ABSTRACT

Objectives. Many systemic diseases including cardiovascular disturbances have been described in psoriatic patients. In the previous studies, left ventricle (LV) subclinical myocardial dysfunction was reported in the psoriasis patients. The T-wave peak to end (Tp-e) interval is a relatively new marker for ventricular arrhythmogenesis and repolarization heterogeneity. Prolongation of this interval represents a period of potential vulnerability to ventricular arrhythmias. However, there is no information available assessing the Tp-e interval and related calculations in patients with psoriasis disease. The aim of this study was to evaluate ventricular repolarization in patients with psoriasis disease by using QT, corrected QT (QTc) and Tp-e/QT ratio, and Tp-e/QTc ratio.

Methods. In this study, retrospective analysis of 30 patients who underwent the psoriasis treatment and of 30 healthy individuals was performed. The severity of the disease was evaluated by the “Psoriasis Area and Severity Index”. QT, corrected QT (QTc), Tp-e interval and Tp-e/QT ratio were measured by means of the 12-lead electrocardiogram. Left ventricular function was evaluated by echocardiography. Results. Baseline characteristics and QT and QTc intervals were similar in both groups. No difference was detected between the groups with regards to Tp-e interval (83.0±9 vs 82.3±10; p=0.81), Tp-e/QT (0.22±0.03 vs 0.23±0.04; p=0.3) and Tp-e/QTc (0.20±0.04 vs 0.19±0.04; p=0.77). Conclusions. These findings suggest that ventricular repolarization in mild to moderate psoriasis patients might be unimpaired. Larger samples and severe degree psoriasis patients are needed to evaluate the arrhythmia risk in psoriasis patients.

Keywords: Psoriasis; Tp-e interval; Tp-e/QT ratio

Introduction

Psoriasis is a chronic autoimmune skin disorder typically characterized by inflammatory plaques with a silver scale on the skin, scalp, nails and joints. Taking into account prevalence and incidence, psoriasis is thought to affect approximately 2-3% of the world population [1]. Many systemic diseases including cardiovascular disturbances have been described in psoriatic patients [2-5]. In the previous studies, LV subclinical myocardial dysfunction was reported in the psoriasis patients especially in severe disease [6-8].
Recent studies indicated that increased T-wave peak to end (Tp-e) interval and Tp-e /QT ratio might be a useful index to predict ventricular tachyarrhythmias and cardiovascular mortality [9,10]. However, there is no information available assessing the Tp-e interval and related calculations in psoriasis patients. The aim of this study was to evaluate ventricular repolarization in patients with psoriasis by using QT, corrected QT (QTC) and Tp-e interval, Tp-e/QT ratio, and Tp-e/QTC ratio.

Methods

The study population consisted of 30 patients with mild to moderate psoriasis (Group I, mean age 39±13 years) and 30 control subjects (Group II, mean age 34±8 years) were included.

Retrospective analysis of study patients was performed. All patients were diagnosed with Psoriasis Vulgaris based on clinical and histopathological findings. Patients with a right bundle or left bundle branch block, pacemaker implantation, coronary artery disease, valvular heart disease, heart failure, pulmonary hypertension and any medication for the prior six months including beta-blockers, antihypertensive drugs, and systemic anti-psoriatic treatment were excluded. All patients were observed to be in sinus rhythm. The ethics committee of our institute approved the study protocol.

The age, gender, height, body weight, as well as the presence of cardiovascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, and smoking) were recorded. Blood pressure was measured once after 15 min in the rest with the auscultatory method using a standard stethoscope and sphygmomanometer. Also, fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) levels were measured.

Evaluation of the Patients

Clinical severity of the disease was assessed according to the psoriasis area and severity index (PASI). The PASI evaluates four body regions: the head, trunk, upper and lower extremities. For each region, the affected area is graded from 0 to 6, and each of the three variables (erythema, thickness, and scaling ) is graded from 0 to 4, the scores from the regions were added to determine a PASI score ranging from 0 to 72 [11]. Nail involvement of the patients was also noted.

Echocardiographic Measurements

A Vivid 7 echocardiographic unit (GE, Norway) with 3.5 MHz probe was used. All echocardiograms were performed by the same investigator. The echocardiographic study was performed in left lateral decubitus position, with parasternal long and apical 2- and 4- chamber views. Quantification by echocardiography was made according to the recommendations of European Association of Cardiovascular Imaging [12].

Measurement of Tp-e, QT and QRS intervals from the 12-lead ECG

All ECGs were scanned. The Tp-e interval was defined as the interval from the peak of T wave to the end of T wave (Figure 1). Measurements of Tp-e interval were performed from precordial leads as it was described [13]. T-wave peak to end interval, QT and RR intervals were measured by a computer based method. The QT interval was defined as extending from the beginning of QRS complex to where T waves descend onto the isoelectric baseline. When a U wave interrupted the T wave before returning to baseline, the QT interval was measured to the nadir of the curve between the T and U waves. The QTC interval was calculated using the Bazett formula: QTC (ms) = QT measured/√RR (sec). All measurements (Tp-e and other surface ECG related ones) were the mean value of three calculations. All the measurements were measured by a blinded investigator.

Statistical Analysis

SPSS version 13.0 (IBM Corporation, USA) was
used for statistical analysis. Data were summarized and organized into tables and analyzed using descriptive statistics which were given as mean±standard deviation. Categorical variables were compared via Fisher exact test. Normally distributed variables were compared across groups using student t-test whereas variables which did not normally distribute were compared using Mann-Whitney U test. p<0.05 was considered as statistically significant.

Results

The psoriasis group consisted of patients with a mild-to-moderate disease with a mean duration of 7.1±5.3 years. Mean PASI score was 7.9±4.3. Nail involvement was detected in 30% of patients with psoriasis (Table 1). None of the patients had psoriatic arthritis.

There were no statistically significant differences between the groups with regard to mean age, sex, heart rate, blood pressures, body mass index. There were no differences between the groups with regards to biochemical parameters (Table 2).

LV end-diastolic and end-systolic dimensions, LV

| Table 1. Specific disease characteristics of patients with psoriasis vulgaris |
|-----------------------------------------------|
| Variables                               | Data |
| Duration of disease (years)               | 7.1±5.3 |
| PASI score                               | 7.9±4.3 |
| Patients with nail involvement (%)       | 30   |
| PASI=Psoriasis Area and Severity Index; Data are presented as means ± SD |

| Table 2. Characteristics of study population and biochemical parameters |
|-----------------------------------------------|
|                                      | Group I (n=30) | Group II (n=30) | p   |
| Age (Years)                            | 39±13   | 34±8    | 0.116 |
| Sex M/F                                | 19 /11 | 19 /11 | 0.640 |
| Body Mass Index (kg/m²)                | 26.9±3 | 24.0±2.3 | 0.118 |
| Systolic BP (mmHg)                     | 117±12 | 112±9.8 | 0.073 |
| Diastolic BP (mmHg)                    | 75.5±8 | 71±7    | 0.116 |
| Heart Rate (bmp)                       | 75±11 | 76±10   | 0.745 |
| WBC count (10³/mm³)                    | 7.65±3.32 | 6.95±2.89 | 0.45 |
| Glucose (mg/dl)                        | 96±10 | 92±7    | 0.122 |
| Total cholesterol (mg/dl)              | 168±45 | 160±40 | 0.234 |
| LDL cholesterol (mg/dl)                | 97±22 | 92±18   | 0.135 |
| LDL=Low density lipoprotein; HDL=High density lipoprotein. Data are presented as means ± SD |

| Table 3. Echocardiographic parameters between the patient group and the control group |
|-----------------------------------------------|
|                                      | Group I (n=30) | Group II (n=30) | p   |
| LVDD (mm)                              | 46±3   | 45±3    | 0.193 |
| LVSD (mm)                              | 26±5   | 27.9±3  | 0.152 |
| LVEF (%)                                | 61.5±2.6 | 63±2 | 0.091 |
| Ventricular septum thickness (cm)       | 0.9±0.2 | 0.91±0.1 | 0.915 |
| LA diameter (cm)                        | 3.6±0.2 | 3.46±0.3 | 0.113 |
| E (m/s)                                 | 0.82±0.13 | 0.84±0.14 | 0.610 |
| A (m/s)                                 | 0.74±0.12 | 0.72±0.11 | 0.522 |
| E/A                                     | 1.1±0.3 | 1.18±0.2 | 0.610 |
| Ea (cm/s)                               | 16.3±0.9 | 16.9±0.4 | 0.836 |
| E/Ea ratio                              | 5.9±1.7 | 5.4±1.3 | 0.230 |

LVDD=left ventricle end-diastolic diameter, LVSD=left ventricle end-systolic diameter, LVEF=left ventricle ejection fraction, LA=left atrium, E=peak mitral flow velocity of early rapid filling wave, A=peak mitral velocity of late filling wave due to atrial contraction, Ea=peak early diastolic velocity. Data are presented as means ± SD.
ejection fraction, LA dimension, and diastolic Doppler indexes were not statistically different between two groups (Table 3).

Groups were compared for calculated Tp-e, QT and QTc intervals and Tp-e/QT and Tp-e/QTc ratios. We have not detected any significant differences between the groups for these calculations (Table 4). In correlation analyzes, there are no significant correlation between the PASI score and Tp-e interval ($r = -0.24, p=0.2$), QT interval ($r=0.11, p=0.54$) and QTc interval ($r=0.29, p = 0.14$) (Table 5).

The overall intraobserver variability in values for the assessment of Tp-e interval and QT interval were 0.95 and 0.90, respectively.

Discussion

Psoriasis Vulgaris is a T-cell-mediated chronic inflammatory disease characterized by the formation of inflamed plaques affecting the skin, scalp, nails and joints [14]. Despite the precise pathogenesis underlying psoriasis are not yet fully elucidated, systemic inflammatory response and oxidative stress are considered the most important mechanisms in the disease’s development [15, 16]. Many systemic diseases including diabetes, hypertension, cardiovascular disturbances have been described in psoriatic patients [2-5].

In the previous studies, LV subclinical myocardial dysfunction was reported in the psoriasis patients especially in severe disease [6-8]. However, there is a scarcity of data on rhythm abnormalities and conduction disturbances in psoriatic patients. In the recent studies have showed that there is a tendency to atrial conduction disturbance in psoriasis patients [17, 18]. Recent studies have also demonstrated an inflammatory background of ventricular arrhythmias and atrial fibrillation [19-22]. Simsek et al. [17] reported that p wave dispersion and QTcD are increased in psoriasis patients. Proietti et al. [23] showed that increased sympathetic arm of the cardiac autonomic modulation in psoriasis patients by heart rate variability analysis. On the other hand, these studies include moderate to severe degree psoriasis patients. In the literature, there is no data about ventricular arrhythmia tendency in mild to moderate psoriasis patients.

Myocardial Repolarization has been evaluated by various methods including QT dispersion (QTd) and corrected QT dispersion (cQTd). Recent studies indicated that Tp-e interval, which is the interval between the peak and the end of T wave on electrocardiogram (ECG), can be used as an index of total (transmural, apicobasal, and global) dispersion of repolarization [24, 25]. Also, increased Tp-e interval might be a useful index to predict ventricular tachyarrhythmias and cardiovascular mortality [9]. Recently, a new index, the Tp-e/QT ratio has been suggested to be a more accurate measure of the dispersion of ventricular repolarization compared to QTd, cQTd, and Tp-e intervals which are independent of alterations in heart rate [10]. Also, these markers may be used as an electrocardiographic index of

Table 4. Electrocardiographic parameters between the patient group and the control group

| Parameters             | Group I (n=30) | Group II (n=30) | p   |
|------------------------|---------------|----------------|-----|
| QT interval (msec)     | 377.4±30      | 356.1±38.0     | 0.47|
| QTc interval (msec)    | 415.1±22      | 431.3±31       | 0.64|
| Tp-e interval (msec)   | 83.0±9        | 82.3±10        | 0.81|
| Tp-e/QT ratio          | 0.22±0.03     | 0.23±0.04      | 0.33|
| Tp-e/QTc ratio         | 0.20±0.04     | 0.19±0.04      | 0.77|

Tp-e= T wave peak to end, QTc= corrected QT, data are presented as means ± SD

Table 5. Correlations between the PASI score and ECG measurements in group I

| Parameters        | r   | p   |
|-------------------|-----|-----|
| Tp-e interval     | -0.24| 0.2 |
| QT interval       | 0.11 | 0.54|
| QTc interval      | 0.29 | 0.14|

ECG= electrocardiography, PASI= psoriasis area and severity index, Tp-e= T wave peak to end, QTc= corrected QT
ventricular arrhythmogenesis and sudden cardiac death [24]. The novel repolarization indexes Tp-e interval and Tp-e/QT ratio had not been studied in psoriasis patients before.

When two groups were compared in our study, QT, QTc, Tp-e interval and Tp-e/QT and Tp-e/QTc ratio were not different in mild to moderate psoriasis patients. According to the results of our study, the risk of ventricular arrhythmias in patients with mild to moderate psoriasis may not increase as much as expected. In our study, normal Tp-e interval and Tp-e/QT interval may be the following reasons: our patients to be younger. Also, they did not have any other cardiovascular risk factor. PASI Index alone is not enough for determining the severity of psoriasis. Several reports have shown that duration of psoriasis and nail involvement are necessary for establishing of psoriasis severity [26, 27]. Only 30% patients had nail involvement. So, we found normal Tp-e interval and Tp-e/QT interval because of the patients’ disease severity may be milder than we assumed.

To the best of our knowledge, this is the first study to investigate Tp-e interval and Tp-e/QT interval in cases of mild to moderate psoriasis. In the present study, we demonstrated that patients with mild to moderate psoriasis had conserved normal ventricular myocardial repolarization.

There are some limitations of this study; our groups were too small for reaching definite conclusions, moreover disease severity was mild to moderate. Thus, measurement of Tp-e interval and Tp-e/QT interval in severe psoriasis patients needs to be studied in future research.

Conclusions

Patients with mild to moderate psoriasis had unimpaired myocardial repolarization. According to the results of our study, the risk of ventricular arrhythmias in patients with mild to moderate psoriasis may not increase as much as expected.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Acknowledgments

We would like to thank dermatology consultant Dr. Serkan Yazici for providing for disease characteristics of Psoriasis Vulgaris patients.

References

[1] Parisi R, Symmons DP, Griffiths CE, Ashcroft DM, Identification and Management of Psoriasis and Associated Comorbidities (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013 Feb;133(2):377-85.
[2] Tseng HW, Lin HS, Lam HC. Co-morbidities in psoriasis: a hospital-based case-control study. J Eur Acad Dermatol Venereol. 2013 Nov;27(11):1417-25.
[3] Ryan C, Menter A. Psoriasis and cardiovascular disorders. G Ital Dermatol Venereol. 2012 Apr;147(2):179-87.
[4] Armstrong AW, Schupp C, Bebo B. Psoriasis comorbidities: results from the National Psoriasis Foundation surveys 2003 to 2011. Dermatology. 2012;225(2):121-6.
[5] Mehta NN, Azfar RS, Shin DB, Neumann AL, Troxel AB, Gelfand JM. Patients with severe psoriasis are at increased risk of cardiovascular mortality: cohort study using the General Practice Research Database. Eur Heart J. 2010 Apr;31(8):1000-6.
[6] Shang Q, Tam LS, Yip GW, Sanderson JE, Zhang Q, Li EK, et al. High prevalence of subclinical left ventricular dysfunction in patients with psoriatic arthritis. J Rheumatol. 2011 Jul;38(7):1363-70.
[7] Shang Q, Tam LS, Sanderson JE, Sun JP, Li EK, Yu CM. Increase in ventricular-arterial stiffness in patients with psoriatic arthritis. Rheumatology (Oxford). 2012 Dec;51(12):2215-23.
[8] Zhao CT, Yeung CK, Siu CW, Tam S, Chan J, Chen Y, et al. Relationship between parathyroid hormone and subclinical myocardial dysfunction in patients with severe psoriasis. J Eur Acad Dermatol Venereol. 2014 Apr;28(4):461-8.
[9] Smetana P, Schmidt A, Zabel M, Hnatkova K, Franz M, Huber, et al. Assessment of repolarization heterogeneity for prediction of mortality in cardiovascular disease: peak to the end of the T wave interval and nondipolar repolarization components. J Electrocardiol. 2011 May-Jun;44(3):301-8.
[10] Gupta P, Patel C, Patel H, Narayanaswamy S, Malhotra B, Green JT, et al. T(p-e)/QT ratio as an index of arrhythmogenesis. J Electrocardiol. 2008 Nov-Dec;41(6):567-74.
[11] Louden BA, Pearce DJ, Lang W, Feldman SR. A Simplified Psoriasis Area Severity Index (SPASI) for rating psoriasis severity in clinic patients. Dermatol Online J. 2004 Oct 15;10(2):7.
[12] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Erande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update form the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015 Mar;16(3):233-70.
[13] Castro Hevia J, Antzelevitch C, Tornés Bárzaga F, Dorantes Sánchez M, Dorticós Balea F, Zayas Molina R, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. J Am Coll Cardiol. 2006 May 2;47(9):1828-34.

[14] Schön MP, Boehncke WH. Psoriasis. N Engl J Med. 2005 May 5;352(18):1899-912.

[15] Fridewald VE Jr, Cather JC, Gordon KB, Kavanaugh A, Ridker PM, Roberts WC. The editor’s roundtable: psoriasis, inflammation and coronary artery disease. Am J Cardiol. 2008 Apr 15;101(8):1119-26.

[16] Kremers HM, McEvoy MT, Dann FJ, Gabriel SE. Heart disease in psoriasis. J Am Acad Dermatol. 2007 Aug;57(2):347-54.

[17] Simsek H, Sahin M, Akyol A, Akdag S, OzkulHU, Gumrukcuoglu HA, et al. Increased risk of atrial and ventricular arrhythmia in long-lasting psoriasis patients. ScientificWorldJournal. 2013 Apr 3;2013:901215.

[18] Calapkorur B, Kelesoglu S, Sarli B, Turasan A, Arine H, Kaya MG. Atrial electromechanical delay is impaired in patients with psoriasis. Med Princ Pract. 2015;24(1):30-5.

[19] Liu T, Li G. Is atrial fibrillation an inflammatory disease? Medical Hypotheses. 2005;64(6):1237-8.

[20] Liu T, Li G, Li L, Korantzopoulos P. Association between C-reactive protein and recurrence of atrial fibrillation after successful electrical cardioversion: a meta-analysis. J Am Coll Cardiol. 2007 Apr 17;49(15):1642-8.

[21] Korantzopoulos P, Kolettis TM, Galaris D, Goudevenos JA. The role of oxidative stress in the pathogenesis and perpetuation of atrial fibrillation. Int J Cardiol. 2007 Feb 7;115(2):135-43.

[22] Kowalewski M, Urban M, Mroczko B, Szmitkowski M. Proinflammatory cytokines (IL-6, TNF-alpha) and cardiac troponin I (cTnI) in serum of young people with ventricular arrhythmias. Pol Arch Med Wewn. 2002 Jul;108(1):647-51. [Article in Polish]

[23] Proietti I, Raimondi G, Skroza N, Pampena R, Bernardini N, La Viola G, et al. Cardiovascular risk in psoriatic patients detected by heart rate variability (HRV) analysis. Drug Dev Res. 2014 Nov;75 Suppl 1:S81-4.

[24] Kors JA, Ritsema van Eck HJ, van Herpen G. The meaning of the Tp-Te interval and its diagnostic value. J Electrocardiol. 2008 Nov-Dec;41(6):575-80.

[25] Antzelevitch C, Sicouri S, Di Diego JM, Burashnikov A, Viskin S, Shimizu W, et al. Does Tpeak-Tend provide an index of transmural dispersion of repolarization? Heart Rhythm. 2007 Aug;4(8):1114-6; author reply 1116-9.

[26] Maradit-Kremers H, Icen M, Ernste FC, Dierkhising RA, McEvoy MT. Disease severity and therapy as predictors of cardiovascular risk in psoriasis: a population-based cohort study. J Eur Acad Dermatol Venereol. 2012 Mar;26(3):336-43.

[27] Radtke MA, Langenbruch AK, Schäfer I, Herberger K, Reich K, Augustin M. Nail psoriasis as a severity indicator: results from the PoSReal study. Patient Relat Outcome Meas. 2011 Jul;2:1-6.