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RESEARCH ARTICLE
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Assessment Of Quality Of Life And Cognitive Function In Patients With Primary Hypothyroidism

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ABSTRACT

Currently, hypothyroidism (HT) is one of the most common forms of endocrine pathology. The prevalence of overt hypothyroidism is 0.2 - 2%, subclinical - 10% (4.5).

The relevance of the problem of hypothyroidism in the clinical practice of doctors of various specialties is due to the fact that with a deficiency of thyroid hormones, severe disorders develop in all organs and systems without exception. The multiorganism of the lesion includes the problems of thyroidology in the sphere of interests of representatives of various disciplines. This fully applies to the effect of hypothyroidism on the mental and neurological status of patients (6,7).

Keywords: *vestibulocerebellar disorders, extrapyramidal disorders, hypothyroid myopathy and myotonic phenomenon, psycho-emotional and intellectual disorders*

INTRODUCTION

The most studied in hypothyroidism in this regard are neuromuscular disorders (hypothyroid myopathy and myotonic phenomenon) and damage to peripheral nerves, the prevalence of which is very variable. Among the signs of organic brain damage, vestibulocerebellar disorders and, less often, extrapyramidal disorders are mentioned. In the structure of chronic encephalopathy in hypothyroidism, psycho-emotional and intellectual disorders are most often described (7.9).

The polymorphism of the clinical picture of mental damage in patients with hypothyroidism is described by local and foreign authors, including the fundamental works of V.G. Baranova (1966) and I.D. Levita (1977), as well as A.K. Dobzhanskaya (1973), B.V. Drivotinova and M.Z. Klebanova (1989), A.P. Kalinin and S.V. Kotova (2009).

However, there is still no consensus on the features of the quality of life (QoL) in patients with hypothyroidism. Assessment of health-related QoL has become a mandatory attribute of modern research. It allows you to determine the impact of a disease or a particular disorder on the state of the patient's key functions, the real effectiveness of therapy and rehabilitation programs, as well as predict the course and outcome of the disease. All of the above shows the relevance of the problem and the feasibility of studying it in the clinic.

Aim of the study

To determine the quality of life in patients with primary hypothyroidism depending on gender using standardized scores of the SF-36 questionnaire scales.

Research material

We examined 78 patients with primary hypothyroidism aged 18 to 59 years, mean age 38.2+7.6 years.

The patients were observed at the Department of Endocrinology and Neurology of AndMI. The cause of primary hypothyroidism (PGT) in all patients was autoimmune thyroiditis (AIT). All patients signed informed consent to participate in the study. Thus, the inclusion criteria for the study were: age from 18 to 59 years, the presence of subclinical hypothyroidism (SH) and overt hypothyroidism (MG). Patients with a history of mental and severe somatic diseases and diseases of the thyroid gland (thyroid gland) accompanied by thyrotoxicosis syndrome were excluded from the study; menopausal syndrome requiring estrogen hormone replacement therapy; diabetes mellitus; autoimmune polyendocrine syndrome; pregnant and lactating.

TABLE 1: Distribution of patients by groups and subgroups

Groups	GT forms	subgroups	gender	n	%
I group (n=55), 70,5%	women	A-subgroup	МГТ	36	65,5%
		B-subgroup	СГТ	19	34,5%
II group (n=23), 29,5%	men	A-subgroup	МГТ	15	65,2%
		B-subgroup	СГТ	8	34,8%
total patients with MHT				51	29,5%
total patients with GTS				27	70,5%
Total				78	100,0%

Depending on the form of hypothyroidism, the patients were divided into 2 groups. Group I included 55 (70.5%) female patients, group II included 23 (29.5%) male patients. Each group was divided into 2 subgroups depending on the form of primary hypothyroidism. Subgroup A consisted of patients with a manifest form of HT, subgroup B - patients with a subclinical form of HT. Group I, subgroup A included 36 (65.5%) patients, group II A subgroup - 15 patients (65.2%). In group I, subgroup included 19 (34.5%) patients, in group II, subgroup B - 8 patients (34.8%) - the percentage was calculated within each group (Table 1). The control group consisted of 20 healthy individuals comparable with the main groups by sex and age.

The examined patients with primary hypothyroidism were aged 48 to 59 years. The average age of women was 42.1±11.7 years, the average age of men was 48.2±8.3 years ($p>0.05$).

All patients underwent a standard clinical and neurological examination (analysis of patient complaints, anamnesis of life and anamnesis of the disease, an objective examination, including the study of neurological status) and a physical examination.

The Mini Mental Status Assessment (MMSE) was used to objectify cognitive impairments. Maximum 30 points, which corresponds to the optimal state of cognitive functions. The lower the final score, the more pronounced the cognitive deficit. In terms of the number of tasks, MMSE significantly outperforms other tests and requires more time to complete, experts note the rather low sensitivity of the test. Also, for neuropsychological testing, a technique was used using a short scale - a battery of frontal dysfunction tests [BPD]. Frontal Asstssment Battery (FAB). In the diagnosis of dementia with a predominant lesion of the frontal lobes, comparison of the FAB results is important. An extremely low FAB result (less than 11 points) indicates frontal dementia. The relationship of cognitive impairment with vascular factors was established using the Khachinsky scale (SH) - in the presence of 7 points and above (average 12-14 points) (2.3).The study of the quality of life (QoL) of patients with PGT was carried out using the General Health Questionnaire SF-36. The questionnaire was filled in by the patients themselves or by questioning patient with written fixation of his answers in the form of the questionnaire.QoL of patients was assessed in points (1).

Statistical processing and visualization of the obtained results were carried out using the software package for statistical analysis STATISTICA v. 10 and built-in functions of Microsoft Office Excel. When conducting

statistical analysis, the critical level of significance of the null statistical hypothesis was taken equal to 0.05.

RESEARCH RESULTS

It should be noted that with MHT in each group, the percentage of detection of comorbid pathology was higher. Cerebrovascular pathology and metabolic syndrome in women with MHT were detected in 30.6% and 36.1% of cases, respectively.

In the framework of this project, the psychological anamnesis was assessed in the subjects. The parameters of the subjects were compared with those of the CG. In patients with MHT, the indicators of cognitive functions (CF) according to MMSE and FAB were significantly lower - 28.0 (27.0÷29.0) points and 17.0 (16.0÷18.0) points than in the CG - 29.5 (28.0÷30.0) points (p=0.006) and 18.0 (17.0÷18.0) points (p=0.022). In patients with hypothyroidism, CI according to MMSE and FAB data were set at 70.5%.

TABLE 2: The structure of cognitive impairment in groups and subgroups

groups	subgroups	Without KN		LKN		UKN		total KN	
		abs	%	abs	%	abs	%	abs	%
I group	**MGT**	3	8,3%	12	33,9%	21	58,3%	33	91,7%
	SGT	11	57,9%	5	26,3%	3	15,8%	8	42,1%
	Total	14	27,5%	17	33,3%	20	39,2%	37	72,5%
II group	**MGT**	2	20,0%	6	40,0%	6	40,0%	12	80,0%
	SGT	6	75,0%	2	25,0%	0	0,0%	2	25,0%
	Total	9	33,3%	8	29,6%	10	37,0%	18	66,7%

Neuropsychological testing with an assessment of the function of memory, attention and thinking revealed signs of CI in group I patients with high MMSE and FAB scores, which were one of the leading (in 72.5%) in the structure of NS lesions in hypothyroidism. In patients of group I, the proportion of mild CI (MCI) was 33.3%, moderate CI (MCI) - 39.2%, in 27.5% of cases CI were not detected (Table 2).

In patients of group II, the proportion of light CI (LCN) was 29.6%, which is significantly lower compared to the same indicators of group II ($p<0.005$). The percentage of moderate CI (MCI) was 37.0%, in 33.3% of cases CI were not detected (v.2). It turns out that in group II there was a larger percentage of patients without CI compared to group I, and in group I, patients with MCI prevailed over patients with MCI in group II - 39.2% versus 37.0%.

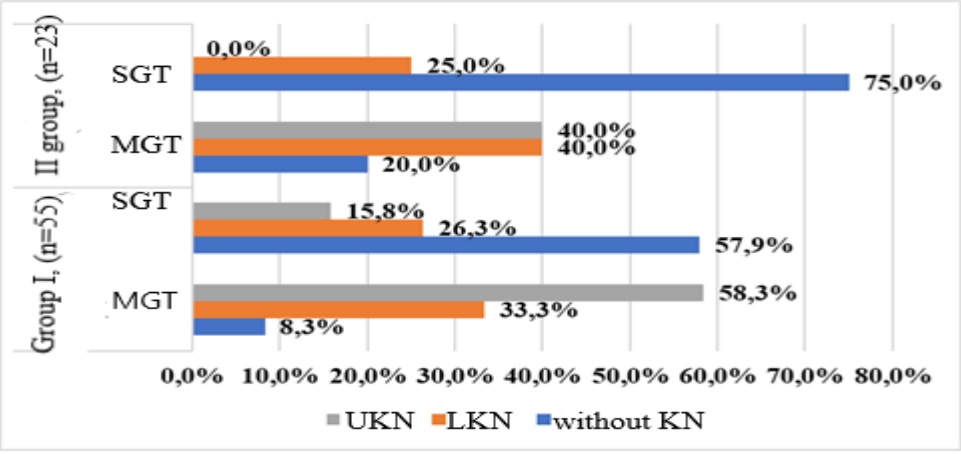

FIGURE 1: The structure of cognitive impairment in patients depending on the form of HT and gender

J Popul Ther Clin Pharmacol Vol 30(14):e249–e255; 10 May 2023.

With regard to the identification of the degree of CI in patients in subgroups, it can be said that patients with GTS in both groups had a greater percentage of patients without CI (Fig. 1). With MHT in both groups, patients with MCI and MCI were significantly more common (58.3%, 40.0%, 33.3% and 40.0%, respectively).

Figure 1 shows that in both groups there was a higher percentage of patients without CI in both groups.

In patients with MHT, short-term memory disorders were found in 40.4%, memorization productivity disorders in 44.2%, a decrease in the rate of memorization in 84.6%, and long-term memory disorders in 25.9%. In terms of short-term memory, patients with MHT without CI, with MCI and MCI significantly differed from each other ($p<0.001$) and the comparison group ($p=0.001$). Memory productivity decreased mainly in MCI ($p<0.05$), delayed recall in patients with MCI and MCI ($p<0.05$). The increase in the severity of CI against the background of decompensation of hypothyroidism was 45.2%; 45.2%; 9.6% without CL MCI MCI is associated with impaired long-term memory and memorization productivity, since in patients with MCI with an increase in the level of TSH, the number of words reproduced by the fifth presentation ($rs = -0.69$; $p = 0.020$) and with delayed reproduction ($rs=-0.90$; $p<0.001$), decreased.

In 71.2% of patients with MHT, impaired attention function was revealed. A decrease in concentration of attention was found in 29.8%, increased instability and exhaustion of attention - in 47.1%. In 1.9% of cases, there were signs of attention rigidity, in 22.1% - an extremely fast pace of work. The decrease in accuracy and concentration of attention prevailed in MCI ($p<0.001$); decrease in attention stability at the first ($p=0.003$) and second ($p=0.002$) minutes, increase in test execution time ($p<0.001$) - with MCI.

Impairments in the function of thinking in MHT were found in 52.9% and were characterized by slowness of mental activity (29.1%) with elements of specific situational thinking (40.0%), accelerated (3.6%) or rigid (23.7%) types of thinking in MCI and MCI, disorders of the analytical and synthetic function (3.6%) - in MCI.

Patients with MHT showed clinical signs of anxiety (43.2%) and depression (20.2%) and their subclinical manifestations (24.0 and 26.9%). With decompensated hypothyroidism, patients with MCI had a higher level of anxiety than patients without CI ($p=0.040$), and in terms of the level of depression they significantly differed from patients with MCI ($p=0.020$), without CI ($p=0.030$) and the comparison group ($p=0.030$). $=0.020$).

Patients with MHT had a lower score on the Khachinsky scale (SH) - 3.0 (2.0÷5.0) points than in the comparison group - 4.5 (3.0÷6.0) points ($p=0.006$). An indicator of SH of 4 points or less was registered in hypothyroidism in 74.0%, 7 points or more - in 2.9%. The sum of scores from 5.0 to 6.0 according to SH was detected in 23.1%, which indicated the contribution of cerebrovascular pathology to the development of CI in hypothyroidism.

The contribution of the identified CF disorders to the clinical manifestations of CI in hypothyroidism was assessed. The analysis group included CF disorders for which a statistically significant relationship with the identified CI was established: thinking disorders ($\chi2=26.87$; $p<0.001$), short-term ($\chi2=56.83$; $p<0.001$) and long-term ($\chi2= 30.85$; $p<0.001$) memory, changes in productivity ($\chi2=17.83$; $p<0.001$) and memorization rate ($\chi2=20.36$; $p<0.001$), impaired concentration ($\chi2=38.18$; $p< 0.001$). Since no relationship has been established between the identified CIs, changes in psycho-emotional status ($p=0.508$; $p=0.213$) and attention span ($p=0.288$), these parameters were not included in the construction of the logistic regression model. Based on the results of the analysis, CF disorders were identified that made the greatest contribution to the clinical manifestations of CI in patients with hypothyroidism: short-term memory ($p<0.001$), attention concentration ($p=0.001$) and long-term memory ($p=0.028$).

Changes in the cognitive status of patients with MHT were of a wave-like character: improvement - worsening - improvement with an increase in positive dynamics, which subsequently consolidated and acquired a stable character. Given that the process of transferring information from short-term memory to long-term memory is accompanied by functional and structural changes supported by the acetylcholinergic system, it can be assumed that

neuroprotective therapy with Cortexin has a direct neurotrophic, neurometabolic effect on cells and mediators of the central nervous system, as well as an effect on visual memory, which can be associated with improved connections between the cortex of the fronto-parietal lobes and subcortical structures [6].

Patients with MHT underwent a course of neuroprotective therapy using Cortexin 10 mg intramuscularly daily for 20 days. The main indicators of the MMSE and FAB scales were studied in dynamics - before and after the treatment (Fig. 2).

Figure 2 shows that there was a positive dynamics of indicators both on the MMSE scale and on the FAB scale, in the group of females there was a greater increase in the indicator on the FAB scale compared to males. Long-term memory recovery is more intense in women.

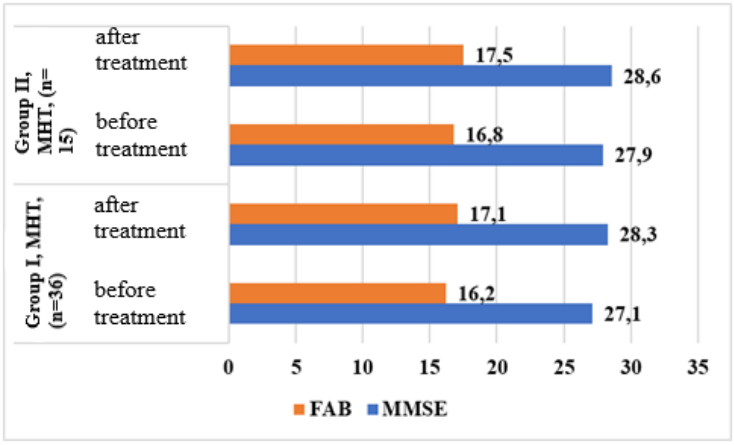

FIGURE 2: Dynamics of MMSE and FAB scores in patients with MHT on the background of neuroprotective therapy

A study of QoL was also conducted in patients of the main study groups using standardized indicators of the scales of the General Health Questionnaire SF-36.

According to most scales of the SF-36 questionnaire, in group I, there were lower values of QOL indicators compared to those in group II, differences in QoL indicators were statistically significant, with the exception of the indicators of the "physical functioning" and "general health" scales. Patients in age groups did not have statistically significant differences in standardized QOL indicators on all scales of the SF-36 questionnaire.

Table 3 presents standardized QoL indicators according to 8 scales of the SF-36 questionnaire (Me and MCR) in patients of the main study groups (with LCR and RBM syndrome) in groups. A statistically significant difference was found between the QoL indicators in group II: the indicators on the "physical functioning" scale and on the "viability" scale were lower in patients with MCI syndrome (U=22.5, p=0.032 and U=16, p=0.009) . On the other scales of the SF-36 questionnaire in group II and on all scales in group I, the QoL indicators did not have statistically significant differences between the main study groups of patients.

TABLE 3: Standardized indicators of the quality of life of the scales of the SF-36 questionnaire (M±δ) in patients with PGT

SF-36 - Brief General Health Assessment Questionnaire, including 36 questions(Short Form Medical Outcomes Study)	**I group**	**II group**
PF - scale "physical functioning"	42,6±9,5	54,1±8,3
RPF - scale "role physical functioning"	37,2±8,1	40,8±7,2

J Popul Ther Clin Pharmacol Vol 30(14):e249–e255; 10 May 2023.

P - scale “pain”	36,4±6,7	54,9±6,8
GH - scale “general health”	47,2±87,6	49,1±6,3
V - scale “viability”	38,5±5,3	54,2±4,6
SF - scale “social functioning”	47,2±4,6	63,4±4,7
REF - scale “role emotional functioning”	40,5±6,1	60,2±5,8
PH - scale “psychological health”	38,4±8,3	54,1±7,8

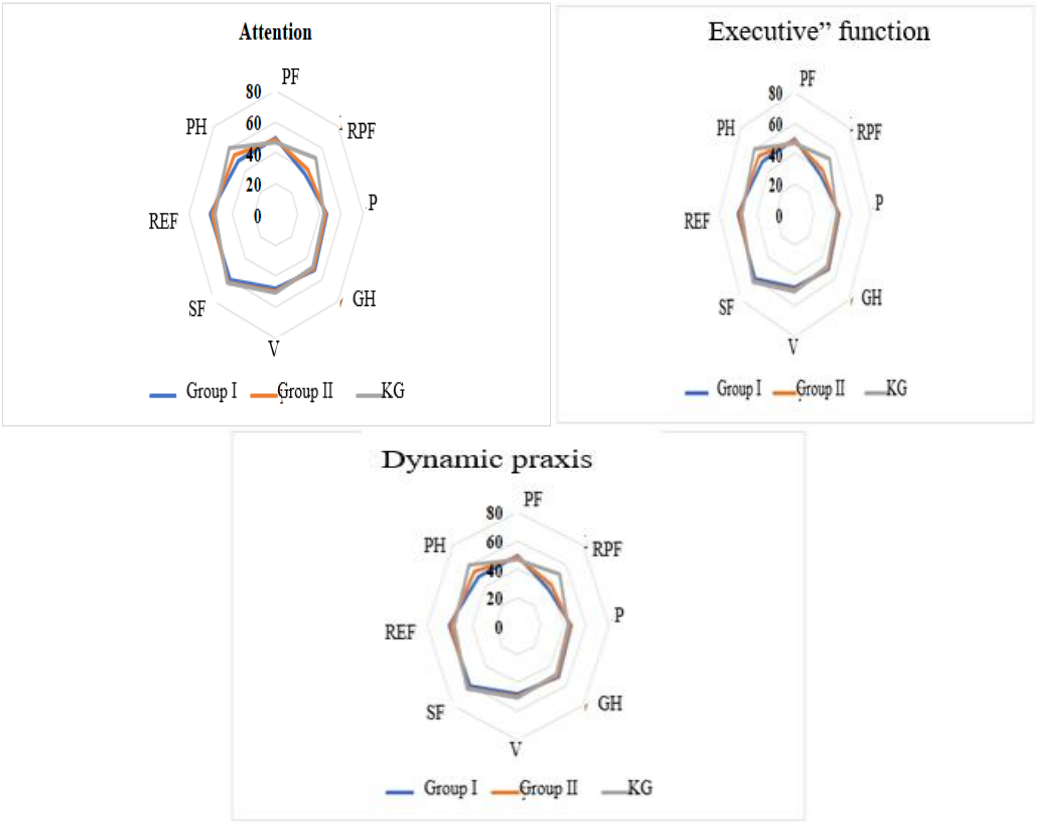

FIGURE 3: Standardized indicators of the quality of life of the SF-36 questionnaire scales in patients with PGT with impaired attention, “executive” function, and dynamic

According to our study, the quality of life of patients with PGT was affected by the profile of MCR. In patients with RBM syndrome, with impaired attention, there was a decrease in the QOL index on the scale of “psychological health” (W=698.5, p=0.024), with a violation of dynamic praxis - on the scale of “physical functioning""(W=325, p=0.003) , in violation of the “executive” function - according to the scale “general health” (W=673.5, p=0.024). Impairments in other cognitive areas did not have a significant impact on QoL indicators according to the scales of the SF-36 questionnaire.

Figure 3 shows the standardized scores of the SF-36 questionnaire for detecting attention disorders, executive function, and dynamic praxis in patients with PGT. In patients of group II, these indicators of cognitive functions had non-significant differences with those of CG, and in patients of group I, differences in scales according to some scales of the SF-36 questionnaire had a significant profile compared to CG.

Emotional-affective disorders influenced the QoL indicators of the SF-36 questionnaire scales in patients with PGT. In patients with asthenic disorder, QoL indicators were reduced on all scales of the SF-36 questionnaire. In patients with depression, QOL indicators were reduced on all scales of the SF-36 questionnaire, with the

exception of the “pain” scale (K=4.7, p=0.095). QoL indicators in patients with increased situational anxiety were reduced on all scales of the SF-36 questionnaire, with the exception of the “role physical functioning” scale (K=5.52, p=0.063). Increased personal anxiety affected the QOL indicators only on those scales that assess the mental component of health; on the scales “physical functioning”, “role physical functioning”, “pain” and “general health”, the QOL indicators did not change statistically significantly (K = 2, 16, p=0.339; K=3.19, p=0.203; K=2.81, p=0.246; K=2.41, p=0.299, respectively).

CONCLUSIONS

The profile of cognitive disorders affects the quality of life of patients with PGT. A significant impact on the quality of life of patients with PGT and RCI syndrome was exerted by disorders of the “executive” function, including dynamic praxis. Patients with RBM syndrome, who, according to the results of neuropsychological testing, had impaired “executive” function, had lower QoL scores on the “general state of health” scale, which characterizes the physical state of health, disease resistance and prospects for treatment, assessed by the patient himself. Praxis is the ability to acquire and use a variety of motor skills, learned and automated sequences of movements. A decrease in the QoL index on the “physical functioning” scale in case of praxis disorder confirms the direct relationship of regulatory CI to self-service and daily physical activity of patients. In patients with PGT and RBM syndrome, attention disturbance correlated with a lower score on the SF-36 mental health questionnaire. This meant that patients with RBM syndrome and impaired attention had anxiety and depressive states, which determined the psychological distress of these patients.

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