Original Article

Evaluation of Cardiac Arrhythmia Incidence in Patients Treated with Oral Moxifloxacin

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Abstract

Background: The effect of moxifloxacin on QT interval is reversible and dose related, mainly provided by weakly but rapidly activated rectifying potassium channel blockade, IKr or human ether-a-go-go-related gene potassium channels. Retrospective data suggested an increase in cardiac event rates with moxifloxacin use. Nevertheless, except for case reports and experimental trials about QT/QTc, there are insufficient data in the literature on the incidence of cardiac arrhythmias detected by electrocardiography (ECG) and Holter monitoring. In this trial, we sought to determine the effects of newly administrated oral moxifloxacin on the incidence of cardiac arrhythmias. **Methods:** Forty-four patients (mean age 34.0 ± 10.4 years) treated with oral moxifloxacin with the indications of upper airway infections, community-acquired pneumonia, and acute exaggerated bronchitis were enrolled. All patients were screened for cardiac arrhythmia before therapy (BT) (0^{th} day), on the 3^{rd} day (during therapy [DT]), and on the 10^{th} day (after therapy [AT]) with ECG and on the 3^{rd} and 10^{th} day with Holter monitorization. Before starting of the therapy, structural heart diseases were excluded using echocardiography, and other exclusion criteria were based on the laboratory tests. **Results:** The mean heart rate (HR) assessed by Holter monitoring was not significantly different during and after antibiotic therapy, although the mean HR measured from surface ECG was significantly reduced during and after antibiotic therapy compared to baseline (BT: 80.3 ± 13.9 beats per minute [BPM] vs. DT: 76.3 ± 11.3 vs. BPM vs. AT: 75.9 ± 106.0 BPM; $P = 0.007$). The mean QT interval value was increased on the 3^{rd} day when compared to 0^{th} day and was similar with the value on the 10^{th} day (BT: 353.1 ± 24.6 msn vs. DT: 363.3 ± 23.7 msn vs. AT: 361.8 ± 20.8 msn; $P = 0.034$). The mean QTc interval was significantly increased on the 3^{rd} day; however, it was decreased to the baseline value AT (BT: 396.4 ± 20.2 msn vs. DT: 404.4 ± 19.3 msn vs. AT: 397.5 ± 21.0 msn; $P = 0.011$). When the Holter monitoring findings of our study were analyzed in terms of gender interaction, minimal and maximal HR and QT dispersion parameters as well as the frequencies of ventricular and supraventricular extrasystoles and other arrhythmia findings were not different between male and females. **Conclusion:** Oral moxifloxacin started on an outpatient basis with the indication of airway infections resulted in a temporary increase in QT interval DT. However, it does not affect QTc and is not related with serious cardiac arrhythmias during Holter monitoring.

Keywords: Arrhythmia, electrocardiography, Holter monitoring, moxifloxacin, QT dispersion, QT/QTc interval

Introduction

Moxifloxacin is a fluoroquinolone used for community-acquired pneumonia, bronchitis exacerbations, and genitourinary diseases but mainly for the treatment of other upper and lower respiratory tract infections.[1,2] The effect of moxifloxacin on QT interval in electrocardiography (ECG) is reversible and dose related, resulted by weakly but rapidly activated

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rectifying potassium channel blockade (IKr)[3] or human ether-a-go-go-related gene (HERG) potassium channels.[4] There are several data reporting an increase in cardiac events related with the usage of oral moxifloxacin.[2,3,5] The common side effects of oral moxifloxacin are well known as gastrointestinal and central nervous system side effects, allergic reactions, skin lesions, tendinitis, QT/QTc prolongation, hypoglycemia, hyperglycemia, and hematologic side effects.[6] QT prolongation is more pronounced with the usage of the certain drugs such as amiodarone. Moxifloxacin should not be used with QT prolonging drugs because of the risk of torsades de pointes (TdP) type of arrhythmia and sudden cardiac death.[7] There is a long list of drugs prolonging QT interval including psychotropic (pimozide, sertindole, ziprasidone, quetiapine, haloperidol, and thioridazine),[8,9] antihistaminic (astemizole and terfenadine), and antimicrobial/antimalarial (erythromycin, cetoconazol, chloroquine, and halofantrine)[3,4] agents. Despite the fact that the risk of TdP with usage of oral moxifloxacin is very low as well as with other fluoroquinolones (<0.01%), it is still suggested to avoid using with other QT/QTc prolonging drugs, especially in high-risk groups.[10] However, except for case reports and experimental trials in the literature, there is not any clinical study evaluating the incidence of cardiac arrhythmias on ECG and Holter monitoring with the usage of oral moxifloxacin.

Methods

This prospective, case–controlled study was conducted at the Department of Cardiology, Faculty of Medicine, Başkent University. In this trial, 44 patients (20 females) between 18 and 75 years of age (mean 34.0 ± 10.4) treated with oral moxifloxacin with the indications of upper airway infections, community-acquired pneumonia, and acute exaggerated bronchitis were enrolled between January 2014 and September 2014. Local Ethical Committee has approved the study, and informed content was drawn from all participants. All patients were screened for cardiac arrhythmia before therapy (BT) (0^{th} day), on the 3^{rd} day (during therapy [DT]), and on the 10^{th} day (after therapy [AT]) with ECG and on the 3^{th} and 10^{th} day using Holter monitorization. Before starting of the therapy, the presence of structural heart disease was excluded using echocardiography. Other exclusion criteria were based on the laboratory tests. Antibiotic regimen was standardized to oral 400 mg moxifloxacin once daily for 7 days.

Exclusion criteria

- Known cardiac arrhythmias (atrial fibrillation, ventricular tachycardia, supraventricular tachycardia, ventricular ectopic beats, and atrial ectopic beats)
- Acquired/congenital long QT syndrome
- Left ventricular systolic dysfunction (ejection fraction [EF] <40%) and/or symptomatic heart failure
- Using QT/QTc prolonging drugs (Class IA and III antiarrhythmic drugs; tricyclic antidepressants), neuroleptics (e.g., phenothiazine, sertindole, and haloperidol), some antibiotics (e.g., halofantrine and pentamidine), and antihistaminics (e.g., therphenadine and astemizole)
- Severe heart valve stenosis and/or regurgitations (>2/4)
- Congenital heart diseases (e.g., mitral valve prolapses, hypertrophic cardiomyopathies, arrhythmogenic right ventricular dysplasia, and Brugada syndrome)
- Cardiopulmonary resuscitation
- Severe hypokalemia (<3.5 mmol/l), hyperkalemia (>5.5 mmol/l), hypercalcemia (>10.5 mg/dl), hypocalcemia (<8.5 mg/dl)
- <18 years of age
- Having other infections except upper and lower airway infections
- Using antibiotics for upper and lower airway infections except moxifloxacin
- Severe hepatic diseases (Child-Pugh Class C or aspartate aminotransferase (ACT) and/or alanine aminotransferase levels are higher 5 times above normal levels) and gallbladder diseases
- Having malignancy
- Thyroid diseases
- Pregnancy and/or breastfeeding period
- Using iron (Fe) preparations, antiacites
- Having allergy to moxifloxacin and other fluoroquinolones.

Transthoracic echocardiography was performed to all patients. The echocardiographic examination was performed at least 15 min after the rest using the GE Vivid 9 Expert (USA) device and the 3V2 transthoracic probe in the left lateral position (two-dimensional, color Doppler echocardiography) using parasternal and apical windows. Echocardiography was performed to each participant in accordance with the American Society of Echocardiography guidelines and the European Standard Echocardiography Guidelines.[11] The EF was calculated according to the modified Simpson's method. Echocardiography was performed and all results were evaluated by the same physician in all patients.

In our study, ECGs were obtained by 12-channel ECG devices using X Hewlett-Packard Pagewriter XLI (Philips, Germany), which is used by our cardiology department. The ECG images were performed by experienced technicians, and poor quality shots were repeated, and all shots were performed in supine position at a speed of 25 mm/s and a calibration of 10 mm/mV. At the time of recording, we tried to prevent speech, coughing, and excessive tremor which could affect the quality of the shooting. The rhythm, heart rate (HR), PR interval, QRS duration, and QT and QTc durations of all were evaluated by ECG. QTc time was calculated based on the Bazett formula. The longest QT time (QTmax) and the shortest QT time (QTmin) were determined in the 12-channel ECG and the QT dispersion (QTmax − QTmin) was calculated manually. All ECGs were evaluated by the physician who performed the study.

The laboratory parameters were studied from venous blood samplings before the initiation of the therapy. The evaluation

of the ECG and Holter monitoring was performed by the same researcher blinded to the other clinical and laboratory data.

Statistics

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL, USA). The normal distribution of the data was evaluated using Kolmogorov–Smirnov test. Those who exhibited normal distribution from numerical variables were shown as mean ± standard deviation, and those without normal distribution were shown as median with percentiles. Categorical variables were expressed as numbers and percentages. In the comparison of two categories, *t*-test (in numerical variables with normal distribution) and Mann–Whitney U-test (in nonnormally distributed numerical variables) were used in independent samples. Chi-square test and Fisher's exact test were used to compare the categorical data. Two-way ANOVA test was used for repeating samples, and Bonferroni corrected *t*-test was used for pair-wise comparisons in comparison of the pre- and post-treatment follow-up variables. The Bonferroni test was used as a *post hoc* test in the interaction of results with gender. Friedman test was used to compare the pretreatment and posttreatment 3rd and 10th day variables, and the Wilcoxon test with Bonferroni correction was used for bilateral comparisons. $P < 0.05$ was considered statistically significant.

Results

Forty-four patients (20 females and 24 males) were included into the study. The average age of the study group was 34.0 ± 10.4 years. In our study, all laboratory parameters were in normal range for all patients, and there was not any structural heart disease. Patient's demographics, laboratory

Table 1: Demographics, laboratory analyses, and echocardiographic findings

Variables	Population (*n*=44)	Female (*n*=20)	Male (*n*=24)	*P*
Baseline characteristics of patients				
Age	34.0±10.4	34.4±11.8	33.7±9.2	0.831
Body mass index (kg/m^2)	24.2±3.3	23.1±3.9	25.0±2.6	0.063
Smoking, *n* (%)	28 (63.6)	8 (40.0)	8 (33.3)	0.757
Laboratory findings				
Potassium (mmol/L)	4.4±0.5	4.3±0.5	4.6±0.5	0.110
Magnesium (g/dL)	2.1±0.3	2.2±0.2	2.1±0.3	0.398
Hemoglobin (mg/dl)	14.2±1.3	13.4±1.2	14.9±1.1	0.001*
WBC (10^3/µL)	8.1±2.3	7.9±2.1	8.3±2.4	0.557
Echocardiographic findings				
Aortic root (cm)	2.7±0.3	2.5±0.2	2.9±0.3	0.001*
Basal septal thickness (cm)	1.0±0.2	0.9±0.2	1.1±0.1	0.003*
Basal posterior wall thickness (cm)	1.0±0.2	0.9±0.2	1.0±0.1	0.004*
LV end diastolic diameter (cm)	4.3±0.4	4.1±0.4	4.5±0.3	0.004*
LV systolic diameter (cm)	2.7±0.3	2.6±0.3	2.8±0.3	0.033*
LA diameter (cm)	3.4±0.3	3.2±0.3	3.5±0.3	0.030*
RA diameter (cm)	3.1±0.3	3.0±0.3	3.3±0.2	0.001*
LV end-diastolic volume (ml)	77.8±14.2	70.1±10.8	84.2±13.7	0.001*
LV end-systolic volume (ml)	31.2±6.5	28.0±5.5	33.8±6.2	0.002*
EF (%)	59.9±2.8	60.5±3.2	59.4±2.3	0.182
M1 (cm/sn)	86.0±19.3	90.6±16.3	82.2±21	0.153
M2 (cm/sn)	67.8±13.7	66.6±13.4	68.8±14.2	0.611
T1 (cm/sn)	61.9±11.3	63.8±10.4	60.4±11.9	0.334
T2 (cm/sn)	50.6±11.8	51.2±13.4	50.1±10.6	0.769
A (cm/sn)	138.7±16.4	138.8±14.8	138.6±18	0.974
MR				
Minimal	18 (40.9)	10 (50.0)	8 (33.3)	0.231
1/4 MR	1 (2.3)	1 (5.0)	-	
TR				
Minimal	18 (40.9)	9 (45.0)	9 (37.5)	0.760
1/4 TR	-	-	-	
Aortic regurgitation	-	-	-	-
Pulmonary regurgitation	90.9±13.5	90.7±15.2	91.1±12.3	0.927
LV diastolic dysfunction				
Grade 1	5 (11.4)	1 (5.0)	4 (16.7)	0.356

*P<0.05 statistically significant. A: Aortic velocity M1: Mitral E velocity, M2: Mitral A velocity T1: Tricuspid E velocity T2: Tricuspid A velocity, MR: Mitral regurgitation, WBC: White blood cells, TR: Tricuspid regurgitation, LV: Left ventricular, RA: Right atrium, LA: Left atrium, EF: Ejection fraction

Table 2: Basal electrocardiography findings (0th day) and Holter findings during therapy (3rd day)

Variables	Population (*n*=44)	Female (*n*=20)	Male (*n*=24)	*P*
Basal ECG findings				
HR (beat/min)	80.3±13.9	78.9±13.5	81.5±14.5	0.536
QRS (msn)	87.9±9.2	85.0±7.8	90.3±9.7	0.055
PR (msn)	153.8±18.1	153.9±18.7	153.8±18	0.979
QT (msn)	353.1±24.6	352.8±24.5	353.4±25.2	0.935
QTc (msn)	396.4±20.2	399.4±26.0	393.9±14.0	0.378
QTmax (msn)	379.5±24.5	378.0±24.8	380.8±24.7	0.707
QTmin (msn)	339.3±21	340.0±20.0	338.8±21.7	0.846
QTd (msn)	39.8±15.5	37.0±16.6	42.1±14.4	0.283
Holter findings during therapy (3rd day)				
HRmin (beat/mn)	56.0±7.3	56.6±4.4	55.6±9.1	0.681
HRmax (beat/mn)	123.7±14.7	128.3±15.1	119.9±13.5	0.057
SVES	170 (0-691)	11 (0-19)	155 (0-691)	0.909
VES	453 (0-4412)	152 (0-370)	854 (0-4412)	0.457
Sinus rhythm (%)	44 (100)	20 (100)	24 (100)	

HR: Heart rate, HRmax: Maxımum heart rate, HRmin: Minimum heart rate, QTc: Corrected QT, SVES: Supraventricular extrasystole, VES: Ventricular extrasystole, ECG: Electrocardiography

analyses, and echocardiographic findings are presented in Table 1. Baseline ECG measurements including HR, QRS, PR, QT, QTc, QTmax, QTmin, and QTd as well as Holter findings including HRmax, HRmin, supraventricular extrasystole (SVES), and ventricular extrasystole (VES) DT are also presented in Table 2. Accordingly, there are no differences between male and gender patients. When the ECG findings BT, DT, and AT were evaluated together in the entire population [Table 3], HR was diminished DT and AT compared to baseline, QT was prolonged DT and AT, but QTc was only prolonged DT. QRS, PR, and QTd parameters were all similar between the groups. On the other hand, when ECG findings BT, DT, and AT were analyzed according to gender [Table 4 and Figure 1], in female patients, but not in male ones, QT distance was prolonged significantly DT and AT (*P* interaction = 0.031). The decrease in HR was significant in males DT and AT (*P* interaction = 0.036), and QTc changes BT, DT, and AT remained similar between male and female patients (*P* interaction = 0.890). QRS, PR, and QTd measurements were comparable between the groups in terms of gender. The comparison of Holter findings DT and AT including HRmax, HRmin, SVES, and VES revealed similar findings [Table 5] which was not affected by the gender [Table 6].

Table 3: Electrocardiography findings before therapy, during therapy (3rd day), and after therapy (10th day)

Variables	Before therapy	3rd day	10th day	*P*
HR (beat/min)	80.3±13.9	76.3±11.3[ŧ]	75.9±10.6[ŧ]	0.034*
QRS (msn)	87.9±9.2	87.7±8.5	88.5±9.4	0.717
PR (msn)	153.8±18.1	156.8±19.3	156.5±18.8	0.400
QT (msn)	353.1±24.6	363.3±23.7[ŧ]	361.8±20.8[ŧ]	0.007*
QTc (msn)	396.4±20.2	404.4±19.3[ŧ,§]	397.5±21.0	0.011*
QTmax (msn)	379.5±24.5	395.5±27.6[ŧ]	395.0±32.6[ŧ]	0.001*
QTmin (msn)	339.3±21.0	352.7±25.6	349.6±27.1[ŧ]	0.008*
QTd (msn)	39.8±15.5	45.5±18.0	45.9±20.5	0.183

[ŧ]There is significant difference before therapy ($P<0.05$), [§]There is significant differences after therapy ($P<0.05$), *$P<0.05$ statistically significant, *P* (int): *P* interaction: The effect of the factor of gender during therapy and after therapy, HR: Heart rate, QTc: Corrected QT, QTd: QTmax − QTmin

Discussion

In our study, we have demonstrated that oral moxifloxacin therapy for the indication of airway infections resulted in a temporary increase in QT interval DT. However, it does not affect QTc and is not related with serious cardiac arrhythmias during Holter monitoring.

It is well known that oral moxifloxacin prolongs the QT/QTc interval. However, there are very few case reports, preclinical studies, and clinical trials of moxifloxacin-related TdP.[12-14] The presence of additional risk factors (such as other drug use) that prolong the QT interval is thought to be an important predisposing factor for TdP development in these reported cases.

The effect of moxifloxacin on QT interval is reversible and dose related. It effects weakly but rapidly activated rectifying potassium channel blockade, IKr[3] or HERG potassium channels.[4] Retrospective data suggested an increase in cardiac event rates with moxifloxacin use.[12] Nevertheless, except for case reports and experimental trials about QT/QTc, there are insufficient data in the literature on the incidence of cardiac arrhythmias detected by ECG and Holter monitoring. In one of the previous prospective studies investigating the influence of quinolone drugs on QT and TdP development, QT interval was shown to prolong about 6 ms as compared to baseline values; however, TdP did not occur after 7 days of single-dose moxifloxacin use among healthy individuals with a mean age of 34 years, who did not have any cardiovascular or renal diseases, who were not using any drugs that could be effective on QT.[15] Similarly, we detected a 10.2 ms increase in QT interval under

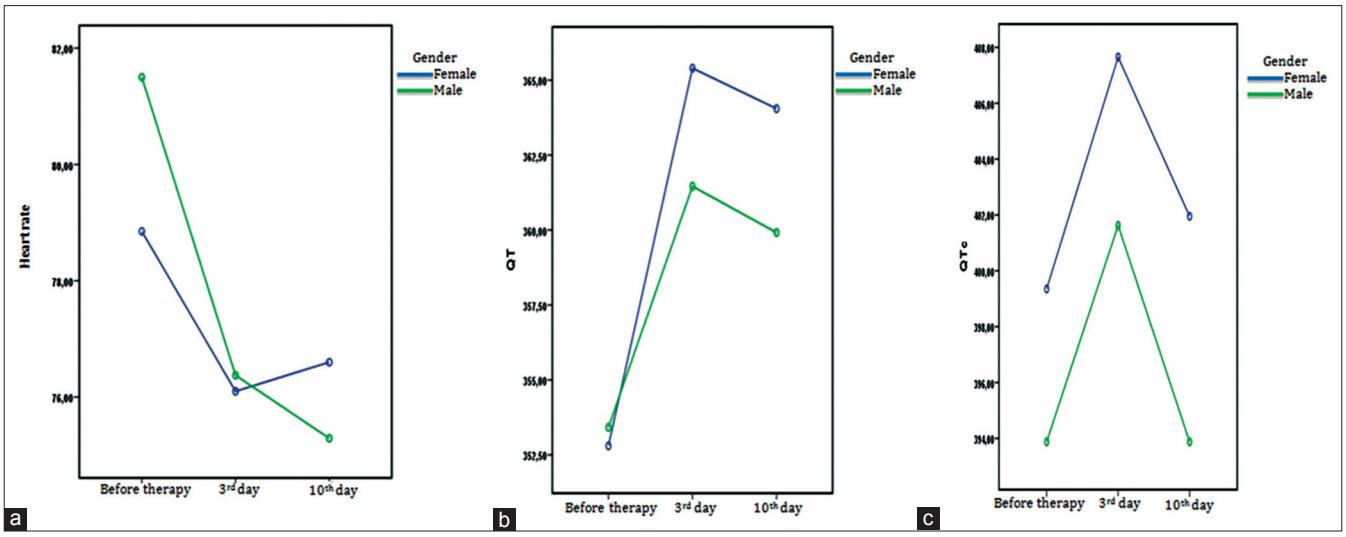

Figure 1: (a-c) Heart rate, QT and QTc, changes before during and after antibiotherapy according to genders

Table 4: Electrocardiography findings before therapy, during therapy, and after therapy according to gender

Variables	Gender	Beforetherapy	3rd day	10th day	*P*	*P* (int)
HR (beat/min)	Female	78.9±13.5	76.1±11.8	76.6±11.7	0.506	0.036*
	Male	81.5±14.5	76.4±10.6	75.3±9.9	0.038‡	
QRS (msn)	Female	85.0±7.8	83.9±7,0	84.6±6.6	0.741	0.635
	Male	90.3±9.7	90.8±8.5	91.8±10.1	0.627	
PR (msn)	Female	153.9±18.7	157.0±18.6	155.6±19.4	0.786	0.906
	Male	153.8±18.0	156.8±20.2	157.3±18.7	0.367	
QT (msn)	Female	352.8±24.5	365.4±25.7	364.1±20.6	0.022‡	0.031*
	Male	353.4±25.2	361.5±22.4	359.9±21.2	0.212	
QTc (msn)	Female	399.4±26.0	407.7±19.8	402.0±22.0	0.262	0.890
	Male	393.9±14.0	401.6±18.8	393.9±19.8	0.116	
QTd (msn)	Female	37.0±16.6	46.0±18.5	50.0±18.9	0.082	0.236
	Male	42.1±14.4	45.0±17.9	42.5±21.5	0.797	

HR: heart rate, QTc: corrected QT , QTd: QTmax- QTmin, ‡significant differences were shown between "before therapy-3rd day" and before therapy-10th day", **P* (int): *P* interaction: the effect of gender factor during therapy and after therapy

Table 5: Holter findings during therapy and after therapy

Variables	3rd day	10th day	*P*
HRmin (beat/min)	56.0±7.3	55.5±6.5	0.587
HRmax (beat/min)	123.7±14.7	126.8±15.4	0.089
SVES	170 (0-691)	220 (0-413)	0.589
VES	453 (0-4412)	752 (0-3377)	0.517

HR: Heart rate, HRmax: Maximum heart rate, HRmin: Minimum heart rate, SVES: Supraventricular extrasystole, VES: Ventricular extrasystole

treatment, and an 8.5 ms increase was detected after treatment compared to baseline values. In our study, QTc interval was detected to increase 8 ms during treatment (on day 3) compared to pretreatment value (day 0); however, it returned to almost pretreatment values after treatment (on day 10). We considered that the detection of prolonged QTc interval after treatment (on day 10) might be associated with higher HR at the beginning (the difference was 5 beats per minute [BPM]) of moxifloxacin therapy. When evaluated with regard to QTc intervals, only 1.1 ms difference was observed between day 0 and 10. In our study, QTc interval did not prolong to cause TdP. In another randomized, double-blind, placebo-controlled study, an QTc prolongation of 4.0% ± 5.1% was observed at 2 h after oral administration of 400 mg/day moxifloxacin in young and healthy cardiac patients, but TdP did not develop in any of them. In the same study, a QTc prolongation of 4.0% ± 5.1% was observed when 800 mg oral moxifloxacin was given daily, but no development of TdP was observed.[16]

Holter ECG was performed to detect drug-induced arrhythmias after initiation of oral moxifloxacin in all patients. In previous studies, Holter ECG was performed on the 1st day of moxifloxacin treatment (3 h after initiation of the therapy). In our study, we decided to perform the first Holter ECG on the 3rd day, because the stable peak effect of oral moxifloxacin (also on QT/QTc) is shown to be on the 3rd day. Furthermore, the other reasons are that the patients are being treated remotely and the antibiotics cannot be taken on the day they are prescribed. For these reasons, we applied Holter and ECG procedures on the 3rd day. There are also animal studies and experimental studies in the literature where QT/

Table 6: Holter findings during therapy and after therapy between genders

Variables	Gender	3rd day	10th day	*P*	*P* (int)
HRmin (beat/min)	Female	56.6±4,4	56.2±5.8	0.765	0.908
	Male	55.6±9,1	55.0±7.1	0.657	
HRmax (beat/min)	Female	128.3±15.1	131.2±14.9	0.368	0.879
	Male	119.9±13.5	123.2±15.3	0.131	
SVES	Female	11 (0-19)	24 (0-52)	0.333	0.340
	Male	155 (0-691)	220 (0-413)	0.377	
VES	Female	152 (0-370)	314 (0-862)	0.333	0.247
	Male	854 (0-4412)	752 (0-3377)	0.302	

HR: Heart rate, HRmax: Maximum heart rate, HRmin: Minimum heart rate, SVES: Supraventricular extrasystole, VES: Ventricular extrasystole, *P* (int): *P* interaction: The effect of the factor of gender during therapy and AT, AT: After therapy

QTc, QT dispersion calculations with telemetric follow-up after oral moxifloxacin, and similar results in terms of QTc and QT dispersion prolongation and no TdP formation are observed.[17,18]

QT dispersion is a gross and estimated measurement of repolarization abnormalities of myocardium; in addition, severe concerns exist about the accuracy of estimation methods.[19,20] All values which have been suggested as upper limit in healthy individuals were noticed not to be safe.[21-23] Therefore, abnormal QT dispersion values in the literature (>100 ms) out of the error limits are suggested to have clinical importance for indicating repolarization abnormality. In our study, we did not detect a difference in QT dispersion values during (on day 3) and after (on day 10) treatment compared to pretreatment values ($P > 0.05$). A statistically significant difference was not observed between genders when QTd interval was evaluated before, during, or after treatment ($P > 0.05$). Before treatment, QTd interval was measured on an average of 37.0 ms in females and 42.1 ms in males. During treatment, these values were found as 46 ms and 45 ms, respectively, for females and males. After treatment, QTd was measured as 50 ms in females and 42.5 ms in males. The differences in QTd before, during, or after treatment were not found statistically significant ($P = 0.236$), and all of these values were within the QT dispersion interval seen in healthy individuals reported in the literature (10–71 ms).

The mean HR assessed by Holter monitoring was not significantly different during and after antibiotic therapy. However, the mean HR measured from surface ECG was significantly reduced during and after antibiotic therapy compared to baseline (BT: 80.3 ± 13.9 BPM vs. DT: 76.3 ± 11.3 BPM vs. AT: 75.9 ± 106 BPM; $P = 0.007$). Since the patients admitted to the hospital had fever leading to tachycardia, the HRs of the patients were reduced during and after antibiotic therapy. When the Holter monitoring findings of our study were analyzed in terms of gender interaction, minimal and maximal HR, QT dispersion parameters, as well as the frequencies of VES and SVES, and other arrhythmia findings were not different between male and females. Mean QT interval value was increased on the 3rd day when compared to 0th day and was similar with the value on the 10th day (BT: 353.1 ± 246 msn vs. DT: 363.3 ± 23.7 msn vs. AT: 361.8 ± 20.8 msn; $P = 0.034$). Mean QTc interval was significantly increased on the 3rd day but was decreased to the baseline value (BT: 396.4 ± 20.2 msn vs. DT: 404.4 ± 19.3 msn vs. AT: 397.5 ± 21.0 msn; $P = 0.011$).

Conclusion

Four hundred milligrams of oral moxifloxacin started on an outpatient basis due to indications of upper and/or lower airway infections results in an increase in QT interval DT. However, it does not affect QTc to critically increased values (>500 msn) and is not related to serious cardiac arrhythmias during Holter monitoring.

Strengths and limitations

The relatively small number of the patients in this study is the most important limitation which precluded adjustment of our results to the general population. Our study has included patients on an outpatient basis. If we were able to add hospitalized patients, we could calculate QT/QTc and other arrhythmia parameters under telemetric or continuous ECG monitoring. Since the dose of oral moxifloxacin was kept constant at 400 mg/day, we could not have any information if any QT/QTc duration changes might occur in patients treated with 400 mg bid. On the other hand, our study has some strength. First, there is not adequate number of clinical data evaluating the possible arrhythmogenic effects of this antibiotic. Second, we did not any drop out during the follow-up period, and all symptoms and any possible changes on the ECG and Holter were carefully and closely monitored. We hope that our study will inspire further clinical studies on this issue.

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Conflicts of interest

There are no conflicts of interest.

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