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Assessment of Voice Changes in Myasthenia Gravis Patients

Myastenia Gravis Hastalarının Ses Değişikliklerinin Değerlendirilmesi

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Abstract

Objective: This study aims to examine the changes between the measurements done in the morning and evening in some acoustic analyses of patients having myasthenia gravis (MG).

Materials and Methods: Twenty-four MG patients diagnosed with Phase-2A (Mildly Generalized MG) according to the classification of Osserman and Genkins by a neurology specialist were involved. Videolaryngostroboscopic examinations and acoustic analyses of these patients were performed in the Ear, Nose, and Throat (ENT) clinic. Perceptual voice assessments were performed using the GRBASI scale, Fo, Shimmer, Jitter, NHR (Noise to harmonic ratio), MPT (Maximum Phonation Time), and s/z rates were calculated.

Results: When the morning and evening vocal measurements of patients were compared according to the GRBASI scale, a significant difference was found between B and A and S values, while no statistically significant difference was found between G, R, and I value. Statistically significant differences were found between cases' Fo, Shimmer, NHR, s/z Ratio, and VHI (voice handicap index) measurements made in the morning and the evening. But no difference was found between the Jitter measurements. A statistically significant difference was found between the morning and evening values of men's Fo and MPT measurements. Again, a statistically significant difference was found between the morning and evening values of women's Fo and MPT measurements.

Conclusion: For Myasthenia Gravis patients, the decrease in muscle power within the day and the tiredness in larynx muscles are an expected process, and it is objectively presented in this study. In addition, further studies are needed to show that possible communication problems can be prevented with sound therapies by evaluating the morning and evening acoustic analyses of MG patients.

Keywords: Myasthenia Gravis, Acoustic Analysis, Praat

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Öz

Amaç: Bu çalışmanın amacı, miyasteni gravis (MG) hastalarının akustik analizlerinin bazı parametrelerinde sabah ve akşam yapılan ölçümler arasındaki değişiklikleri incelemektir.

Gereç ve Yöntemler: Osserman ve Gengkins sınıflandırmasına göre bir nöroloji uzmanı tarafından Faz-2A (Hafif Genelleştirilmiş MG) tanısı almış 24 MG hastası dahil edildi. İşitsel-Bilişsel ses muayeneleri GRBASI ölçeği kullanılarak gerçekleştirilmiş ve Fo, Shimmer, Jitter, NHR (Noise to harmonic ratio), MPT (Maximum Phonation Time) ve s / z oranları hesaplanmıştır.

Bulgular: Hastaların sabah ve akşam ses ölçümleri GRBASI ölçeğine göre karşılaştırıldığında, B, A ve S değerleri arasında anlamlı fark bulunurken, G, R ve I değerleri arasında istatistiksel olarak anlamlı bir fark bulunmadı. Sabah ve akşam yapılan vakaların Fo, Shimmer, NHR, s / zRatio ve VHI (ses handikap indeksi) ölçümleri arasında istatistiksel olarak anlamlı farklılıklar bulundu. Ancak, Jitter ölçümleri arasında hiçbir fark bulunamadı. Erkeklerin Fo ve MPT ölçümlerinin sabah ve akşam değerleri arasında istatistiksel olarak anlamlı fark bulundu. Yine kadınların Fo ve MPT ölçümlerinin sabah ve akşam değerleri arasında istatistiksel olarak anlamlı fark bulundu.

Sonuç: Myasthenia Gravis hastaları için gün içinde kas gücünün azalması ve gırtlak kaslarındaki yorgunluk beklenen bir süreçtir ve bu çalışmada objektif olarak sunulmuştur. Böylelikle MG hastalarının sabah ve akşam akustik analizlerinin değerlendirilmesiyle olası iletişim problemlerinin ses terapileri ile önlenebileceği düşünülmektedir.

Anahtar Kelimeler: Miyastenia Gravis, Akustik Analiz, Praat

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Introduction

Myasthenia gravis (MG) is characterized by muscle weakness and anormale fatigability (1-2). Being an autoimmune disease caused by specific antibodies developing against the acetylcholine receptor (AChR) in final motor plaque, the main characteristic of MG is weakness and fatigue in muscles due to repetitive activities. In 2/3 of patients, the first symptom is eccentric ocular muscle stiffness (2-3). On the other hand, from the aspect of prevalence, isolated or early laryngopharyngeal or extremity weakness is seen more rarely (4). Besides the studies reporting the prevalence of oral, pharyngeal, and laryngeal complaints as 30%, there are also studies reporting that dysphagia is the most frequent "first symptom" with a prevalence of 6% (5-6).

As mentioned above, MG can affect many muscle groups, including the larynx muscles. But the laryngeal symptoms have been reported to be relatively rarer in MG in proportion to other symptoms mentioned. Especially the respiratory insufficiency due to vocal fold paralysis, the myasthenia crisis, and stridor and dysphonia due to bilateral vocal fold paralysis is among the laryngeal symptoms seen in MG (7). In MG patients, the muscle power decreases towards evening, and the acoustic quality declines.

This study examines the differences between morning and evening measurements of some parameters in acoustic analyses of MG patients.

Materials and Methods

This study was carried out with the approval of Kayseri Training and Research Hospital's Planning and Coordination Council Nr.46 dated 15.10.2015 Kayseri in the neurology policlinics of Erciyes University Medical Faculty Hospital and Kayseri Training and Research Hospital. Patients diagnosed with MG between 15/10/2014 and 14/12/2015, had videolaryngostroboscobic examinations, and whose acoustic analyses had been performed in the ENT clinic were included in the study. Before examining patients, the ethics committee approval and patient informed consent forms were obtained.

In this study, after their verbal/written consents, 24 MG patients were diagnosed with Phase 2A (Mildly Generalized) MG using the Osserman and Gengkins classification (1) by a neurology specialist after it was proved via videolaryngostroboscopy under laboratory conditions that there was no organic or psychogenic vocal pathology. Patients having organic and/or psychogenic vocal diseases were excluded from the study. Morning and evening acoustic analyses and specific socio-demographical characteristics of the patients were recorded on a data collection form. All the examinations were performed in a silent room in the mornings and evenings. Examinations, recordings, and evaluations were performed by an ENT specialist who had acoustic education. Praat software was utilized for acoustic analyses. The same ENT specialist had performed the videolaryngostroboscopic examination of the patients. In an analysis of the data, the SPSS software's version 15 was utilized. The difference between the dependent groups' mean values was examined via the Wilcoxon test. The statistical significance level was $p<0.05$.

Acoustic Analysis Criteria:

The auditory/vocal evaluations were performed using the GRBASI scale, Fo, Shimmer, Jitter, Noise to harmonic ratio(NHR), Maximum Phonation Time (MPT), and s/z ratios were calculated. All the evaluations were performed in a silent room in the mornings and evenings. The patients were asked to speak the (/a/) voice for 10 seconds at 15cm distance to the Audio-Technical AT2005USB microphone, and they were recorded. The examinations, records, and evaluations were performed by an ENT specialist who had acoustic education.

Moreover, in subjective evaluation of vocal problems of the patients, the Turkish version of the Voice Handicap Index (VHI) developed by Jacobson et al. VHI was utilized (8-9). VHI is a 30-item questionnaire consisting of 10 questions for each of functional (F), physical (Fi), and emotional (E) aspects. The patient

scores each item between 0 and 4, and the highest score is 120. The higher the score is, the more severe the vocal problem (9).

For acoustic analyses, the Praat software was developed by Paul Boersma and David Weenink from the Phonetic Science Department of Amsterdam University (10). Praat is developed for acoustic analyses of voice and speech samples and provides the user with script memory for batch processing; it allows spectrograph, density, and pulse analyses.

Videolaryngostroboscopic Evaluation:

For videolaringostroboscopy, the 900 Karl Storz brand rigid endoscope, XION Endostrob-DX, and NEC Multisync LCD 1990SX screen were used. The videolaryngostroboscopic evaluation of the patients was performed by the same ENT specialist.

Statistical Analyses:

In analyses of data, the SPSS software's version 15 was utilized. The normal distribution of the variables was examined via visual (histogram, Stem-and-leaf graph, and normality plots with tests) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. The percentage, mean, standard deviation, median, minimum, and maximum values were used as the definitive analyses. The Wilcoxon test was used to determine a difference between the mean values of dependent groups. The statistical significance level was $p<0.05$.

Results

The mean age was 38. 62.5% (n=15) of the patients were male and 37.5% (n=9) were female. As seen in Table 1, when the morning and evening acoustic measurements of patients were compared following the GRBASI scale; while statistically significant differences were found in B (Breathiness), A (Asthenia), and S (Strain) values ($p<0.05$), no significant difference was found in G (Grade), R (Roughness), and I (Instability) values ($p>0.05$) (Table 1).

A statistically significant difference was found between the morning and evening Shimmer apq11, NHR, and s/z Ratio ($p<0.05$). But no significant difference was found between Jitter ppq5 measurements ($p>0.05$). (Graphic 1)

VHI evaluations of patients' voices before the MG diagnosis and actual ones were performed, and significant differences were observed between the results ($p<0.05$).

A statistically significant difference was found between male participants' morning and evening Fo and MPT measurements ($p<0.01$). Statistically, a significant difference was also found between female participants' morning and evening Fo and MPT measurements ($p<0.05$). (Table 2)

Discussion

Coursing with spontaneous remissions or deteriorations, MG does not affect the sensation, reflexes, or coordination (11-12). Besides that, the clinic of the patients may vary significantly. Moreover, while generalized weakness is observed in 85% of the patients, the muscular loss is symmetrical (12-13).

Considering the emergence of myasthenia cases by age, it exhibits bimodal distribution between 20 and 30 in females and over 50 in males. In contrast, it shows unimodal distribution over 50 years of age in males. Besides that, as in other autoimmune diseases, it is more frequently seen in females than in males. This difference decreases in older adults, is not seen in babies (< 1-year-old), and is rarely found in children

Table 1
Morning and evening acoustic measurements of patients are compared in accordance with GRBASI scale

	Definitive Statistics					Wilcoxon Test	
	Mean	**Standard Deviation**	**Median**	**Min.**	**Max.**	**Z value**	**p**
G_morning	1.25	0.85	1.00	0.00	3.00	-1.538	0.124
G_evening	1.54	0.51	2.00	1.00	2.00		
R_morning	0.79	0.72	1.00	0.00	2.00	-1.057	0.290
R_evening	1.00	0.66	1.00	0.00	2.00		
B_morning	0.71	0.69	1.00	0.00	2.00	-2.070	0.038*
B_evening	1.21	0.93	1.00	0.00	3.00		
A_morning	1.04	0.95	1.00	0.00	3.00	-3.948	0.000*
A_evening	2.21	0.72	2.00	1.00	3.00		
S_morning	1.04	0.75	1.00	0.00	2.00	-2.478	0.013*
S_evening	1.83	1.01	2.00	0.00	3.00		
I_morning	1.26	0.96	1.00	0.00	3.00	-1.474	0.140
I_evening	1.57	0.79	2.00	0.00	3.00		

G:grade of hoarseness R:roughness B:breathiness A:asthenia S:strain I: instability

Table 2
Morning and evening fundamental frequency (Fo) and maximum phonation time (MPT) measurements of participants

Gender			N	Mean	Std. Deviation	Median	Wilcoxon Test	p
Male	Fo	Morning	15	189.40	38.53	195	-3.408	0.001*
		Evening	15	115.13	25.30	114		
Male	MPT	Morning	15	17.07	2.22	17	-3.195	0.001*
		Evening	15	14.20	2.54	15		
Female	Fo	Morning	9	182.22	36.42	177	-2.073	0.038*
		Evening	9	131.78	28.83	118		
Female	MPT	Morning	9	12.22	1.86	12	-2.232	0.026*
		Evening	9	11.00	1.32	11		

MPT: Maximum Phonation Time Fo: fundamental frequency

between 1 and 10 years of age (14). In this study, all the patients were adult males and females, and most were male (62.5). A higher percentage of males may lead to selection-based bias. Moreover, since it is unknown how long the patients speak in their daily lives depending on their jobs, it might have led to a difference in acoustic analyses. Since there is no professional voice use that will make a significant difference between the daily voice usage amounts of the patients, the average voice usage amounts have been accepted as similar. Further studies must specify how long the participant spoke on the day of measurement and any difference.

The symptoms in myasthenia patients generally start in the third decade (14). In this study, they started after 27 years of age. In addition to that, the association with thymoma is more frequent in males than in females (14), but this condition was not examined in our study.

In a study of Heller et al. (15), where they examined the acoustic, speech, and laryngeal characteristics of Sjogren patients, they reported no difference between the genders in terms of Jitter measurement. At the same time, there was a statistically significant difference between males and females in terms of Shimmer measurements. This study compared patients' morning and evening measurements with myasthenia, an autoimmune disease like Sjogren syndrome. While there was no difference between Jitter measurements performed in the morning and evening, the morning average of Shimmer measurements was higher than the evening average. Despite that, the difference between the genders was not discussed.

VHI, although it is not suitable for frequent application, is of perfect distinguishing power in separating healthy persons from people having laryngeal diseases. This distinguishing power is also seen in a study

of Kalsen et al. on 126 healthy persons and 355 patients with vocal diseases in Norway. VHI averages of every group from dysphonic patients to aphonic patients were significantly higher than that of the control group. The acoustic problems increase as the VHI score increases (16). In a study by Heller et al., the mean VHI score of Sjogren symptom patients was 43±23. Interestingly, the first test score in this study (10.54 ± 2.73) was significantly higher than the score on the fortieth day (8.29 ± 2.63).

Maximum Phonation Time (MPT) is the longest duration of making noise with a single breath. Although it varies depending on the age, gender, and accompanying disease, the mean values were 20 seconds for males and 15 seconds for females.

The s/z ratio, an indicator of glottic efficiency, has been reported to be equal to or lower than 1.0 in normal voices. High s/z ratio should be examined from the aspect of the laryngeal lesion (16). In this study, the morning and evening s/z ratios were higher than 1.0. Evening s/z ratios of myasthenia patients, significantly higher than morning values, are important since they indicate the change of pathology during the day. This study is the first study comparing the acoustic measurements of myasthenia patients throughout the day.

In a study by Xu et al., where the clinic and electro-physiologic larynx characteristics of myasthenia gravis (n=32) patients and normal individuals (n=36) were studied, the Fo average of MG patients was found to be 172.5 ± 50.4 Hz while that of normal individuals was found to be 187.4 ± 60.3 Hz; no difference was found between the groups (4). Similarly, in our study, the morning Fo average of the myasthenia patients (187.83 ± 37.40 Hz) was significantly higher than the evening average (121.83 ± 27.94 Hz). When the morning Fo value was normal, there were significant decreases in evening values.

The high Fo values detected in our patients were thought to be due to MG's inability to use the vocal fords effectively. In addition, when the literature is examined, it has been shown that high Fo values may also be present in the female group (17,18).

In the study of Xu et al., NHR is significantly lower in myasthenia patients (18.4±1.9 dB) compared to the normal group (22.8±2.9 dB). Similarly, in our study, the evening NHR average (15.329±6.42 dB) is significantly lower when the morning average (25.85±3.97 dB) is normal.

This study also has some limitations. First, there is not equal distribution of gender because the study was carried out with applicants. Second, the gender-based comparison could not be performed because enough patients could not be achieved. The strength of this study is that it is the first study comparing the acoustic measurements of myasthenia patients within the day.

In addition, by evaluating the morning and evening acoustic analyzes of MG patients, the idea arises that possible communication problems can be prevented by applying etiological treatments and medical treatments, as well as sound therapies. Diaphragm and breathing exercises, strengthening of the vocal fold, resonance, and lax vox therapies to be performed in these patients, and voice breaks that develop towards the end of the day and increase contractions to relatively more acceptable levels may be the subject of future studies.

Conclusions

As mentioned above, MG can affect many muscle groups, including the larynx muscles. But the laryngeal symptoms have been reported to be relatively rarer in MG in proportion to other symptoms mentioned. This study shows the differences between morning and evening measurements of some parameters in acoustic analyses of MG patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the Erciyes University ethics committee.

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Authors declared no conflict of interest.

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