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Title: Voice Characteristics in Patients with Thyroid Disorders

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Abstract

Objective: This study investigated acoustic and perceptual characteristics of the voice of patients with thyroid gland disorders such as hypothyroidism and hyperthyroidism immediately after the diagnosis was made and six months later, after using drug therapy.

Materials and Methods: The study includes 20 female outpatients with hypothyroidism and 27 female outpatients with hyperthyroidism. The criterion for the selection of the patients was a thyroid gland disorder medical diagnosis, no history of voice disorders and absence of other possible causes of voice changes. Acoustic, perceptual and aerodynamic parameters were assessed. Acoustic analysis was performed by specific software. Experienced speech and language pathologists made perceptual voice assessment by using grade, roughness, breathiness, asthenia, and strain (GRBAS) scale.

Results: Significant differences in patients with hypothyroidism were established on parameter amplitude perturbation, jitter and noise-to-harmonics ratio between pretreatment and posttreatment period, in which patients took drug therapy. In group of patients with

hyperthyroidism significant difference was noted only on aerodynamic parameter maximum phonation time. There were a significant differences in all perceptual parameters in both groups of patients ($p<0.05$) in pre and posttreatment, except on grade and asthenia parameter in the group of patients with hypothyroidism and parameter grade was borderline insignificant in the group of patients with hyperthyroidism

Conclusion: Voice quality is affected by thyroid disease. Thyroid gland disorders cause minor changes in acoustic voice parameters of patients with hypothyroidism and hyperthyroidism, but perceptual deviations in these patients are especially noticeable.

Keywords: Hypothyroidism, hyperthyroidism, voice

Introduction

It is well known that hormones have a major impact on voice quality. Although there are numerous hormones in the body, evidence has shown direct effects of the sex hormones and thyroid hormones particularly on the voice [1]. Disturbances in the function of parathyroid glands and thyroid gland diseases are one of the most common endocrine disorders that can cause phonation disturbances [2]. The most common thyroid gland disorder is hypothyroidism, caused by an underactive thyroid not producing enough hormones [3]. Endocrine disbalance, such as hypothyroidism, is one of the common causes of tissue irritation [4]. Symptoms of hypothyroidism are even more subtle than symptoms of hyperthyroidism, and changes in the voice are one of the well-known symptoms in hypothyroidism [5]. Changes in the voice may even occur in cases of milder thyroid failure, since thyroid hormone receptors have been found to be present in human larynx, which proves that thyroid hormone acts on the larynx tissue [6]. Hypothyroidism can cause notable voice changes such as low voice, roughness, reduced range and vocal fatigue [7].

Hyperthyroidism or excessive thyroid hormone production can lead to dysphonia. The most frequent change that can occur is the reduction of the fundamental frequency of the voice. Other changes may include hoarseness, roughness, loss of voice [1, 8], but also trembling voice, reduced intensity of voice and audible breathing [7, 9]. Follow-up studies show that voice changes are present in 27% of patients with hyperthyroidism and in 2-98% of patients with hypothyroidism [10].

Patients with untreated thyroid gland diseases suffer from a wide range of symptoms that have a very high impact on various aspects of quality of life [10]. There is currently a small number of studies

available on the impact of thyroid diseases on voice production, and thyroid gland dysfunction is mainly reported after surgery in terms of the paralysis of the recurrent laryngeal nerve or the superior laryngeal nerve and its impact on patients' voice [11].

The aim of this study was to determine the acoustic and perceptual characteristics of the voice of patients with thyroid gland disorders such as hypothyroidism and hyperthyroidism immediately after the diagnosis was made and six months later, after using drug therapy.

Materials and Methods

Patients

The subjects were female patients with thyroid gland disorders such as hypothyroidism and hyperthyroidism who were treated at the Clinic Centre. The criterion for the selection of the patients was a thyroid gland disorder medical diagnosis, no history of voice disorders, absence of other known causes of voice changes, and no patients who previously had any surgery or trauma in the head and neck. The diagnosis was made by a specialist in nuclear medicine based on a typical clinical examination, determination of hormones in serum (TSH, T3, T4), ultrasound and palpatory examination. After the medical diagnosis of thyroid gland disease was made by specialist in nuclear medicine, the patients were subjected to an examination by the ENT specialist in order to exclude the existence of other possible causes of voice changes and then patients were instructed to record their voice by speech and language pathologist. Only 47 did so. The patients were divided into two groups: the first group was made of 20 patients, (mean age 45 years) with hypothyroidism (age range 26-71 years), while the second group was made of 27 patients (mean age 50 years) with hyperthyroidism (age range 26-74 years).

Research tools and data collection

The study was conducted at the Ear, Nose and Throat Clinic of the University Clinical Center. The speech and language pathologist made an acoustic and perceptual evaluation of the patient's voice. The first evaluation of the patient's voice was done after diagnosing thyroid gland disease and the examination by an ENT specialist (pretreatment), and the second evaluation was done after the period of six months (posttreatment). During this period, patients took drug therapy, coordinated by a specialist in nuclear medicine.

To record the patient's voice, the AKG 190ES microphone was used, placed at a distance of 30 cm in accordance with the recommendations of Union of European Phoniatricians (UEP) for using the microphone [12], and at 45°. Recording was conducted in sound isolation booth with noise level less

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than 40dB. Average of three trials of prolongation of vowel /a/ was used for the acoustic analysis, that is, its middle part of the acoustic waveforms for at least 2 seconds. Acoustic voice analysis was performed using computer software "Speech Training for Windows, Version 4.00 - Dr. Speech "and" EZ Voice Plus (TM) v.2.0.". Acoustic vocal parameters that were assessed were the average fundamental frequency (F0), frequency perturbations (jitter), amplitude perturbations (shimmer), harmonics-to-noise ratio (HNR).

Perceptual voice assessment was conducted using the GRBAS scale [13]. The patients read a standard text for 2 minutes and their voices were recorded. Voice recordings were assessed by three experienced speech and language pathologist, who were already familiar with the GRBAS scale, in a double blind randomized fashion. The scale is intended for a perceptual assessment of voice quality. This scale evaluates five vocal characteristics assigned on a scale of 0–3, where 0 is normal or absence of deviance, 1 is slight deviance, 2 is moderate deviance and 3 is severe deviance. These five elements are: grade (G), a description of the degree of hoarseness, which relates to the overall voice quality, integrating all deviant components; roughness (R), the perceptual irregularity of vocal fold vibrations, abnormal fluctuations in fundamental frequency or amplitude of vibration, breathiness (B), an auditive impression of air leakage through the insufficient glottic closure, asthenia (A) voice denotes weakness and lack of power and strain (S) reflects a perception of vocal hyperfunction. The parameters of aerodynamic measurements were evaluated as well, maximum phonation time of vowel sound "a" (MPT).

The present study was approved by the Ethics Committee of University Clinical Center. All the participants have signed an informed consent form before they were submitted to research procedures.

Statistical Analysis

Statistical analysis was performed using the software package SPSS (version 24.0, IBM Corp.; Armonk, New York, USA). Descriptive statistics parameters were calculated. The normality of data distribution was tested using Shapiro-Wilk test. Paired-samples t-test was used to determine differences in acoustic parameters of voice in two related samples of patients in pretreatment and posttreatment. Wilcoxon signed rank test calculated differences of repeated mesurements for perceptual parameters, for two related samples. A statistical significance level of 95% ($p<0.05$) was considered to be the significance limit for all statistical tests.

Results

Figure 1 and 2 shows the percentage of patients with hypothyroidism and hyperthyroidism with abnormal acoustic and aerodynamic parameters.

Figure 1.

Percentage of patients with hypothyroidism with abnormal F0 was the same in the pretreatment period and in the posttreatment in which patients used drug therapy (30% of patients). Jitter was within normative values. Only 10% of patients with hypothyroidism had abnormal shimmer and HNR in posttreatment, and MPT was abnormal in 25% of patients compared to 35% in the initial evaluation.

Figure 2.

Percentage of patients with hyperthyroidism with abnormal F0 in pretreatment and posttreatment was not changed, as well as in patients with hypothyroidism, but a percentage of patients with abnormal values of other measured acoustic and aerodynamic parameters has decreased in posttreatment period in which patients used drug therapy.

Furthermore, tests were conducted in order to test whether there are significant differences in acoustic and aerodynamic parameters in general, between pretreatment and posttreatment.

Table 1 clearly shows that a significant difference was found in the variable describing amplitude perturbations (shimmer) in patients with hypothyroidism ($p=0.032$), where it was clear that this parameter has significantly decreased in posttreatment. There is also significant difference on the variable describing the harmonics-to-noise ratio (HNR) ($p=0.017$). In this group of patients, the mean value was improved in this voice parameter in posttreatment. Although values of parameter jitter were in the normal range in patients with hypothyroidism in pretreatment, there was a significant difference between pretreatment and posttreatment ($p=0.03$). There were no significant changes in pre and posttreatment on variables describing the frequency of the voice. The fundamental frequency was even lower in posttreatment. Although insignificant, the mean value of parameter MPT has improved in posttreatment.

Comparison of acoustic voice parameters in patients with hyperthyroidism in the pretreatment and posttreatment showed significant differences only in parameter MPT ($p=0.004$). As in the patients with hypothyroidism, the F0 showed a slight decrease in voice pitch. Although insignificant, the patients with hyperthyroidism did have better results on the jitter, shimmer and HNR in posttreatment.

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Table 1.

The perceptual voice assessments were also compared, pre and posttreatment, in patients with hypothyroidism and hyperthyroidism (Table 2). Significant differences were found in all parameters in group of patients with hyperthyroidism, except on parameter grade, but only in parameters roughness, breathiness and strain in group of patients with hypothyroidism.

Table 2.

Discussion

Although the relationship between the thyroid hormone and the larynx is still insufficiently investigated [6], the position of the thyroid gland in the neck region and its direct connection to the larynx can justify the presence of voice changes in people with thyroid gland disorders [14]. The result of this study showed that values of the parameters describing the voice frequency ranged within normal values and there was no change in voice frequency between pretreatment and posttreatment in which period patients took thyroid replacement therapy. Colton [15] state that women usually produce a basic frequency of voice between 180 HZ and 220 Hz and at the age of 40-49 years, F0 is 214 Hz [15].

Although jitter was within normal values, patients with hypothyroidism showed significant improvement in posttreatment on this parameter. The minor glottic pulse irregularities were even less noticeable after posttreatment period. Most researchers consider that the normal value of jitter in adults ranges between 0.5 and 1% [16].

The results also show that the patients with hypothyroidism had the biggest deviation in the variables describing amplitude perturbations and HNR, and in these parameters were established significant differences in pre and posttreatment. The overall average shimmer value for females is 0.25 dB and critical values 0.48 dB [17]. In pretreatment, 40% of patients with hypothyroidism had abnormal shimmer but in posttreatment only 10% of these patients. Signal-to-noise ratio also improved in posttreatment. The higher HNR indicates better voice quality [18]. The value of the aerodynamic variable in the pretreatment was slightly below normal values and in posttreatment, it was on the lower limit of normal values. MPT is approximately 15-20 seconds for adults [4].

When it comes to hypothyroidism, Birkent et al. [19], established that after thyroidectomy was performed and appropriate substitution therapy was applied, a statistically significant increase in the F0 parameter was found, although this parameter was abnormal even prior to the therapy. The MPT

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parameter was reduced after therapy, although not in a way that was statistically significant, while the other objective parameters (jitter, shimmer, APQ, PPQ, and NHR) showed no significant changes after hormone replacement. This was not the case in this study, but these were patients treated only with drugs. In cases of primary hypothyroidism, before substitution therapy was applied, the fundamental frequency, voice turbulence index and soft phonation index differed significantly from the control values of patients who did not have hypothyroidism [20]. Not all, but a certain number of patients in this study had voice deviations. Jitter, shimmer, and HNR seem to determine the basic perceptual elements of voice quality: grade, roughness, and breathiness [21]. This support results of the perceptual analysis in this research, except for parameter grade that was borderline insignificant. Voice hoarseness and loss of voice range are major features of hypothyroidism. Hoarseness has a gradual onset and a slow progression, thus limiting the patient to notice any voice changes [22]. Therefore, the voice quality may be affected by thyroid gland disease, and some of the symptoms that are referred to in the literature regarding hypothyroidism are loss of vocal range, reduced voice frequency, especially in women, vocal fatigue, hoarseness, low voice, decreased voice intensity [23]. In some cases, mild dysphonia may occur as a result of mild thyroid deficiency. Hoarseness is common symptom in patients with hypothyroidism. Kadakia, Carlson and Sataloff [1] state that according to Ritter, mechanism of action of the thyroid hormone to the voice is unknown in patients with hypothyroidism, but it is believed to be related to increased levels of polysaccharides and the fluid accumulation in the lamina propria in the vocal folds, paresis of the cords due to the thyroid gland enlargement, myedema of the cricothyroid muscle and neural edema of the vagus nerve [6]. Thickening lead to decreasing of vibratory capacity. Singers with hypothyroidism may complain about the limitations associated with the higher vocal range and vocal fatigue. In a number of cases regarding patients who are singers and who experienced voice problems and hypothyroidism, there was an increase in voice clarity after using small doses of thyroid replacement [24]. Speech disorders in most patients with thyroid hypofunction and voice changes correlate with serum TSH levels [21]. Birkent et al. [19] state that dysphonia associated with hypothyroidism may vary in relation to the amount and duration of hormone deficiency. Certain degrees of changes in the patient's thyroid status will affect the patient's voice regardless of the absolute value of TSH level at the start of hormone replacement. It is believed that the supplementations of thyroid hormones are usually sufficient to control the symptoms of hypothyroidism [1].

The assessment results of the acoustic voice parameters in patients with hyperthyroidism show that the parameters describing the frequency characteristics were within the limits of normal values in

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most patients, but 29.63% of patients had abnormal F0, in pre and posttreatment. There was significant improvement in pre and posttreatment only on variable MPT. MPT is indirect measure of laryngeal function widely used in studies of patients with voice problems [21] including those with breathy and weak voice [25]. On the other hand, the results of perceptual evaluation show significant differences in all observed variables, except in parameter grade, in pre and posttreatment. Hyperthyroidism is often the cause of hoarseness or roughness which is often overlooked [8]. Voice hoarseness is one of the problems that patients often complain about when they come to vocal therapy, although it can often be associated with infection or injuries [4]. Apart from hoarseness, a number of patients with a high degree of hyperthyroidism complained of vocal disruption [24]. Although some symptoms are very specific in hyperthyroidism, the sensitivity in these patients when it comes to certain symptoms is low (2.9% to 28.3%). In addition to hoarseness, a frequent symptom of hyperthyroidism is reported to be a deep voice. However, the absence of symptoms does not mean the absence of thyroid gland disorders [26].

During study which was conducted with the help of 96 patients with thyroid gland disorders, a high prevalence of deviant perceptual voice features was determined. Most of these abnormalities were mild to moderate deviations, and only 8% of patients had clinically significant perceptual abnormalities [23]. The results of study show that there are voice changes in patients with thyroid gland disorders, which was especially evident in perceptual evaluation. The voice changes in these patients are not negligible, bearing in mind that the literature states the presence of symptoms of voice changes in patients with thyroid pathology ranging from 9% to 38% [14]. Patients with thyroid pathology, apart from other symptoms, may also complain about voice changes [27], the most common of which is hoarseness, breathiness, strain and uncertainty how the voice will sound [28]. Cases of a low voice, rough voice, reduced vocal range and vocal fatigue were also reported [7]. Although this study found significant differences in posttreatment period, in which period patients were under drug therapy in only a small number of acoustic parameters, which do not include parameters describing the fundamental frequency and not the same parameters in patient with hypothyroidism and hyperthyroidism, Birkent et al. [19] state that it is possible, with the exemption of the F0 parameter, that other acoustic estimation parameters cannot detect the subtle changes in the mass of the vocal fold and unlikely to detect any change without significant vibratory or epithelial disease. In any case, the patient comes to have voice changes that have been caused by the thyroid gland disorders and these changes may disappear completely which usually takes three to six months, after achieving euthyroidism [22].

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Limitations of this study is a small number of patients. Moreover, even though we recorded all patients in the morning after the morning routine in order to diminish fluctuations of acoustic voice parameters during the day, and enforced the controlled use of voice prior to recording, these factors could still affect the voice parameters. Further studies should focus on the correlation of changes in patient's thyroid status and patient's voice in regard to thyroid hormones.

Thyroid gland disorders cause changes in the voice of these patients. Changes in the perceptual characteristics of the voice of patients are particularly evident, while the acoustic characteristics are less affected by changes, especially variables describing the frequency of voice. The biggest deviations in the voice of these patients show the acoustic parameters of shimmer and HNR. There was improvement in voice of patients with thyroid gland disorders after the posttreatment period, during which patients took drug therapy. The results of the conducted study indicate the importance of assessing and treating the symptoms of changes in the voice of patients with thyroid gland disorders and possible the effect of hormone replacement therapy and especially on the perceptual voice features. Since there are a small number of studies on the effect of thyroid hormone supplementation and the long-term follow-up of voice discrepancies after the application of therapy further studies should aim at monitoring the effects of thyroid hormone replacement therapy on the voice of patients with hypothyroidism and hyperthyroidism.

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Table 1. Results of the t-test on differences in acoustic voice parameters in patients with hypothyroidism and patients with hyperthyroidism in pretreatment and posttreatment

Variable	Hypothyroidism					Hyperthyroidism				
	Pretreatment		Posttreatment			Pretreatment		Posttreatment		
	Mean	SD	Mean	SD	p	Mean	SD	Mean	SD	p

F0	192.35	25.85	189.41	20.5	0.566	195.39	33.65	192.04	24.58	0.575
Shimmer (dB)	0.51	0.46	0.27	0.18	**0.032**	0.44	0.36	0.31	0.2	0.12
Jitter (%)	0.31	0.2	0.2	0.06	**0.03**	0.31	0.26	0.24	0.09	0.209
HNR	8.45	5.04	11.53	3.6	**0.017**	8.21	4.11	9.89	3.82	0.1
MPT	14	5.69	15.15	6.51	0.353	13.88	5.44	16	4.74	**0.004**

Abbreviations: F0-average fundamental frequency; shimmer-amplitude perturbations; jitter-frequency perturbations; HNR- harmonics-to-noise ratio; MPT- maximum phonation time;

* Paired-samples t-test, P-value < .05 is significant

Table 2. Results of the Wilcoxon signed rank test on the differences in perceptual voice parameters in patients with hypothyroidism and patients with hyperthyroidism in pretreatment and posttreatment

Variable	**Hypothyroidism**		**Hyperthyroidism**	
	Z	p	Z	p
Grade	-1.823	0.068	-1.897	0.058
Roughness	-2.373	**0.018**	-2.956	**0.003**
Breathiness	-1.89	**0.059**	-2.06	**0.039**
Asthenia	-1.298	0.194	-2.913	**0.004**
Strain	-2.058	**0.040**	-2.98	**0.003**

* Wilcoxon signed rank test; Z-standardized test statistic; P-value < .05 is significant

Figure legend

Figure 1.

F0-average fundamental frequency; shimmer-amplitude perturbations; NHR-harmonics-to-noise ratio; MPT-maximum phonation time of vowel sound "a"

Figure 2.

F0-average fundamental frequency; shimmer-amplitude perturbations; jitter-frequency perturbations; NHR-harmonics-to-noise ratio; MPT-maximum phonation time of vowel sound "a"

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