = 34$ )  $91.3 + 8.6$ . Patients receiving levothyroxine had a 21% greater improvement in quality of life than patients receiving iodine ( $r < 0.05$ ).

## Discussion

Our studies have shown that levothyroxine is indicated for the treatment of migraine and subclinical hypothyroidism comorbidities the addition resulted in a significant reduction in headache duration and encounter volume, and a significant improvement in quality of life. At the same time, the level of anxiety and depression in patients was significantly reduced ( $r < 0.05$ ).

A 2017 study by Bougea A. and a number of scientists also found a decrease in the number of migraine headaches (from 14.68 attacks to 1.86 per month) when 45 patients with hypothyroidism and aura-free migraine were examined after taking 50-100mg levothyroxine for 2 months. decreased), headache severity was found to decrease from 6.54 to 1.23. Significant improvement in quality of life was observed after treatment (4).

In addition, a 2016 study by Lima C. and a number of other scientists found a decrease in the number of headaches after levothyroxine treatment in both subclinical and overt hypothyroidism (7).

According to a study by Abou Elmaaty and a number of scientists in 2020, hypothyroidism in patients with migraine and tension headaches (headaches) significantly more common were found (1).

There are several hypotheses about the relationship between migraine and hypothyroidism. One of these is that changes in the immune system under the influence of migraine are thought to cause autoimmune diseases of the thyroid gland [16]. According to Silva JE and Bianco SD, in patients with migraine, there is a decrease in the function of the sympathetic nervous system in the intermittent period, which in turn increases the risk of developing hypothyroidism [14].

2013 Aloisi AM. and the role of the hormone TTG in the mechanism of pain origin has been explained in the results of research by a number of scientists [3]. Some scientists believe that there is a two-way relationship between migraine and hypothyroidism, and suggest that there are common genetic and external factors that cause changes in the immune and autonomic systems in the development of these two diseases [13].

## CONCLUSION

Our results suggest that migraine and subclinical hypothyroidism levothyroxine intake significantly reduces the rate and number of migraine headaches when comorbid. It also has a significant reduction in anxiety and depression. Improvement in quality of life was observed in our patients after levothyroxine administration. Therefore, based on the above results, we

recommend that hormonal tests be performed to assess thyroid function in patients with migraine.

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