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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Use of thyroid hormones in hypothyroid and euthyroid patients – a THESIS questionnaire survey of Serbian physicians

Biljana Nedeljković-Beleslin[1], Roberto Attanasio[2], Laszlo Hegedüs[3], Endre V. Nagy[4], Roberto Negro[5], Enrico Papini[6], Petros Perros[7], Jasmina Ćirić[1], Miloš Žarković[1]

[1]University of Belgrade, Faculty of Medicine, University Clinical Centre of Serbia, Clinic of Endocrinology, Diabetes, and Metabolic Disorders, Belgrade, Serbia;
[2]Associazione Medici Endocrinologi, Scientific Committee, Milan, Italy;
[3]Odense University Hospital, Department of Endocrinology and Metabolism, Odense, Denmark;
[4]University of Debrecen, Faculty of Medicine, Department of Medicine, Division of Endocrinology, Debrecen, Hungary;
[5]Vito Fazzi Hospital, Division of Endocrinology, Lecce, Italy;
[6]Regina Apostolorum Hospital, Department of Endocrinology and Metabolism, Rome, Italy;
[7]Royal Victoria Infirmary, Department of Endocrinology, Newcastle upon Tyne, United Kingdom

SUMMARY

Introduction/Objective Hypothyroidism is a common disease and treatment with levothyroxine (LT4) is effective. However, variations in management are frequent.
The aim of this study was to identify practices and attitudes of Serbian physicians relating to the treatment of hypothyroidism.

Methods An anonymized questionnaire was distributed electronically to members of the Serbian Thyroid Society, Serbian Association of Endocrine Surgeons, and Section for Endocrinology of the Serbian Medical Society.

Results Out of 170 invitations, 99 responses were received. LT4 was the first choice for the treatment of hypothyroidism in 90% of patients. After starting LT4 replacement therapy most respondents would recheck thyroid-stimulating hormone (TSH) in 4–6 weeks (n = 51, 62%) and in eight weeks (n = 29, 35%). In total, 61% of respondents (n = 60) indicated that they would consider treating euthyroid patients with LT4, the commonest indication being female infertility with high levels of thyroid antibodies (54%, n = 50). More than half respondents (58%, n = 45) would recommend combined LT4 + LT3 therapy for patients on LT4 with normal serum TSH who still complain of symptoms of hypothyroidism. 53% (n = 41/77), reported that the frequency of patients with normal serum TSH who still complain of hypothyroid symptoms is less than 5%.

Conclusion LT4 was the first choice of therapy for the treatment of hypothyroid patients, whereas LT3 + LT4 combination treatment is considered in patients with persistent symptoms of hypothyroidism despite normalization of TSH. The most common indication for thyroid hormone treatment in euthyroid patients was female infertility with high levels of thyroid antibodies. Alternative LT4 formulations like liquid solution or soft-gel capsules –formulations presently not available in Serbia, were largely reserved for specific conditions (interfering drugs, malabsorption, inability to take LT4 in the fasting state, unexplained poor biochemical control of hypothyroidism).

Keywords: THESIS; survey; Serbia; thyroid hormones; hypothyroidism; levothyroxine

INTRODUCTION

Hypothyroidism is a common disease affecting approximately 3% of the European population [1]. The treatment of choice for hypothyroidism is levothyroxine (LT4). For optimal efficacy, the traditional tablet formulation requires that patients avoid concomitant ingestion with food, drinks, and certain medications. Some comorbidities influence the bioavailability of LT4 and may mandate repeated-dose adjustments. In such situations, other formulations, like LT4 oral solution could have an increased absorption rate in comparison to LT4 tablets, and potentially could be a better choice [2]. As 5–10% LT4 treated hypothyroid patients have persistent complaints despite serum thyroid-stimulating hormone (TSH) values within the reference range, the combination of LT3+LT4 therapy has been proposed as an experimental treatment modality [3].

Although numerous papers publications including the European Thyroid Association (ETA) guidelines [4] are available concerning this topic, the choice of therapy is influenced by local/regional conditions and traditions.

In Serbia, LT4 tablets is the only formulation currently available, and the only formulation included in National guidelines on hypothyroidism published by the Serbian Thyroid Society and the Ministry of Health [5]. The health care system in Serbia is mainly public and based on universal health coverage but private healthcare is also available. The majority

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Correspondence to:
Biljana NEDELJKOVIĆ BELESLIN
University of Belgrade
Faculty of Medicine
Clinic of Endocrinology, Diabetes and Metabolic Disorders
University Clinical Centre of Serbia
Belgrade
Serbia
biljana_beleslin@yahoo.com

of hypothyroid patients are managed by endocrinologists in secondary care. The Balkan Peninsula and the Serbian region are iodine deficient. Iodine prophylaxis was introduced in 1951 and a recent national survey established that iodine deficiency disorders have been eliminated [6].

LT4 is an effective treatment for hypothyroidism, however, controversies such as the use of combination treatment or unorthodox indications and variations in management exist. This study was part of a larger project investigating thyroid practices across Europe.

The aim was to identify practices and attitudes of Serbian physicians relating to the treatment of hypothyroidism.

METHODS

A total of 99 members of either the Serbian Thyroid Society, Serbian Association of Endocrine Surgeons, or Section for Endocrinology of the Serbian Medical Society participated in a web-based survey investigating the treatment of hypothyroidism. The survey was conducted using Lime-Survey, an open-source online survey tool. Lime-Survey was hosted on servers belonging to the Faculty of Medicine, University of Belgrade. The Treatment of Hypothyroidism in Europe by Specialists: An International Survey (THESIS) questionnaire was translated and adapted to Serbian by a bilingual clinician and further checked by two senior physicians fluent in English. The survey contained 25 questions, eight related to the demographic and professional characteristics of the responder, and 17 related to hypothyroidism treatment. Survey responses were collected anonymously and stored electronically. The survey platform automatically blocked repeated submissions from the same computer. A total of 170 physicians were invited, and 99 responded and participated in the survey following two reminders (response rate 58%). According to the latest Health Statistical Yearbook of the Republic of Serbia, from 2019, the total number of practicing endocrinologists and endocrine surgeons is 184 and 10, respectively [7]. The survey opened on 25 September 2020 and closed on 26 November 2020.

Statistical analysis

Statistical analysis was performed using multinomial regression for nominal variables, ordinal logistic regression for ordinal data and logistic regression for binomial data. For table analysis, χ^2 and Fisher exact test were used. Statistical significance (alpha error) was at 0.05 level. R statistical environment was used for the analyses.

Ethical approval

Responses on the online platform were collected anonymously. Respondents agreed to fill out the survey voluntarily, were aware that they could at any point leave the survey and did not receive any incentives. Personal identifiable data were not collected. Institutional board review was not necessary as the survey was anonymous.

RESULTS

The demographic and professional characteristics of the participants

The demographic and professional characteristics of the participants are presented in Table 1. Most of the physicians were women aged 40–60 years, with 20–40 years of medical practice. The vast majority of respondents were endocrinologists and were employed at university centers. Importantly, nearly all respondents managed hypothyroid patients in their routine practice. Twenty-seven (27%) of 99 respondents were not members of any endocrine society. Twenty-seven (27%) were members of the ETA, two (2%) of the American Thyroid Association, and 66 (66%) of the other national societies. Some of the respondents were members of multiple societies.

Table 1. Characteristics of respondents

Gender	n (%)
Male	30 (30.3%)
Female	69 (69.7%)
Age (years)	**n (%)**
20–30	4 (4%)
31–40	19 (19.2%)
41–50	34 (34.3%)
51–60	33 (33.3%)
61–70	9 (9.1%)
70 +	0
Years of medical practice	**n (%)**
< 20	40 (40.4%)
21–40	58 (58.6%)
> 40	1 (1%)
Specialization*	**n (%)**
Endocrinology	65 (66%)
Internal medicine	53 (54%)
Pediatric Endocrinology	4 (4%)
Nuclear Medicine	1 (1%)
Surgery	6 (6%)
Other	0
Place of employment*	**n (%)**
University Centre	71 (72%)
Regional hospital	15 (15%)
Private clinic	19 (19%)
General Practice	1 (1%)
Basic researcher	4 (4%)
Treats thyroid patients	**n (%)**
Daily	65 (68%)
Weekly	29 (30%)
Rarely	2 (2%)
Missing	3 (3%)
Number of patients with hypothyroidism treated	**n (%)**
10–50 / year	9 (9.4%)
51–100 / year	23 (24%)
> 100 / year	62 (64.6%)
rarely	2 (2%)
Missing	3 (3%)

*Total is greater than the number of respondents because some respondents choose multiple answers

First choice of therapy for hypothyroidism

LT4 was the primary choice of therapy for the treatment of hypothyroid patients for most respondents in this survey (Table 2). Generally, they reported that for most

Table 2. First choice of therapy for the treatment of hypothyroid patients

Thyroid hormone	Responses, n (%)
LT4	88 (90%)
LT3	2 (2%)
Desiccated thyroid extract	1 (1%)
LT4 and LT3 combination	7 (7%)
Missing	1

Table 3. Responses on indications for thyroid hormone treatment in euthyroid subjects

Indications	Responses, n (%)	Total responses, (n)
Unexplained fatigue	29 (32%)	92
Obesity resistant to life-style interventions	21 (23%)	92
Severe hypercholesterolemia, as a complementary treatment	26 (28%)	92
Depression resistant to anti-depressant medications	22 (24%)	92
Female infertility with a high level of thyroid antibodies	50 (54%)	92
Simple goiter growing over time	25 (27%)	92
No, treatment is never indicated for these patients	36 (39%)	92

of their patients they have control over the type of LT4 brand that they prescribe (n = 82; 92% responders, 89 responses). Thirty-three percent of physicians (n = 28 out of 86) thought that LT4 tablets are least liable to variable absorption compared to 27% (n = 23 out of 86) who selected soft-gel capsules, and 11% (n = 9 out of 86) liquid solution. Twenty-six respondents (30%) did not expect significant differences between the preparations.

Monitoring thyroid hormone treatment

After starting LT4 replacement therapy most respondents would recheck TSH in 4–6 weeks (n = 51, 62%) and in eight weeks (n = 29, 35%). Only 1% (n = 1) would recheck TSH after two weeks, and 1% (n = 1) based their choice of interval on clinical assessment. Even after switching to a different formulation or changing from one manufacturer's LT4 tablet to another most respondents would recheck TSH in 4–6 weeks (n = 34, 42%, 82 responses) and in eight weeks (n = 22, 27%, 82 responses). However, a number of physicians would not recheck TSH (n = 14, 17%, 82 responses) or would recheck TSH according to clinical judgment (n = 12, 15%, 82 responses).

Treating patients with dietary supplements

Dietary supplements were deemed to be acceptable in addition to thyroid hormones mainly in patients with hypothyroidism due to autoimmune thyroiditis (n = 57, 70%, 82 responses).

Treating euthyroid subjects with thyroid hormones

In euthyroid patients, almost 40% (n = 36 out of 92 responses) of respondents would never recommend LT4. The most common indication for thyroid hormone treatment in euthyroid patients was female infertility with a high level of thyroid antibodies (54%, n = 50 out of 92 responses). For all other indications, the distribution of those who would recommend thyroid hormone was similar (23–31%). The results are presented in Table 3.

Using different LT4 formulations

Table 4 summarizes the preferences of the respondents regarding the administration of LT4 as a tablet, soft-gel capsule, and liquid solution. Soft-gel capsule and liquid solution are presently not available in Serbia. In all clinical scenarios, the liquid solution was the last choice.

Combination treatment with LT4 + LT3

Regarding the possible indications for combined LT4 + LT3 treatment, more than half respondents would recommend combined LT4 + LT3 therapy to patients with normal serum TSH who still complain of symptoms suggestive of hypothyroidism (Table 5).

Table 4. Responses on the choice of LT4 formulations in different clinical scenarios.

Scenario	Formulation	Total responses, (n)
A patient who self-reports intolerance to various foods raising the possibility of celiac disease, malabsorption, lactose intolerance, or intolerance to common excipients	Tablets 24 (28%) Soft-gel capsules 29 (34%) Liquid solution 11 (13%) No major changes with the different formulations 22 (26%)	86
A patient established on generic LT4 who has unexplained poor biochemical control of hypothyroidism*	Tablets 46 (56%) Soft-gel capsules 16 (20%) Liquid solution 8 (10%) No major changes with the different formulations 12 (15%)	82
A patient with poor biochemical control who is unable (due to a busy lifestyle) to take LT4 fasted and separate from food/drink	Tablets 17 (21%) Soft-gel capsules 31 (38%) Liquid solution 14 (17%) No major changes with the different formulations 20 (24%)	82
A patient established on LT4 who has good biochemical control of hypothyroidism but continues to have symptoms	Tablets 37 (45%) Soft-gel capsules 17 (21%) Liquid solution 4 (5%) No major changes with the different formulations 24 (30%)	82

Persistence of hypothyroid symptoms despite normal serum TSH

About half of the respondents (53%) considered that the frequency of patients with normal serum TSH who still complain of hypothyroid symptoms is less than 5% and that this has not changed in the last five years (49%).

Physicians with hypothyroidism in relation to their own treatment

Five respondents (7%) indicated that they had hypothyroidism. One experienced excessive

Table 5. Possible indications for combined LT4 + LT3 treatment

Possible indications	Responses, n (%)*	Total responses, n
For a short period, in patients recovering from protracted hypothyroidism	17 (22%)	78
In patients with normal serum TSH who still complain of symptoms suggestive of hypothyroidism	45 (58%)	
In hypothyroid patients with normal serum TSH who complain of unexplained weight gain	10 (12%)	
Due to the low quality of available evidence, combined therapy should never be used	24 (31%)	

TSH – thyroid-stimulating hormone

Table 6. Perceptions about the persistence of hypothyroid symptoms despite normal serum thyroid-stimulating hormone

Frequency	Responses, n (%)	Total responses, n
< 5%	41 (53%)	78
6–10%	17 (22%)	
11–30%	7 (9%)	
> 30%	0	
Not sure	13 (17%)	
Trends		
I am seeing more such cases	8 (10%)	78
I am seeing fewer such cases	13 (17%)	
No change	38 (49%)	
Not sure	19 (24%)	

tiredness and none of them tried combination treatment with LT4 + LT3 or desiccated thyroid extract. Out of 69 non-hypothyroid physicians, 51 (74%) would not try combination treatment with LT4 + LT3 or desiccated thyroid extract if they experienced persistent symptoms on LT4. However, out of 51 physicians who would not treat themselves 32 (62.7%) would treat their patients with the LT4 + LT3 combination.

Correlations between baseline characteristics and responses

Multivariate analysis of answers based on the respondents' age, gender, specialization, and years of medical practice did not influence physicians' answers while the place of employment and number of patients treated per year showed some trends.

Physicians treating a high volume of hypothyroid patients (over 100 patients per year) tended to monitor the serum TSH at eight weeks rather than to 4–6 weeks after initiation of LT4 treatment compared to other physicians ($p = 0.047$, OR = 2.9).

University-based physicians (57%) were less inclined than other physicians (90%) to use combined LT4 + LT3 to treat persistent symptoms in patients with normal TSH ($p < 0.01$, OR = 0.1).

By multivariate analysis using the place of employment and number of patients treated, the use of LT4 + LT3 to treat obesity was less likely by university-based physicians ($p < 0.01$ OR = 0.04) and by physicians treating a large number of patients (over 100, $p < 0.01$, OR = 0.08), than the rest of the responders. Using the same multivariate analysis, university-based physicians strongly agreed with the statement that LT4 + LT3 combination should never be used ($p < 0.01$, OR = 7.6), compared to other physicians.

Endocrinologists employed at university centers agreed with the statement that chronic fatigue syndrome was the cause of the persistence of hypothyroid symptoms despite normal serum TSH (OR = 7.3), while those who treated more than 50 thyroid patients per year disagreed with this statement (OR = 0.09).

Only 1 out of 10 endocrinologists employed at university hospitals considered "normal serum TSH in hypothyroid patients who complain of unexplained weight gain" as possible indications for combined LT4 + LT3 treatment.

A total of 43% of endocrinologists employed at university hospitals would never use LT4 + LT3 therapy due to the low quality of available evidence (OR = 6.2).

DISCUSSION

The current study was the first of its kind among Serbian endocrinologists.

The typical Serbian endocrinologist respondent is female, 40–60 years old with 20–40 years of medical practice. Most endocrinologists are employed at a university center and are members of the national endocrine society.

Almost all guidelines indicate that LT4 is the only recommended option for the treatment of hypothyroidism. The ETA recommendations commented on the possibility of LT4 + LT3 combination therapy also, but rather as a short-term trial or last option in patients who do not respond sufficiently to LT4 treatment [4]. Attitudes of Serbian physicians are in line with these recommendations. LT4 is the first choice of therapy for 90% of Serbian physicians. At variance with evidence-based recommendations, 7% of the physicians would use the LT4 + LT3 combination as the first choice, although this formulation is not available on the Serbian market.

After the start of the LT4 replacement therapy, most respondents would recheck TSH in 4–6 weeks (62%) and in eight weeks (35%). The volume of patients seen significantly influenced the choice of monitoring interval, as physicians treating with more than 100 patients per year tend to use an eight-week monitoring interval ($p = 0.047$, OR = 2.9, compared to physicians with a lower-case load who monitor their patients at shorter intervals). Similarly, after a change of the LT4 manufacturer, most respondents would check TSH in 4–6 weeks (42%) and in eight weeks (27%). On the other hand, 17% would not check TSH at all, or according to clinical judgement (15%). The longer interval between thyroid function tests preferred by respondents with the high number of hypothyroid patients can be explained that by the assumption that in a busy practice prolonging the monitoring interval also reduces the clinician's workload (either perceptually or really). However, we could not confirm a similar trend after the LT4 manufacturer change scenario. A significant percentage of physicians (32%) would not routinely check TSH

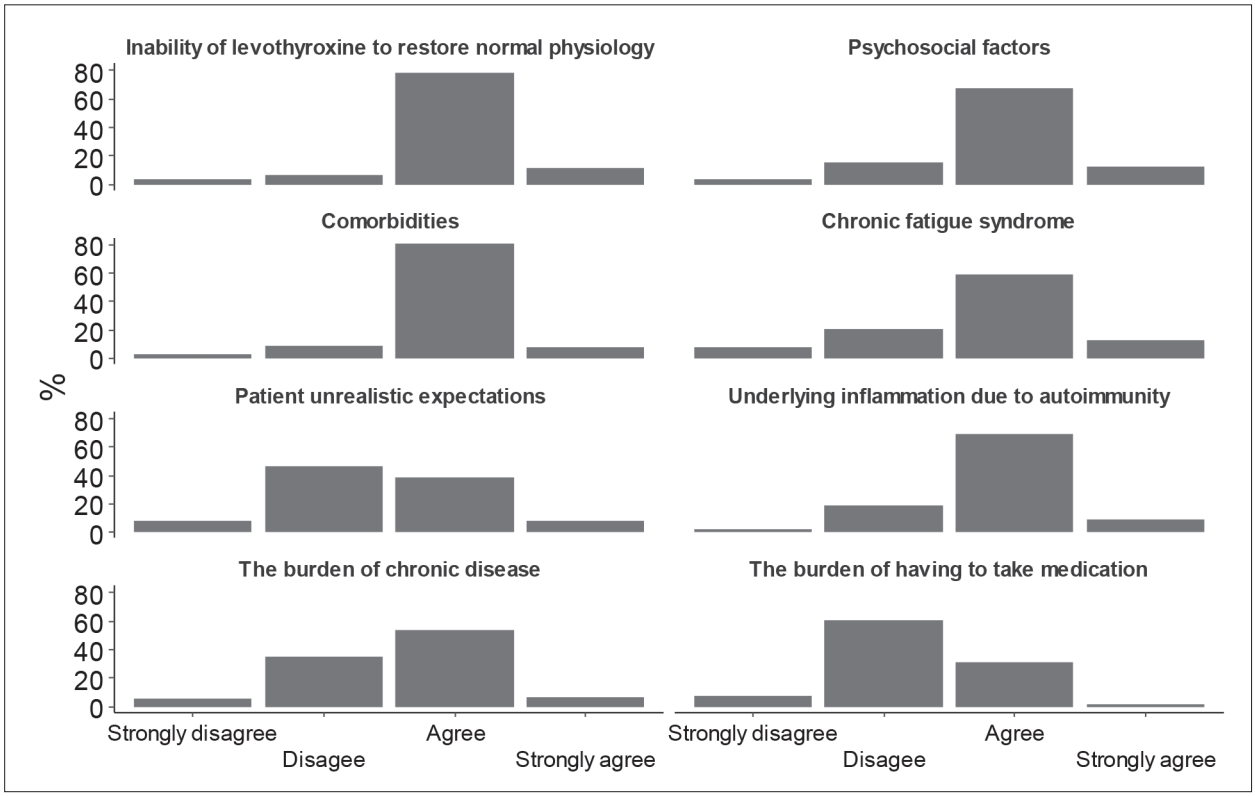

Figure 1. Distributions of a degree of agreement with the explanations for the persistence of hy-pothyroid symptoms despite normal serum thyroid-stimulating hormone; counts on the y-axis

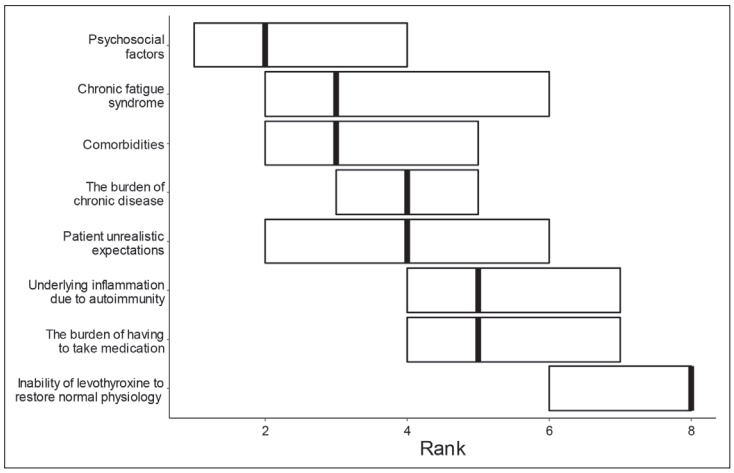

Figure 2. Physician's ranking of the explanations for the persistence of hypothyroid symp-toms despite normal serum thyroid-stimulating hormone (1 is the most likely and 8 is the least likely explanation); the bold line represents the median and boxes the 95% confidence limits

after a change in the formulation of LT4, probably based on confidence in the bioequivalence of the preparations.

More than half respondents (58%) would recommend combined LT4 + LT3 therapy to patients with normal serum TSH who still complain of symptoms suggestive of hypothyroidism. On the other hand, 31% reported no indication for combined treatment due to the low quality of available evidence for efficacy. Of the latter, the majority worked at the university clinic ($p < 0.001$, OR = 7.64). However, 21 out of 99 respondents did not answer this question. Working at the university clinic was the only factor we could identify for not answering this question ($p = 0.035$, OR = 3.55). Even if we assume that all missing responses from university-affiliated physicians are negative, the conclusion remains unchanged: respondents working at university clinics consider that there is no indication for combined treatment ($p = 0.002$, OR = 6.50).

This approach of the majority of Serbian respondents appears not consistent with the ETA guidelines that recommend only a short trial of treatment for patients who complain of hypothyroid like symptoms after the attainment of biochemical euthyroidism.

Among Serbian physicians' dietary supplements are a popular adjunct to the treatment of hypothyroidism mainly in patients with hypothyroidism due to autoimmune thyroiditis (70%). Only 8.5% of physicians responded that supplements should never be used. Despite lack of evidence, many ETA members recommend selenium supplementation in Hashimoto's thyroiditis [8].

Physician perceptions of persistence of hypothyroid symptoms despite normal serum TSH in Serbia are different to the previously published data of THESIS study from other European countries. In Serbia, 53% of the physicians think that the prevalence of patients with normal TSH and persistent symptoms of hypothyroidism is less than 5%. Also, 49% of Serbian physicians think that there has been no change in number the prevalence of such patients over recent years and 17% think it is decreasing. This pattern is more similar to Romanian and Bulgarian data and different to the Danish data implying that regional differences

in patient perception of symptoms and/or physicians' approach to patient complaints [9]. Also, this survey was conducted during the COVID-19 pandemic, when most physicians were working in the COVID hospitals. That could have influenced physicians' perceptions of their current and previous experiences.

Almost 40% of respondents would never recommend LT4 treatment for euthyroid patients. The most common indication for thyroid hormone treatment in euthyroid patients was female infertility with high levels of thyroid antibodies (54%). Such practice is in contrast with the available evidence – a large prospective study and a recently published randomized clinical trial refuted any benefit of LT4 treatment for female infertility with a high level of thyroid antibodies [10, 11]. Surprisingly, all other indications were also selected in significant percentages (23–31%) which are not in line with current recommendations and differ from the results of other THESIS publications [12, 13, 14]. Such an approach to patients that implies unnecessary treatment with LT4 carries the risk of over-replacement which can have detrimental long-term physical and psychological consequences [15]. It is interesting to note that physicians affiliated with university hospitals were significantly less likely to treat euthyroid patients for non-evidence-based indications (fatigue OR = 0.35, obesity OR = 0.29, hyperlipoproteinemia OR = 0.25, depression OR = 0.33), except for female infertility with high levels of thyroid antibodies and goiter increasing in size. Therefore, the only risk factor for the use of LT4 for some non-evidence-based indications was working in a non-university hospital. However, we could not identify other or universal risk indicators for this physician behavior. Furthermore, we did not explore patient preferences that could significantly influence physicians' behavior.

The development of new oral formulations as liquid preparation and soft gel capsules represents the most recent advance regarding LT4 therapy. They are mainly indicated for specific conditions, like malabsorption, interfering drugs, inability to take LT4 in the fasting state or unexplained poor biochemical control of hypothyroidism [16]. However, Serbian endocrinologists still preferred tablets and thought that there were no major changes with the different formulations. The liquid solution was the least chosen formulation for all clinical scenarios as presented in Table 4. This is most probably due to a fact that tablets from only two manufacturers are available in Serbia. Considering that soft-gel capsules and liquid solution are more expensive, and they are not available in Serbia, Serbian endocrinologists do not recommend and do not have experience with them.

Interest in measuring satisfaction and quality of life (QOL) with regards to healthcare has grown in recent years and is considered an important patient-reported outcome measure [17, 18]. Population studies have confirmed that 5–30% of patients with a diagnosis of hypothyroidism treated with LT4 alone continue to have symptoms compared to controls even when the serum is within the normal reference range [19, 20, 21].

Most physicians agreed that the main reasons for the persistence of hypothyroid symptoms despite normal serum TSH include psychosocial factors, the inability of LT4 to restore normal physiology, presence of underlying inflammation due to autoimmunity, comorbidities, and chronic fatigue syndrome.

Major determinants of Serbian physician opinions and preferences are practice volume and practice settings. Physicians working in the university setting and at high volume practices had different opinions and preferences compared to other physicians.

From the patients' point of view, an online survey by the British Thyroid Foundation [22] showed that there was no association between satisfaction or QOL with a type of thyroid hormone replacement treatment for hypothyroidism. Patient expectations, poor experiences with healthcare professionals and lack of information from the general practitioner on hypothyroidism had a major impact on satisfaction and QOL.

Limitations of the survey

Since the survey was conducted during the COVID-19 pandemic the number of physicians who participated in this survey may not be representative especially of those employed at regional hospitals. Also, those who responded were about 50% of the total number of relevant clinicians in Serbia.

CONCLUSION

Serbian physicians preferred LT4, as the first choice of therapy for the treatment of hypothyroid patients. LT3 + LT4 combination treatment is mainly considered in patients with persistent symptoms of hypothyroidism who are biochemically euthyroid. In a biochemically euthyroid patient, the most common indication for thyroid hormone treatment was female infertility with a high level of thyroid antibodies. Alternative LT4 formulations, like liquid solution or soft-gel capsules, were recommended for patients with suspected or proven malabsorption, use of interfering drugs, lifestyle issues and unexplained poor biochemical control of hypothyroidism.

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Употреба тироидних хормона код хипотироидних и еутироидних болесника – анкета лекара у Србији *THESIS*

Биљана Недељковић-Белеслин[1], Роберто Атаназио[2], Ласло Хегедиш[3], Ендре В. Нађ[4], Роберто Негро[5], Енрико Папини[6], Петрос Перос[7], Јасмина Ћирић[1], Милош Жарковић[1]

[1]Универзитет у Београду, Медицински факултет, Универзитетски клинички центар Србије, Клиника за ендокринологију, дијабетес и болести метаболизма, Београд, Србија;
[2]Италијанско удружење клиничких ендокринолога, Научни комитет, Милано, Италија;
[3]Универзитетска болница Оденсе, Одељење за ендокринологију и метаболизам, Оденсе, Данска;
[4]Универзитет у Дебрецину, Медицински факултет, Одељење медицине, Одсек за ендокринологију, Дебрецин, Мађарска;
[5]Болница „Вито Фаци", Одсек за ендокринологију, Леће, Италија;
[6]Болница „Ређина Апостолорум", Одељење за ендокринологију и метаболизам, Рим, Италија;
[7]Болница краљице Викторије, Одељење за ендокринологију, Њукасл на Тајну, Уједињено Краљевство

САЖЕТАК

Увод/Циљ Хипотиреоза је често обољење које се ефикасно лечи левотироксином (ЛТ4), мада постоје извесне контроверзе везане за терапију.

Циљ рада је био испитивање ставова лекара у Србији према терапији хипотиреозе.

Методе Анонимна анкета је електронским путем послата члановима Српског тироидног удружења, Српског удружења ендокриних хирурга и члановима Ендокринолошке секције Српског лекарског друштва.

Резултати Од укупно 170 лекара којима је анкета упућена, 99 је одговорило. ЛТ4 је био прва линија лечења хипотиреозе за већину учесника анкете (90%). После започињања супституције ЛТ4 већина учесника би поновила хормон штитне жлезде (ТСХ) за 4–6 недеља (*n* = 51; 62%) или осам недеља (*n* = 29; 35%), 61% учесника анкете (*n* = 60) лечило би еутироидне болеснике са ЛТ4, а најчешћа индикација је био женски инфертилитет са високим нивоом антитироидних антитела (54%, *n* = 50). Више од половине учесника (58%, *n* = 45/77) препоручила би комбиновану терапију ЛТ4 + ЛТ3 болесницима на ЛТ4 са нормалним вредностима ТСХ који и даље имају симптоме хипотироидизма. Укупно 53% учесника (*n* = 41/77) сматра да је учесталост болесника са нормалним ТСХ који се и даље жале на симптоме хипотироидизма мања од 5%, а 49% има утисак да се то није променило за последњих пет година.

Закључак ЛТ4 је био прва линија лечења хипотиреозе, док би комбиновану терапију ЛТ3 + ЛТ4 већина учесника препоручила болесницима са перзистентним симптомима хипотиреозе упркос нормализованом нивоу ТСХ. Најчешћа индикација за лечење хормона штитне жлезде код еутироидних болесника је био женски инфертилитет са високим нивоом антитироидних антитела. Алтернативне формулације ЛТ4, попут течног раствора или гел-капсула које нису доступне у Србији, у анкети су углавном биле резервисане за специфична стања (лекови који ометају апсорпцију, стварна или сумња на малапсорпцију, немогућност узимања ЛТ4 наште, необјашњива лоша биохемијска контрола хипотироидизма).

Кључне речи: *THESIS*; анкета; Србија; тироидни хормони; хипотиреоза; левотироксин