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Heart rate variability and turbulence analysis in patients with psoriasis

Psöriazisli hastalarda kalp hızı değişkenliği ve türbülans analizi

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ABSTRACT

Objectives: Psoriasis vulgaris (PV) is a chronic inflammatory skin disorder with increased incidence of many systemic abnormalities. However, the effects of psoriasis on autonomic nervous system have not been previously well-defined. Impaired autonomic function with an increase in sympathetic activity may be associated with ventricular arrhythmias and sudden cardiac death in the general population. Heart rate turbulence (HRT) is a non-invasive test to reflect the increased sympathetic tone and abnormal baroreflex sensitivity. The aim of current study was to investigate the effect of psoriasis on cardiac autonomic function by using HRT and heart rate variability (HRV) parameters as possible indicators of increased risk for ventricular arrhythmias and sudden cardiac death.

Materials and methods: The study comprised 20 psoriatic patients without cardiovascular involvement and age and sex matched 20 healthy subjects. The severity of the disease was evaluated by the "Psoriasis Area and Severity Index". The HRV and turbulence analysis were assessed from a 24-hour Holter recording.

Results: There were no statistically significant differences between the two groups with respect to clinical, demographic and biochemical characteristics. When HRT parameters were compared; the values of the turbulence onset and slope in psoriatic patients were not significantly different from the control group ($p>0.05$). HRV parameters except for high frequency power (significantly lower in psoriatic patients, $p<0.05$) also did not differ between the both groups ($p>0.05$).

Conclusion: Psoriasis appeared not to be associated with impaired autonomic function regarding to HRT and HRV values. Further investigations are needed to confirm these results.

Key words: Heart rate variability; psoriasis; turbulence analysis.

ÖZET

Amaç: Psöriasis Vulgaris (PV), çok sayıda sistemik hastalık insidansının arttığı gösterilen bir kronik yangısal deri hastalığıdır. Ancak PV'in otonom sinir sistemi üzerine olan etkisi iyi tanımlanmamıştır. Artmış sempatik aktivite ile seyreden bozulmuş otonomik işlev bozukluğu, genel populasyonda ani kalp ölümü ve ventriküler aritmilerle ilişkilidir. Kalp Hızı Türbülansı (KHT), anormal barorefleks duyarlılığını ve artmış sempatik tonusu gösteren invaziv olmayan bir testtir. Bu çalışmanın amacı; artmış ventriküler aritmi ve ani kardiyak ölüm riskinin muhtemel göstergeleri olan KHT ve kalp hızı değişkenliği (KHD) parametrelerini kullanarak, PV'nin kardiyak otonomik fonksiyon üzerine olan etkisini saptamaktır.

Gereç ve yöntem: Çalışmaya kardiyovasküler tutulumu olmayan 20 psöriatik hasta ve yaş-cinsiyet yönünden benzer 20 sağlıklı birey dahil edildi. Hastalık ciddiyeti, "Psöriasis Alan Şiddet İndeksi" kullanılarak değerlendirildi. KHD ve türbülans analizi, 24 saat-Holter kayıtları ile elde edildi.

Bulgular: İki grup arasında, klinik, demografik ve biyokimyasal karakteristikler açısından istatistiksel anlamlı farklılık yoktu ($p>0.05$). KHT parametreleri karşılaştırıldığında, psöriatik hastalarda turbulans onset ve slop değerleri kontrol grubundan farklı değildi ($p>0.05$). Yüksek frekans gücü haricinde (psöriatik hastalarda daha düşük, $p<0.05$) KHD parametreleri, 2 grup arasında farklılık göstermedi ($p>0.05$).

Sonuç: KHD ve KHT değerleri açısından, PV bozulmuş otonomik fonksiyon ile ilişkili gözükmemektedir. Bu sonuçları doğrulayacak daha ileri araştırmalar gereklidir.

Anahtar kelimeler: Kalp hızı değişkenliği, psöriazis, türbülans analizi

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INTRODUCTION

Psoriasis vulgaris (PV) is a chronic, inflammatory, immune-mediated skin disease and clinically characterized by chronic erythematous plaques, generally at the elbows, knees, scalp, and lumber area. Patients with psoriasis have been shown to have an increased incidence of cardiovascular diseases compared with the general population.[1-3] Heart valve abnormalities, arterial hypertension and arterial atherosclerosis are most frequently observed cardiovascular diseases.[4-9]

Analysis of Heart Rate Variability (HRV) has been used to assess autonomic function and to quantify risk in a wide variety of both cardiac and non cardiac disorders.[10] Decreased HRV is a reflection of increased sympathetic and decreased vagal activity, which has a strong association with ventricular arrhythmias and sudden cardiac death in the general population, and especially in cardiac patients.[11] However, the predictive value of HRV alone is modest.[11] Heart Rate Turbulence (HRT) is a noninvasive method to assess autonomic function and has been shown to be an independent predictor of mortality and more predictive value than HRV on mortality.[12]. The disappearance of HRT means the loss of normal autonomic function.[13] HRV parameters were studied in patients with psoriatic arthritis.[14] and influence of psoriasis on heart rate and arrhythmia development were also reported previously.[15] However, no studies have previously evaluated HRT parameters in psoriatic patients.

The aim of the present study was to determine HRT and HRV parameters in psoriatic patients, and to compare them with the control subjects.

MATERIALS AND METHODS

Study population

The study was performed in Ministry of Health, Diskapi Yildirim Beyazit Research and Educational Hospital. Two groups of participants, matched for sex and age, were studied after obtained written informed consent. The study protocol was approved by the institutional ethics review board and conforms to the principles outlined in the Declaration of Helsinki 2008.

A total of 40 patients with PV were evaluated. However, after removal of patients with exclusion criteria, only 20 psoriatic subjects were included in the study. Nine psoriatic patients with cardiac involvement, 4 psoriatic patients who did not have a good echocardiographic picture and the patients who had not any PVC on holter recordings were excluded from the study. The study comprised a total of 20 patients with PV (9 female, 11 male; mean age 41.0±10.8 years) without cardiovascular involvement and age and sex matched 20 non-psoriatic subjects (12 female, 8 male; mean age 42.9 ± 14.7 years) (Table 1).

Among the received therapy, there were topical steroids. None of the patients used systemic steroids during the course of the disease but 10 of the patients were under the medication of local steroids. All subjects of the study did not use drugs that may influence HRT parameters.

The diagnosis of psoriasis was made using a dermatological examination by a specialist. Severity of the disease was evaluated by "The Psoriasis Area Severity Index" (PASI) scale in all psoriasis cases.[16] Each subject provided a detailed medical history and all patients and controls were evaluated via a physical examination, and 24-hour holter monitoring.

Patients having known coronary artery disease, heart failure and/or left ventricular ejection fraction (LVEF) <50%, diabetes mellitus, hypertension, thyroid disorder, connective tissue or other inflammatory disorders, moderate or severe valve insufficiency or stenosis, hepatic dysfunction, renal diseases, patients with arthropathy and any findings of cardiac involvements of PV in echocardiographic examinations were excluded from the study. In addition, patients with atrial fibrillation or without PVCs, or PVCs preceded by noise or artifacts were excluded from HRV and HRT analysis and also the subjects who use drugs that may influence HRT parameters were excluded from the study. All subjects were recommended not to drink alcohol and any caffeinated beverages during the study. Patients without any known atherosclerotic disease and any findings of left ventricular hypertrophy, left ventricular diastolic dysfunction, left ventricular wall motion abnormalities, valvular pathologies, especially mitral and tricuspid valve prolapsed on echocardiography were accepted as patients who lack of cardiac involvement. A GE Vivid 3 echocardiography machine with a 2.5-MHz transducer was used

to determine underlying structural heart disease in the study.

Holter Analysis

All subjects underwent 24-hour holter monitoring. Holter electrocardiograms (ECGs) were carefully analyzed by expert cardiologists blinded to the study using the DMS CardioScan 12 Holter system (DM Software Inc., Stateline, NV, USA).

The HRV analysis was assessed over a 24-hour period and was performed in time domains and power spectral analyses according to the European Society Cardiology/ North American Society of Pacing and Electrophysiology guidelines.[11] The following time-domain and power spectral parameters were calculated:

Standard deviations of all NN intervals (SDNN); mean of the standard deviations of all NN intervals for all 5-minute segments of the entire recording (SDNNI); standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording (SDANN); the square root of the mean of the sum of the squares of differences between adjacent NN intervals (rMSSD); the number of pairs of adjacent NN intervals differing by more than 50 ms divided by the total number of all NN intervals (pNN50); the very low frequency range power (VLF power); and the high frequency range power (HF power); the low frequency range power (LF power); and low-frequency /high-frequency power ratio (LF/HF ratio).

HRT parameters were calculated according to the method reported by Schmidt et al.[12]. Two numerical descriptors were estimated: turbulence onset (TO) reflecting the initial phase of sinus rhythm acceleration and turbulence slope (TS) describing deceleration phase. HRT onset was defined as the difference between the mean of the first two sinus rhythm RR intervals following the compensatory pause after a premature ventricular complex (PVC) and the mean of the last two sinus rhythm RR intervals preceding the PVC, expressed as a percentage of the former. It is calculated using the equation; TO = ((RR1 + RR2) - (RR-2 + RR-1)) / (RR-2 + RR-1) * 100 with RR-2 and RR-1 being the first two normal intervals preceding the PVC and RR1 and RR2 the first two normal intervals following the PVC. Positive values for TO indicate deceleration, negative values indicate acceleration of the sinus rhythm.

The HRT slope was defined as the maximum positive slope of a regression line assessed over any sequence of five subsequent sinus rhythm RR intervals within the first 20 sinus rhythm intervals after PVC, expressed as millisecond (ms) per beat. TS was calculated based on the averaged tachogram. Filtering algorithms were used to eliminate inappropriate RR intervals and VPCs. The HRT onset or slope was defined as abnormal if the onset was ≥0% or the slope was ≤2.5 ms/beat.

Statistical analysis

Using an SPSS package 11.5, the results were expressed as mean ± standard deviation or frequency expressed as percent. Data were tested for normal distribution using the One-Sample Kolmogorov-Smirnov test. Categorical variables were compared using χ^2 test. If expected count less than 5 in a cell, Fisher's exact test, otherwise Pearson chi-square test was used to compare categorical variables. For continuous variables, difference between two groups was assessed by using unpaired t - test. A two-tailed P values less than 0.05 was considered as statistically significant.

RESULTS

Clinical and demographic characteristics of both groups and the comparisons are summarized in Table 1. There were no statistically differences between the two groups with respect to age, gender, smoking, history of hypertension, and hyperlipidemia. The mean ages were 41.0±10.8 years for the PV group, and 42.9±14.7 years for the control group ($p>0.05$). We also did not find any statistical differences between the psoriatic and control groups in terms of the means of LVEF (78.2±6.9 vs. 75.7±8.0, $p>0.05$ respectively). The mean of disease duration in the PV group was 17.5±6.7 y and the mean of PASI scale was 13.2 ± 6.4 (Table 1) which is compatible with the literature that describes the severe psoriasis as 10-17 in PASI scale.[16, 17-18]

Table 1. Baseline clinical characteristics of the psoriasis and control groups

	Psoriasis group (n=20)	Control group (n=20)	P
Age (years)	41.0 ± 10.8	42.9 ± 14.7	0.644
Gender (male/female)	11/9	8/12	0.342
Body mass index (kg/m^2)	28.2 ± 5.2	27.4 ± 3.5	0.621
Smokers (%)	4 (20%)	5 (25%)	1.0*
Hyperlipidemia (%)	2 (10%)	2 (10%)	1.0*
PVC count per day	244.5 ± 736.1	261.6 ± 455.6	0,931
Mean heart rate (beat/min)	78.2 ± 6.9	75.7 ± 8.0	0.291
Left ventricular ejection fraction (%)	70 ± 5.5	66.7 ± 4.5	0.057
Duration of the disease (years)	17.5 ± 6.7	-	-
PASI scale	13.2 ± 6.4	-	-

* If expected count less than 5 in a cell, Fisher's exact test, otherwise Pearson chi-square test was used to compare categorical variables.
PASI; The Psoriasis Area Severity Index, PVC; premature ventricular contraction. p< 0.05 was considered as statistically significant.

Table 2. Results of heart rate turbulence analyses

	Psoriatic Group n = 20	Control Group n = 20	P value
HRT onset (%)	-2.2 ± 5.4	-2.8 ± 7.3	0.777
HRT slope (ms/beat)	19.4 ± 14.6	28.9 ± 28.6	0.237
Abnormal HRT onset, n (%)	6 (30%)	4 (20%)	0.285*
Abnormal HRT slope, n (%)	1 (5%)	3 (15%)	0.619*

* Fisher's exact test was used to compare these categorical variables.
HRT; heart rate turbulence. p< 0.05 was considered as statistically significant.

Table 3. Results of heart rate variability parameters

	Psoriatic Group n = 20	Control Group n = 20	P
pNN50 (%)	10.3 ± 8.4	14.9 ± 10.2	0.132
SDNN (ms)	144.6 ± 39.0	149.7 ± 44.9	0.710
SDNNI (ms)	54.0 ± 13.1	59.2 ± 12.0	0.209
SDANN (ms)	135.3 ± 38.5	135.3 ± 45.4	0.999
rMSDD (ms)	31.3 ± 11.0	45.3 ± 29.5	0.059
Total Power	3063.0 ± 1293.6	3554.8 ± 1529.2	0.286
VLF Power (ms^2)	2165.0 ± 910.8	2552.0 ± 1036.9	0.783
LF Power (ms^2)	645.0 ± 323.0	820.0 ± 425.6	0.157
HF Power (ms^2)	223.5 ± 163.3	394.8 ± 256.0	0.018
LF/HF Ratio	3.5 ± 1.3	2.8 ± 1.9	0.214

HF = high frequency; LF = low frequency; pNN50 = the number of pairs of adjacent NN intervals; rMSSD = root mean square of successive differences; SDNN = standard deviation of all NN intervals; SDNNI = mean of the standard deviations of all NN intervals for all 5-minute segments; SDANN = standard deviation of the 5-minute mean RR intervals; VLF = very low frequency. p< 0.05 was considered as statistically significant.

When HRT parameters were compared between psoriatic and control groups, the values of the TO and TS were similar (TO; -2.2±5.4 vs. -2.8±7.3, p = 0.777 and TS; 19.4±14.6 vs 28.9±28.6, p = 0.237, respectively, Table 2). For the HRV parameters in psoriatic patients; SDNN 24 hour, SDANN index, SDNN index, rMSSD, pNN50, total power, VLF power, LF power, LF/HF ratio did not differ significantly from control subjects (Table 3). Only HF power was significantly lower in psoriatic patients than control subjects (223.5±163.3 vs. 394.8±256.0, p = 0.018, respectively, Table 3).

DISCUSSION

Clinical, pharmacological and experimental data is supporting neurogenic mechanisms and the role of the nervous system in the pathogenesis of psoriasis.[19] However, there is insufficient evidence concerning the effect of psoriasis on cardiac autonomic function by using HRV and HRT analyses[14,15]

Although the cardiac pathologies associated with PV have been described in previous reports[20,21], this is the first study to evaluate the effect of PV on cardiac autonomic function by HRT analysis. In the current study we found that HRT and HRV analyses in psoriatic group did not differ significantly with the control group. Only HF power was found significantly lower in psoriatic patients than control subjects. The HF component is indicated as a marker of vagal modulation. This component is respiration-mediated and determined by the frequency of breathing. The LF/HF ratio reflects the global sympatho-vagal balance and can be used as a measure of this balance. With an average normal adult in resting conditions, the ratio is generally between 1 and 2.[11,22] In our study, this ratio was increased but psoriatic group did not differ from the control group significantly in LF/HF ratio (Table 3).

Impaired autonomic function with an increase in sympathetic activity is associated with ventricular arrhythmias and sudden cardiac death in the general population.[11] Markuszeski et al.[15] studied heart rate and arrhythmia in patients with PV. Heart rate was significantly higher in patients with PV than in the control group. There was a positive correlation between the increased heart rate in psoriatic patients and severity of the disease.[15] Our results are not supporting the findings of this study. Mean heart rate and the count of PVCs in psoriatic group was found similar to the control group in our study.

Novikova et al.[14] studied HRV parameters in patients with psoriatic arthritis. They reported that significantly lower values of HRV parameters were detected in psoriatic arthritis patients when compared with the control group. There was a significant negative correlation between HRV and disease duration, psoriatic arthritis activity.[14] However, our results are in conflict with this study. In the current study, we did not find any statistically significant differences between both groups with respect to HRV parameters except for HF power analysis.

HRT is a noninvasive test to reflect increased sympathetic tone and abnormal baroreflex sensitivity. It has been used to investigate autonomic function in different patient groups.[23-26] HRT is the physiological, bi-phasic response of the sinus node to PVCs and consists of a short initial acceleration followed by a deceleration of the heart rate. The PVC causes a brief disturbance of the arterial blood pressure (low amplitude of the premature beat, high amplitude of the ensuing normal beat).[12] When the autonomic control system is intact, this change is registered immediately with an instantaneous response in the form of HRT. If the autonomic control system is impaired, this reaction is either weakened or entirely missing.[12] In addition to HRV parameters, HRT parameters estimated as TO and TS also found similar to the values of control subjects in our study.

Factors known to affect autonomic nervous system are; age, gender, cigarette use, diabetes mellitus, and coronary artery disease. Cagirci et al.[27] studied influence of heavy cigarette smoking on HRT and HRV parameters. The study demonstrated that heavy smoking has a negative effect on autonomic function. Impaired HRV and HRT parameters were detected in that study. In our study, our selection criteria ensured that all factors affecting the cardiac autonomic function either were excluded or two groups had similar clinical and demographical data.

When considered the limitations of this study, small number of the study patients is the major limitation. Larger studies are needed to support our results. We did not have psoriatic patients having arthropathy in which inflammation may be more severe. As a last limitation, coronary artery disease

can not be strictly excluded since coronary angiography was not performed in the study population.

In conclusion, findings of the current study have suggested that PV appeared not to be associated with the increased risk for ventricular arrhythmias or sudden cardiac death, as the HRT and HRV values of psoriatic patients were found to be similar to those of the control subjects. Further investigations with larger groups and the evaluation of different types of the disease will be needed to confirm our results.

Conflict of interest: none declared

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