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Araştırma Makalesi / Original Article

EVALUATION OF AUTONOMIC NERVOUS SYSTEM WITH HEART RATE TURBULENCE IN PATIENTS WITH STROKE

İNME GEÇİREN HASTALARDA OTONOMİK SİNİR SİTEMİNİN KALP HIZI TURBULANSI İLE DEĞERLENDİRİLMESİ

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ÖZET

Giriş: Serebrovasküler hastalıklar sonrası genellikle otonomik disfonksiyon gelişmektedir. Otonomik disfonksiyonu gösteren testlerden biri de kalp hızı türbülansıdır. Bu çalışmada bizim amacımız kalp hızı türbülansı parametrelerini kullanarak akut iskemik inme sonrası otonomik disfonksiyonu değerlendirmektir.

Yöntemler: Çalışmaya 30 akut iskemik inme ile hastaneye yatırılan hasta ve 15 sağlıklı birey dahil edildi. Hastaların yatışları esnasında çekilen bilgisayarlı tomografi ve manyetik rezonans görüntüleri incelendi. Sağ hemisfer, sol hemisfer ve beyin sapı- serebellum lezyonu olarak 3 sınıfa ayrıldı. Hastaların hastaneye yatışlarının ilk 24 saati içerisinde takılmış olan holter EKG(elektrokardiyografi) kayıtları incelendi. Kalp hızı türbülansı parametreleri olan türbülans başlangıcı (TB) ve türbülans eğimi (TE) kontrol grubu ile kıyaslandı.

Bulgular: Çalışmaya alınan gruplar arasında cinsiyet, yaş, hipertansiyon, hiperlipidemi sigara kullanımı ve biyokimyasal parametreler açısından anlamlı bir farklılık yoktu. TB ve TE değerleri kontrol grubu ile kıyaslandığında anlamlı fark saptanmadı. (TB -0.004970 (±0.02), -0.013627 (±0.01) p: 0.14, TE 6.81(±7.30), 7.67 (±5.30) p: 0.11). Sol hemisfer lezyonlu hastalarda TB ve TE için daha fazla anormal değer saptanmasına karşın istatistiksel fark saptanmadı.

Sonuç: Akut inme ile kalp hızı türbülansı arasında ilişki gösterilememiştir.

Anahtar Kelimeler: İnme, Kalp Hızı Türbülansı, Otonomik Disfonksiyon

ABSTRACT

Introduction: Autonomic dysfunction usually develops after cerebrovascular diseases. Heart rate turbulence is one of the tests to show autonomic dysfunction. We aimed to evaluate autonomic dysfunction using heart rate turbulence parameters after acute ischemic stroke in this study.

Methods: We included 30 patients hospitalized with acute ischemic stroke and 15 healthy individuals in the study. Computed tomography and magnetic resonance images taken during the hospitalization of the patients were examined. It was divided into 3 classes the right hemisphere, left hemisphere, and brainstem cerebellum lesions. Holter ECG(electrocardiography) records inserted within the first 24 hours of hospitalization of the patients were examined. Turbulence onset (TO) and turbulence slope (TS) parameters, which are heart rate turbulence parameters, were compared with the control group.

Results: There was no significant difference between the groups included in the study in terms of gender, age, hypertension, hyperlipidemia smoking, and biochemical parameters. When TO and TS values were compared with the control group, no significant difference was found. (TO -0.004970 (± 0.02), -0.013627 (± 0.01) p: 0.14, TS 6.81 (± 7.30), 7.67 (± 5.30) p: 0.11). Although there were more abnormal values for TO and TS in patients with left hemisphere lesions, no statistical difference was found.

Conclusion: No relationship has been shown between acute stroke and heart rate turbulence.

Keywords: Stroke, Heart Rate Turbulence, Autonomic Dysfunction

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INTRODUCTION

Stroke is a clinical condition characterized by the focal or global loss of brain functions that causes death or neurological deficit, and lasts longer than 24 hours. There is no different cause other than vascular etiology in stroke (1).

Cardiac complications such as arrhythmias or sudden death due to cardiovascular autonomic dysfunction may occur after acute stroke. Increased sympathetic autonomic system activity and changes in the parasympathetic autonomic system are thought to play a role in the occurrence of these complications (2).

The effect of cerebral hemispheres on cardiac autonomic modulation is not fully known. However, clinical and experimental studies have shown that the insular cortex, amygdaloid nucleus, and lateral hypothalamus are effective in autonomic function (3-4). It is known that different cerebral regions contain the source of different sympathetic nervous system pathologies (5). Right-hemisphere lesions affect the sympathetic nervous system more than left-hemisphere lesions (6).

Stroke increases cardiac arrhythmias and causes myocardial damage. Clinical studies in patients with acute stroke have shown that increased sympathetic activity and/or decreased vagal activity increase the propensity for cardiac arrhythmia.6 These changes in the balance of the autonomic nervous system cause an increase in early mortality and morbidity after stroke, independent of heart disease (7).

Heart rate turbulence, which is an indicator of baroreceptor sensitivity, is a non-invasive method that can be used in the evaluation of autonomic nervous system function. Both sympathetic and parasympathetic components of the autonomic nervous system can be evaluated by heart rate turbulence. Transient decrease in blood pressure due to premature ventricular contraction causes activation of baroreceptors and this activation causes vagal inhibition. Thus, the heart rate increases and the R-R interval shortens. At the same time, transient relative hypotension stimulates the sympathetic arc. Increased sympathetic activity leads to a gradual increase in vascular resistance and systolic blood pressure. As a result, vagal activity increases again and cycle intervals are prolonged. Therefore, a healthy interaction of both parasympathetic and sympathetic systems is required for normal heart rate turbulence. A pathology in one or both of these systems can cause abnormal heart rate turbulence (8-9).

Heart rate variability has been shown in many studies to assess autonomic dysfunction after stroke and to predict poststroke cardiac mortality (10-11). However, heart rate turbulence, another parameter in determining autonomic dysfunction, has not been studied in the acute post-stroke period. We think that the relationship between stroke and HRV may also be compatible with HRT in patients with stroke. Because it is known that there is a strong relationship between HRT and HRV. In this study, we classified the cerebral lesions in acute stroke according to their hemispheric localization and aimed to evaluate the changes in the autonomic nervous system with heart rate turbulence.

METHODS

Study Population

We included 30 patients with acute ischemic stroke within 24 hours and 15 healthy individuals who had no disease and no pathology in the 24-hour Holter ECG(electrocardiography), whose 24-hour Holter ECG record was taken in the cardiology outpatient clinic for any reason. When selecting the control group, we made sure that the individuals were of similar ages to the patient group. It was checked from hospital records that they did not use drugs that affect heart rate and that they did not have cardiovascular or cerebrovascular disease.

Patients with no lesion detected on cranial MRI, patients with lesions in more than one of the localizations specified in the patient subgroups, and patients who were admitted to the hospital 24 hours after their stroke, were excluded from work. Patients; no difference was observed in terms of complete blood count, liver-kidney function tests, blood electrolyte levels, ECG recordings, and treatments received in the first 24 hours at the time of admission.

Computed tomography and/or cranial MRI(magnetic resonance imaging) images of the patients were scanned. The acute lesion responsible for the clinical condition was identified. The localization of the lesions was classified into 3 sections the right hemisphere, left hemisphere, and brainstem-cerebellum. Lesions smaller than 15 mm were excluded from the study. Patients who had a 24-hour Holter ECG in the first 24 hours of hospitalization were included in the study. Patients with atrial fibrillation, diabetes mellitus, previous stroke, cardiac prosthetic valve, severe heart failure, kidney and liver failure, and patients using drugs known to affect the cardiac rhythm were also excluded from the study.

Informed consent forms were obtained from the patients. The study was performed following the Declaration of Helsinki and was approved by the local ethics committee (Decision Date/No: 04.05.2018/2018/121).

Heart Rate Turbulence Analysis

In all patients and controls, 24-hour Holter ECG monitoring was applied (Lifecard CF Digital Holter Recorder, Spacelabs Healthcare Company, WA, USA). 24-hour Holter ECG monitoring was applied within 24 hours after hospitalization. HRT (heart rate turbulence) parameters, turbulence onset (TO), and turbulence slope (TS) were automatically calculated by a computer program(HRT View, Version 0.60-0.1 Software Program, Munich, Germany). Each contraction considered by the software as a premature ventricular contraction was visually evaluated before analysis, and artifacts were excluded from the study.

TO and TS parameters were used to evaluate HRT. T0 was defined as the amount of early acceleration in sinus rate that occurred immediately after premature ventricular contraction. T0 was calculated by the formula below and expressed as a percentage (%) (12).

TB = [(RR1 + RR2) - (RR -2 + RR -1) / (RR -2 + RR -1)] x 100 (%)

TS was defined as the rate of deceleration following the early acceleration in the sinus rate and was expressed in milliseconds per contraction. TS was calculated as the maximum positive regression slope obtained over any 5 consecutive sinus rhythm RR intervals out of the RR interval of the first 15 sinus rhythms after premature ventricular contraction. TO ≤ 0% and TS ≥2.5 ms / RRi interval were considered normal.

Statistical Analysis

Statistical analysis was performed using the SPSS (Statistical Package for the Social Sciences ver.15.0, SPSS Inc, Chicago, Illinois, USA) package program. Whether the numerical variables showed normal distribution was tested with the Kolmogorov-Smirnov Test. Numerical variables were expressed as mean ± standard deviation. The chi-square test was used for comparison of categorical data, and the Kruskal-Wallis test was used for comparison of parametric data. p ≤0.05 was considered statistically significant. Power analysis was done using the g power package program. However, the specified number of patients could not be reached.

RESULTS

The mean age was 65.2 (±10.6) in the patient group and 65.7 (±8.6) in the control group. 10 33% (10) of the patient group and 40% (6)of the control group were women. Demographic characteristics of individuals in the study are summarized in Table 1.

Table 1. Baseline clinical characteristics of the study participants

Parameter	Patients (n=30)	Control (n=15)	P value
Age, years	65.2 (±10.6)	65.7 (±8.6)	1.000
Female n(%)	10 (%33.3)	6 (%40.0)	0.746
HT	16 (%53.3)	8 (%53.3)	1.000
HL	15 (%50.0)	6 (%40.0)	0.752
Smoke	13 (%43.3)	8 (%53.3)	0.546

HT: Hypertension, HL: Hyperlipidemia

HRT parameters, TO and TS did not significantly differ between the two groups, as shown in Table 2.

Table 2. Heart rate turbulence parameters

Parameter	Patients	Control	P value
TO (%)	-0.004970 (±0.02)	-0.013627(±0.01)	0.14
TS (ms/RRi)	6.81(±7.30)	7.67(±5.30)	0.11

TO: Turbulence onset, TE: Turbulence Slope

We categorized the parameters as normal-abnormal, assuming ≥0% for TO and 2.5 ms / RR for TS as abnormal values. 9 of 14 patients (%64.3) with left hemisphere lesions had abnormal TO and/or TS values (in 2 patients, both TO and TS were abnormal). 3 of 7 patients (%42.9) with brainstem-cerebellum lesions had abnormal TO and/or TS values (in 1 patient, both TO and TS were abnormal). Only 1 of the patients with right hemisphere lesions had an abnormal TS value. In the healthy control group, there were no patients with abnormal TO or TS values. Although more patients in the group with left hemisphere lesions had abnormal values, there was no statistically significant difference between the three groups as shown in Table 3.

Table 3. Abnormal heart rate turbulence parameters

Parameter	Right hemisphere (n=9)	Left hemisphere (n=14)	Brainstem-cerebellum (n=7)	P value
Abnormal TO (≥ %0)	0	5	1	0.10
Anormal TS (≤ 2,5000 ms/RRi)	1	6	3	0.24

TO: Turbulence onset, TE: Turbulence Slope

DISCUSSION

CVD (cerebrovascular disease) can cause dysrhythmia without organic heart disease. The worst consequence of these dysrhythmias is sudden cardiac death. It has been suggested that dysrhythmias developing as a result of CVD are due to the effect of the autonomic nervous system, but its mechanism is not fully understood (13-14). The clinical use of non-invasive tests to determine the effects of stroke on cardiac autonomic regulation is limited. The two most applicable tests are heart rate variability and heart rate turbulence. It is known that there is a significant decrease in heart rate variability parameters in patients with stroke (15-16). However, no study has yet been conducted to evaluate autonomic dysfunction after stroke by heart rate turbulence. We could not find a significant difference in this study in which we compared the post-stroke heart rate turbulence parameters in the patient and control groups.

Autonomic dysfunction after cerebral infarction has been demonstrated in several studies. Barron et al. showed that cardiac autonomic innervation decreased after any hemisphere infarction and that parasympathetic innervation decreased significantly associated with a right hemisphere lesion (17). In another study, Oppenheimer et al. showed that heart rate variability decreased in patients with acute left hemisphere stroke and the effects of the left insular lesion (4).

Recent studies indicate that the most important region mediating cardiovascular autonomic regulation is the insular cortex. The insular cortex is connected with other important autonomic regions, but its relationship with the cardioregulatory center is not fully known (3). It is known that sympathetic cardiovascular tone increases with stimulation

of the right insular cortex, whereas parasympathetic activity increases with stimulation of the left insular cortex (4). In another study, it was shown that various arrhythmias increased in patients with right insular cortex lesions (6).

It has been suggested that autonomic cardiovascular dysfunction in patients with stroke is due to parasympathetic dysfunction. Tokgözoğlu et al. observed a significant decrease in heart rate variability parameters in a series of 62 patients with stroke and found these findings significantly associated with the lesion of the right insula (5). Meglic et al. reported a significant decrease in heart rate variability parameters in lesions affecting only the medullary region in the brainstem in their study (2). In another study, it was found that transient autonomic nervous system dysfunction developed in the early period in patients with stroke, and this was more common in patients with right hemisphere lesions and hemorrhagic stroke (18).

In our study, we classified the lesions as the right hemisphere, left hemisphere, and brainstem-cerebellum. However, we did not evaluate whether the lesions affected the insular cortex.

Also, the fact that all of the patients we included in the study had an ischemic stroke and there were no patients with hemorrhagic stroke may have affected our result. Heart rate turbulence, which we use to evaluate autonomic dysfunction, has more complex interactions than other tests. Therefore, we may not be able to show the significant difference shown in heart rate variability in patients with stroke.

The most recent study between ischemic stroke and HRT was shown in a study by Candemir et al. Significant abnormalities were detected in HRT parameters, especially in patients with right and left cerebral infarction. However, the limited number of patients requires this result to be supported by more studies (3).

In a stroke, especially in the acute phase, closer follow-up and treatment of patients to protect them from complications such as arrhythmia and sudden death may affect the prognosis positively. To detect autonomic nervous system dysfunction after acute stroke, we need long-term, well-attended prospective studies that evaluate central regions (insular cortex, amygdaloid nucleus, and lateral hypothalamus) with known effects on autonomic function.

Limitations

The most important limitation of our study is the small number of patients and control groups. Also, the absence of strokes that affect the insular cortex and hemorrhagic strokes may have caused significant results. Finally, the fact that the number of patients specified in the Power analysis could not be reached may have caused the study data to be meaningless.

CONCLUSION

We could not show a relationship between heart rate turbulence parameters used in the diagnosis of cardiovascular autonomic dysfunction and ischemic stroke.

Ethics Committee Approval: The study was performed following the Declaration of Helsinki and was approved by the local ethics committee (Decision Date/No: 04.05.2018/2018/121).

Informed Consent: Informed consent forms were obtained from the patients.

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