Evaluation of Cardiovascular Autonomic Dysfunction According to Heart Rate Turbulence and Variability in Patients with Benign Paroxysmal Positional Vertigo

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ABSTRACT

Introduction: The relationship between benign paroxysmal positional vertigo (BPPV) and cardiovascular autonomic dysfunction is not clear. Disruption of the balance between the sympathetic and parasympathetic systems causes various diseases. It is believed that disorders of the parasympathetic system, particularly, may be responsible for causing BPPV. Heart rate variability (HRV) and HRT (heart rate turbulence), which show autonomic dysfunction, are two non-invasive tests that show the relationship of the heart rate with the autonomic nervous system. The purpose of the present study was to evaluate the relationship between autonomic dysfunction and BPPV in patients with BPPV by using HRV and HRT, which are non-invasive laboratory parameters.

Patients and Methods: A total of 100 age- and gender-matched volunteers and 100 patients with BPPV were selected for the study between January 2015 and January 2020. We obtained HRT and HRV parameters from 24-hour ECG Holter recordings. We considered a TO above 0 and a TS above 2.5 to be abnormal. We compared the parameters between groups.

Results: A significant difference was observed between the BPPV and control groups in the HRV parameters SDNNI (p= 0.036), SDANN (p= 0.045), and HRT parameter TS (p= 0.048). We showed that abnormal TO (p= 0.025) and TS (p= 0.038) values were significantly higher in the patient group.

Conclusion: Parasympathetic autonomic dysfunction was demonstrated by the lower HRV and HRT values observed in the patients with BPPV compared to the control group in the present study. The present findings must be confirmed with a much larger number of patients and multi-center studies.

Key Words: Benign paroxysmal positional vertigo; autonomic nervous system disorders; dizziness

Benin Paroksismal Pozisyonel Vertigolu Hastalarda Kardiyovasküler Otonomik Disfonksiyonun Kalp Hızı Türbülansı ve Değişkenliğine Göre Değerlendirilmesi

ÖZET

Giriş: *Benign Paroxysmal Positional Vertigo* (BPPV) ile otonomik disfonksiyonun ilişkisi net değildir. Sempatik ve parasempatik sistem arasındaki dengenin bozulması çeşitli hastalıklara sebep olmaktadır. Özellikle parasempatik sistem bozukluklarının BPPV'ye sebep olabileceği düşünülmektedir. Otonomik disfonksiyonu gösteren HRV (*heart rate variability*) ve HRT (*heart rate turbulence*) kalbin kalp hızının otonomik sinir sistemi ile ilişkisini gösteren iki non-invaziv testtir. Bu çalışmadaki amacımız BPPV'li hastalarda otonomik disfonksiyon ile BPPV arasındaki ilişkiyi non-invaziv bir laboratuvar parametresi olan HRV ve HRT parametrelerini kullanarak değerlendirmektir.

Hastalar ve Yöntem: Çalışma için Ocak 2015-Ocak 2020 tarihleri arasında yaş ve cinsiyet uyumlu 100 gönüllü, 100 BPPV hastası seçilmiştir. Hastaların 24 saatlik EKG holter kayıtları analiz edilmiştir. Bu kayıtlardan HRT ve HRV parametreleri elde edilmiştir. Parametreler gruplar arasında kıyaslanmıştır. TO 0´ın ve TS 2.5'in üzeri anormal kabul edilmiştir. Gruplardaki anormal TS ve TO değerleri kıyaslanmıştır.

Bulgular: HRV parametrelerinden SDNNI (p= 0.036) SDANN (p= 0.045) ve HRT parametrelerinde TS (p= 0.048) arasında BPPV ve kontrol grubu arasında anlamlı derecede farklılık izlendi. Anormal TO (p= 0.025) ve TS (p= 0.038) değerleri hasta grupta anlamlı düzeyde daha fazla izlendi.

Sonuç: Bu çalışmada BPPV'li hastaların kontrol grubuna göre HRV ve HRT değerlerinin düşük olması, parasempatik otonomik disfonksiyonu olduğunu düşündürmektedir. Mevcut bulguların çok daha fazla hasta sayısı ve çok merkezli çalışmalarla doğrulanması gerekmektedir.

Anahtar Kelimeler: Benin paroksismal pozisyonel vertigo; otonomik sinir sistemi bozuklukları; baş dönmesi

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INTRODUCTION

Vertigo is perceived as an imaginary illusion of movement. Positional vertigo is defined as the sensation of rotation caused by gravity with the relative change in head position. The most common cause of positional vertigo is benign paroxysmal positional vertigo (BPPV), which is defined as an inner ear disorder characterized by recurrent episodes of positional vertigo. It is known to affect approximately 5.6 million people (17-42%) annually in the US[1]. Twenty percent of BPPV patients can recover spontaneously in one month and 50% in three months. Although BPPV affects all three canals, posterior canal BPPV (85-95%) is the most common. The second most common is lateral/horizontal canal BPPV (5-15%), and superior/anterior canal BPPV is very rare (1%). Physiopathologically, the displacement of otoconia in the canal (canalothiasis) is the most common cause and results in nystagmus and vertigo. Horizontal-rotatory nystagmus observed during the Dix-Hallpike Test is particularly diagnostic for posterior BPPV. Canalith Reposition Maneuver (Epley) and Semont Maneuver are used in the treatment. In the diagnosis of lateral canal BPPV, horizontal nystagmus in the Supine Head Roll Test (Pagnini-Lempert or Pagnini-McClure Roll Test) is diagnostic. Gufoni Maneuver can be used in treatment. Most patients are relieved with these maneuvers and require less medical treatment[2].

The autonomic nervous system operates in a state of delicate balance between sympathetic and parasympathetic innervation. The relations of the vestibular system with the autonomic system have been the subject of curiosity of researchers to date. It is known that patients and animals that have vestibular dysfunctions also have clinical presentations of autonomic dysfunction and patients with autonomic dysfunction present with symptoms such as dizziness and tinnitus. The mechanism by which the vestibular system and the autonomic system are affected and the cause-effect relationships are not clearly known yet[3]. The Head Up Tilt Test, which evaluates orthostatic hypotension and autonomic dysfunction, and beat-to-beat systolic pressure measurements were used to investigate this relation[4]. However, the measurement of heart rate variability (HRV) and heart rate turbulence (HRT) parameters using a 24-hour Holter monitor, which has not been previously studied, is considered the most common noninvasive testing method for evaluating the sympathetic and parasympathetic systems. Heart rate turbulence refers to the physiological short-term baroreflex-regulated fluctuations in the sinus rhythm following premature ventricular contraction (PVC). Turbulence onset (TO) values, which indicate the initial increase in heart rate following a ventricular premature beat, and turbulence slope (TS) values, which reflect the subsequent heart rate slowing, are utilized to evaluate heart rate turbulence (HRT)[5].

Heart rate variability is also very important in the evaluation of autonomic dysfunction like HRT, which is called cyclic fluctuations in heart function between successive heartbeats (i.e. RR intervals) and at rest. The retraction of vagal tone and increased sympathetic activity, leading to decreased HRV, is believed to be associated with the development of life-threatening arrhythmias[6].

The purpose of the present study was to evaluate the relationship between autonomic dysfunction and BPPV in patients with BPPV using non-invasive laboratory parameters such as HRV and HRT.

PATIENTS and METHODS

Study Design and Patient Selection

A total of 100 age- and gender-matched volunteers and 100 BPPV patients were selected for the study between January 2015 and January 2020. The 100 volunteers consisted of patients who applied to the otolaryngology outpatient clinic for any reason, and BPPV patients were patients who applied to the otolaryngology clinic with dizziness and were then diagnosed with idiopathic BPPV by various maneuver tests (e.g. Dix-Hallpike, Supine Roll). Permission was obtained from the local ethics committee for the study, and informed consent was obtained from the patients. The study was approved by the local Ethics Committee (30.04.2021-2021/06). The study was conducted in accordance with the guidelines of the Declaration of Helsinki, the principles of Good Clinical Practice, and with due respect for the rights and dignity of all participants involved. Verbal informed consent was obtained from participants following a brief explanation of the aim of the study.

Inclusion and Exclusion Criteria

The diagnosis of BPPV was established based on a history of new-onset vertigo that occurred during specific positional changes and was confirmed through maneuver tests. All patients with BPPV were treated with the Canalith Reposition Maneuver for the affected canal.

The exclusion criteria were vestibular neuritis or head injury, use of drugs affecting the autonomic system (e.g. anticholinergics, antiarrhythmics, sympathomimetics, parasympathomimetics), those with neurological and metabolic diseases, hypertension and diabetes, patients with chronic vertigo and any heart disease (e.g. atrial fibrillation, other rhythm disorders, myocardial infarction).

Serum electrolyte values, atrial conduction times measured on ECG, and echocardiography parameters were normal in all patients and the control group.

Measurements

The 24-h Holter ECG (Reynolds Medical Pathfinder Software Version V8.255; Reynolds Medical, Hertford, UK) monitoring was performed for all patients. Holter ECG monitoring was conducted on the day of BPPV diagnosis for the patient group. Holter records were kept by excluding the artifacts. Since the HRT data could not be obtained in patients without PVC, such patients were excluded from the study.

The HRT parameters (TO and TS) were calculated by using a computer software (HRT View Software Version 0.60-0.1, Munich, Germany), and TO was expressed as the percentile difference between the 2 RR intervals that were measured just after a VPB and just before a VPB. The TS value was defined and calculated as the maximum positive slope of a regression curve obtained from any set of five consecutive RR intervals in the first 20 sinus rhythm intervals after a VPB. The TO value was calculated separately for each VPB and the final data were defined as the mean values of these individual measurements. An abnormal TO value was defined as ≥0%, while an abnormal TS value was defined as ≤2.5 ms/RR[7].

The HRV analysis was made in all participants according to the Guidelines of the European Society of Cardiology and the North American Society of Pacemakers and Electrophysiology, and HRV measurements were made from 24-hour Holter ECG recordings[8]. The evaluation of HRV was performed by using a computer program (Cardioscan 12.0, DMS, Ventura, CA, the USA). The 6-hour part at night was determined following the marked day-night shift in the length of RR intervals.

The HRV measurements included the standard deviation of all normal sinus RR intervals over 24 hours (SDNN), the mean value of all normal sinus RR intervals (SDNNI) for all 5-minute segments, the standard deviation of the mean normal sinus RR intervals for all 5-minute segments (SDANN), the root-mean-square difference of the sequential normal sinus RR interval (rMSSD), and the percentage of the consecutive normal sinus RR intervals >50 ms (sNN50).

Statistical Analysis

All analyses were made by using the SPSS software version 24 (IBM Corp., Armonk, NY, the USA). A p-value of <0.05 was considered significant. Distributions of HRT and HRV parameters in MS and control groups were analyzed by using the Shapiro-Wilk Test. Continuous data that did not have a normal distribution were compared with the Mann-Whitney U-Test. Categorical parameters were evaluated and compared with the Chi-square Test. The HRT and HRV values were adjusted for age with the Covariance Analysis. For descriptive statistics, frequencies were used in categorical data, and median and interquartile ranges were used for non-normally distributed quantitative data. Correlation analyses were performed by using Spearman's Rank Correlation Coefficients. Additionally, a post-hoc power analysis was performed to confirm that the current study had sufficient power (99%).

RESULTS

Among the 100 BPPV patients, 66 were female and 34 were male, and the mean age was 41.6 ± 10.2. Among the 100 control patients, 64 were female and 36 were male, and the mean age was 40.8 ± 9.8 years (Table 1).

There were no differences in the mean heart rates between the groups. SDNN, rMSSD, sNN50, and TI results of HRV parameters were statistically similar between the two groups. Also, HRV parameters such as SDNNi, and SDANN were significantly different in the BPPV group when compared to the control group (50.18 ± 21.92; 54.23 ± 20.26 p= 0.036; 116.12 ± 46 ± 94; 122.91 ± 39.18 p= 0.045 respectively). There was no significant difference between the two groups in TO, one of the HRT parameters. Significant differences were detected in TS one of the HRT parameters between the groups (35.19 ± 25.15; 13.15 ± 9.11 p= 0.048, respectively) (Table 2).

A TO value of ≥0% and an S value of ≤2.5 ms/RR were considered abnormal. Significant differences were observed between the two groups in terms of abnormal TO and TS parameters (68%; 19% p= 0.025, 64%; 21% p= 0.038) (Table 3).

Table 1. Demographic characteristics of the patients with BPPV and controls

	Patients with BPPV (n= 100)	Controls (n= 100)	p
Age (years) (mean±SD)	41.6 ± 10.2	40.8 ± 9.8	0.435
Sex (number of females)	66/100 (66%)	64/100 (64%)	0.387

SD: Standard deviation.

Table 2. HRT and HRV parameters of the patients with BPPV vs controls

		Patients with BPPV	Controls	p
HRT	TO	-0.04 ± 0.03	-0.08 ± 0.36	0.124
	TS	35.19 ± 25.15	13.15 ± 9.11	0.048
HRV	SDNN	128.98 ± 47.92	135.95 ± 42.14	0.224
	SDNNI	50.18 ± 21.92	54.23 ± 20.26	0.036
	SDANN	116.12 ± 46 ± 94	122.91 ± 39.18	0.045
	rMSSD	35.51 ± 30.60	35.09 ± 19.50	0.214
	sNN50	10853.05 ± 1267.53	9835.14 ± 8869.78	0.156
	TI	34.84 ± 12.42	34.12 ± 6.5	1

HRT: Heart rate turbulence, HRV: Heart rate variability, BPPV: Benign paroxysmal positional vertigo, TI: Triangular index, TO: Turbulence onset; TS: Turbulence slope, SDNN: Standard deviation of NN intervals, SDNNI: SDNN index, SDANN: Standard deviation of the average NN intervals for each 5-min segment, rMSSD: Root-mean-square of successive RR interval differences, sNN50: Percentage of successive RR intervals that differ by more than 50 ms.
*p< 0.05

Table 3. Abnormal HRT parameters of the patients with BPPV and controls

	Patients with BPPV	Controls	p
Abnormal TO	68/100 (68%)	19/100 (19%)	0.025*
Abnormal TS	64/100 (64%)	21/31 (21%)	0.038*

SD: Standard deviation, HRT: Heart rate turbulence, BPPV: Benign paroxysmal vertigo, TO: Turbulence onset, TI: Triangular index.

DISCUSSION

Despite previous studies demonstrating various causes of vertigo's pathophysiology, the mechanisms of the vestibular system are still not fully understood. Vertigo associated with autonomic dysfunction (AD), orthostatic hypotension (OH), or mitral valve prolapse (MVP) may be the cause of dizziness experienced by an individual who has an autonomic disorder. Since the pathophysiology of such diseases is complex, their treatment becomes more difficult. These patients are often misdiagnosed with conditions such as hypoglycemia, chronic fatigue syndrome, neurocardiogenic syncope, or psychiatric disorders[3]. Vertigo that is associated with autonomic dysfunction has been reported in many previous studies, which showed that dysautonomia on postural changes may play important roles in the development of vertigo, and is provoked by disturbances of the autoregulatory mechanisms of cerebral blood flow[9]. Many non-invasive tests (e.g. Hyperventilation Test, Tilt Test) were used in the past for vertigo and dizziness to monitor autonomic dysfunction[10].

The semicircular canals are responsible for sensing the angular head movement in three-dimensional space providing input from the central nervous system (CNS) required for rapid mobility, stable vision, and autonomic control of cardiovascular and other gravity-sensitive systems. Disturbances altering the canal mechanics result in pathological inputs to the CNS often leading to attenuating symptoms[11]. The most important pathology in BPPV is the mechanical stimulation of vestibular receptors by displaced otoconia in the Semicircular Canals (SCCs) without a true rotation of the head[12]. It was shown that the vestibular system participates in autonomic regulation that regulates cardiovascular control during body movement and postural changes[13].

One-third of patients who have BPPV have some abnormality in the autonomic system response, as indicated by orthostatic hypotension with the Tilt Test or by the blood pressure response during the Valsalva Maneuver. The rate of autonomic dysfunction is higher in patients with residual vertigo than in those without[14]. Despite the occasional success of repositioning treatments in BPPV patients, the underlying pathophysiological mechanisms remain largely unknown. Notably, the mechanism of autonomic dysfunction has not been investigated in relation to BPPV thus far.

The HRV parameter is used to evaluate the tonic vagal activity[15]. Vagal tone is dominant during rest, but vagal and sympathetic activities are in a constant balance. Decreased HRV is detected in patients with multiple sclerosis, heart failure, diabetic neuropathy, or myocardial infarction[8,14,15]. It was shown in the study of Kim HA et al. that the residual dizziness after successful treatment in BPPV may be partly related to sympathetic neural autonomic dysfunction[14].

It was observed in our study that HRV parameters such as SDNNi, and SDANN were decreased significantly in BPPV patients when compared to the control group.

The deterioration in HRT parameters indicates cardiac autonomic dysfunction associated with decreased baroreflex sensitivity and decreased parasympathetic activity. In many previous studies, abnormal HRT parameters were reported in various diseases, and the findings were associated with an impaired baroreflex response[17,18]. In the present study, significant differences were detected between the TS one of the HRT parameters between BPPV and the control group. Based on these findings, it can be suggested that there is a decrease in baroreflex sensitivity and parasympathetic activity in individuals with BPPV.

The decreased HRV and HRT parameters observed in BPPV patients indicated a decrease in autonomic functions, specifically a decrease in the parasympathetic system, along with an increase in sympathetic activity.

The main limitation of our study was the absence of Spectral HRV Analysis, which resulted in the measurement of only parasympathetic tone while the measurement of overall parasympathetic tone could not be conducted. Another limitation of the study was the lack of a gold standard diagnostic test for evaluating autonomic dysfunction. However, similar methods were employed in all studies in the literature.

CONCLUSION

Benign paroxysmal positional vertigo is the most common known cause of peripheral vertigo. Although two main pathophysiological mechanisms such as cupulolitiasis and canalolithiasis were emphasized in this regard, its pathophysiology has not yet been fully elucidated. In conclusion, in the present study, the lower HRV and HRT values of patients who have BPPV when compared to the control group showed parasympathetic autonomic dysfunction. The current findings need to be validated through larger sample sizes and multi-center studies to ensure their robustness and generalizability.

Ethics Committee Approval: The study was approved by Afyonkarahisar Health Sciences University Clinical Research Ethics Committee (Decision no: 2021/6, Date: 30.04.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

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