Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2021;46(2):691-698
DOI: 10.17826/cumj.856174

ARAŞTIRMA / RESEARCH

Electrocardiographic findings and cardiac safety of hydroxychloroquine+azithromycin in hospitalized patients with COVID-19

Hastanede yatan COVID-19 hastalarında elektrokardiyografik bulgular ve hidroksiklorokin + azitromisin tedavisinin kardiyak güvenliği

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Cukurova Medical Journal 2021;46(2):691-698

Abstract

Purpose: The aim of this study was to determine the novel arrhythmia markers (Tpe, cTpe, cTpe/cQT) in addition to standard evaluation of 12-derived electrocardiography (ECG) and effects of therapy in patients with COVID-19.
Materials and Methods: We evaluated 12-derived ECG in 51 patients with COVID-19 at the pre-treatment stage and on the 2nd and 5th days of the treatment, retrospectively. Patients were treated by either hydroxychloroquine (HCQ) + azithromycin or HCQ alone. Severe COVID-19 patients were defined with the presence of clinical signs and symptoms of pneumonia plus SpO2<90%, or respiratory rate > 30 breathe/minute.
Results: While 68.6% of patients received HCQ + azithromycin combination therapy, 31.4% of patients received HCQ monotherapy. On the 2nd day of the treatment, heart rate was the only statistically significant variable either on the treatment of HCQ + azithromycin or HCQ alone. On the 5th day of treatment, in addition to the heart rate, Tpe and cTpe levels were also statistically significant among the whole treatment regimens. Although Tpe statistically significantly increased in both treatment strategies during treatment, increasing relative Tpe ratios were similar between both of the treatment strategies.
Conclusion: The results of our study suggests that those off-label drugs (HCQ/azithromycin) have an acceptable cardiac safety profile in COVID-19 disease during short hospitalization.
Keywords:. Arrhythmia, corrected QT, COVID-19, Tpeak- Tend interval

Öz

Amaç: Bu çalışma ile COVID-19 hastalarında 12-derivasyonlu elektrokardiyografinin (EKG) standart değerlendirmesine ek olarak yeni aritmi belirteçlerini ve tedavi etkisininin araştırılması amaçlanmıştır.
Gereç ve Yöntem: Toplam 51 COVID-19 hastasının 12-derivasyonlu EKG si tedavi öncesi, tedavinin 2. ve 5. günlerinde geriye dönük olarak değerlendirildi. Hastalar COVID-19'a yönelik hidroksiklorokin (HCQ) + azitromisin veya sadece HCQ tedavisi aldı. Ciddi COVID-19 hastaları, pnömoni bulgularına ek olarak SpO2<90% veya solunum sayısı >30/dk olarak tanımlandı.
Bulgular: Hastaların %68,6'ı HCQ + azitromisin kombinasyon tedavisi alırken, %31,4 hasta sadece azitromisin tedavisi aldı. Tedavinin 2. gününde, kombinasyon tedavisi alanlarda ve sadece azitromisin alanlarda sadece kalp hızı istatistiksel olarak anlamlı değişken olarak bulundu. Tedavinin 5. gününde kalp hızına ek olarak ve cTpe değerleri her iki tedavi rejiminde istatistiksel olarak anlamlı olarak bulundu. Tedavi süresince her iki tedavi rejiminde Tpe düzeyleri istatistiksel anlamlı olarak artmasına rağmen, rölatif artış oranları istatistiksel olarak gruplar arası benzer bulundu.
Sonuç: Çalışma sonuçlarımız, kısa süreli hastanede yatan COVID-19 hastalarında kullandığımız HCQ/ azitromisin tedavisinin kabul edilebilir düzeyde kardiyak etki profiline sahip olduğunu göstermektedir.

Anahtar kelimeler: Aritmi, düzeltilmiş QT, COVID-19, Tpik- Tson intervali

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Geliş tarihi/Received: 09.01.2021 Kabul tarihi/Accepted: 30.04.2021 Çevrimiçi yayın/Published online: 20.05.2021

INTRODUCTION

COVID-19 pandemic is not only one of the worst economic and social problems experienced during the last century, but it is a disaster that disrupts healthcare as well. COVID-19 pandemic has been observed in the hospitals and especially the intensive care units with highly morbidity and mortality[1]. Virus transmitted via aerosols primarily during inspiration and less frequently by contact from contaminated surfaces. Clinical presentation may vary from the mild flu infection (fever, cough) and atypical pain to severe shortness of breath and overt myocardial infarction[2]. Although patients with COVID-19 primarily admitted to hospital by findings of respiratory distress (non-productive cough, crackels, ground-glass opacity and bilateral shadowing on computed tomography, pneumonia etc.), underlying cardiovascular disease or risk factors (older age, hypertension, diabetes mellitus) were the main reasons for further intensive care unit visits. Cardiac manifestations of COVID-19 have been described continuously, however, many of them consist of case studies[2-4]. Studies showed that cardiac ischemia-related parameters (D-dimer, troponin, fibrinogen, etc.) increased in COVID-19 patients and these may be associated with increased cardiac risk and death in COVID-19 patients[,5,6]. Although sinus tachycardia is the most common arrhythmia in patients with COVID-19, QT prolongation, ST/T wave changes, torsade de pointes, and ventricular tachycardia/fibrillation are responsible for poor prognosis[7]. The mechanisms of these arrhythmias which display reentry in myocardial ischemia and triggered activity/early afterdepolarizations in QT prolongation, may be concluded as VF/VT and torsade de pointes, respectively[8]. According to our knowledge, increased cardiac risk may not be only associated with the direct influences of COVID-19 viruses and its co-morbidities, but also with off-label treatments of COVID-19 which were the potential risk for ventricular arrhythmias and death[9-11]. Because of these safety concerns, we evaluated the effects of hydroxychloroquine (HCQ) + azithromycin (AZM) by novel arrhythmia markers (Tpe, cTpe, cTpe/cQT) in addition to standard evaluation of 12-derived electrocardiography (ECG).

MATERIALS AND METHODS

Hatay Mustafa Kemal University Non Interventional Clinical Research Ethics Committee (no.32, date: 06.07.2020) approved the current study. This study was also designed in accordance with the Helsinki Declaration.

This study included 51 laboratory confirmed (had positive PCR results) COVID-19 infection patients (41 male, 10 female) who were hospitalized in the infectious disease clinic. Patient inclusion period was between 1 April and 1 June 2020. We evaluated 12-derived ECG and laboratory parameters in patients with COVID-19 at the pre-treatment stage and on the 2nd and 5th days of treatment, retrospectively. Patients were treated by either HCQ + AZM or HCQ alone. The selection of therapy with HCQ ± AZM was based on the treating physician's decision and given according to the local healthcare system guidelines[12]. Both HCQ (loading dose 400 mg two times on day 1 and maintenance dose 200 mg twice daily on days 2-5) and AZM (loading dose 500 mg on day 1 and maintenance dose 250 mg daily on days 2-5) were given orally for 5 days. All patients in HCQ alone group were also given levofloxacin (LEV) or moxifloxacin (MXF) for seconder bacterial infections. Severe COVID-19 patients were defined with the presence of clinical signs and symptoms of pneumonia plus SpO2<90%, or respiratory rate > 30 breathe/minute. Moderate COVID-19 disease course was defined with pneumonia with SpO2 ≥ 90% on room air.

Electrocardiographic analysis

Heart rate (per minute), QRS, corrected QT (cQT), Tpeak- Tend interval (Tpe), corrected Tpe (cTpe), and cTpe/cQT intervals were analyzed from 12-derived ECG by at least two cardiologists who were blinded to the patients' data. Examinations were performed on the precordial leads. QRS was measured from the beginning of the QRS to the end of the S wave, and reflects ventricular depolarization. The QT interval was measured from the beginning of the QRS complex to the end of the tangent of T wave at the point of the isoelectric line. The Tpe interval was measured from the peak point of T wave to the end of the tangent of T wave crossing isoelectric line (the difference between QT interval and QT peak interval)[13]. cQT and cTpe were measured by means of Bazett formula: cQT = QT√ (R–R interval) and cTpe = Tpe√(R–R interval), respectively. T wave in which amplitude was below 1.5 mm was not appropriate for evaluation. Patients with U wave and flat T wave were not included into the data either. There was no a patient with a deep or biphasic T waves, or any cases with suspicion and evidence for ischemia/acute coronary syndrome.

Laboratory analysis

Demographic data, serum electrolytes, C-reactive protein (CRP), procalcitonin, D-dimer, fibrinogen levels, clinical course, comorbidities, medications were evaluated from the database. Patients under the age of 18 were not included in the current study.

Statistical analysis

All statistical analyses were performed using the SPSS software, version 21.0 for Mac (SPSS Inc, Chicago IL, USA). The normality of variables was tested by the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages and were compared with Chi-square test or Fisher's exact test. Non-normally distributed continuous variables were presented as median with q1-q3 (25th and 75th percentiles) and compared by the Kruskal-Wallis test and the Mann-Whitney U test between the groups. The Wilcoxon signed rank test was used for the comparison of non-normally distributed variables at different time points in each treatment group. The Spearmen rank-order correlation test was used to determine correlations between different variables. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 51 laboratory confirmed (had positive PCR results) COVID-19 patients with a mean age of 44.9 ± 15,9 years were included in the current study. The baseline characteristics of the patients in the HCQ + AZM and HCQ + LEV/MXF groups were summarized in Table 1. There were 28 patients suffering from chronic comorbidities; hypertension (15%), coronary artery disease (11%), diabetes mellitus (7%), cerebrovascular diseases (5%), chronic kidney disease (4%), heart failure (4%), chronic obstructive pulmonary disease (4%), and Alzheimer's disease (1%). In HCQ + AZM group, only 1 patient had a history of donepezil usage that has a known risk of QT prolongation and Torsades de Pointes (TdP). Additionally, 1 patient had a history of furosemide usage and 2 patients had a history of hydrochlorothiazide usage that have a risk of QT prolongation and TdP only under certain conditions (excessive doses, in patients with electrolyte imbalance-hypokalemia-hypomagnesemia, or when taken with interacting drugs which may trigger the deterioration of serum electrolytes), whereas in HCQ + LEV/MXF group only 2 patients had a history of hydrochlorothiazide usage[14].

Severe disease occurred in 31,4% (n=16) of all COVID-19 patients while 68,6% (n=35) of the patients had a moderate disease course. Severe COVID-19 prevalence was higher in HCQ + LEV/MXF group than HCQ + AZM treatment group (p=0.002). While 68,6% of patients received HCQ + AZM treatment regimen, 31,4% (n=16) of patients received HCQ + LEV/MXF. No clinical cardiac event was observed during the study period.

Although, baseline electrocardiographic parameters were similar between severe and moderate COVID-19 patients, some alterations occurred during the treatment period. According to Wilcoxon signed rank test, on the 2nd day of treatment heart rate was the only statistically significant variable when compared to the pre-treatment stage in the whole study population ($Z=-3.592$, $p<0.001$).

On the 5th day of the treatment, all patients were successfully discharged as PCR negative and without moderate-severe symptoms. On the 5th day of the treatment; while the heart rate was significantly decreased ($Z=-2.353$, $p=0.019$), Tpe ($Z=-2.836$, $p=0.005$) and cTpe ($Z=-2.156$, $p= 0.031$) levels were significantly increased in the whole study population (Table 2). Similarly, on the 5th day of the treatment; potassium was significantly increased ($Z=-4.580$, $p<0.001$) while D-dimer ($Z=-2.793$, $p=0.005$), procalcitonin ($Z=-4.297$, $p<0.001$) and CRP ($Z=-3.374$, $p= 0.001$) levels were significantly decreased in the whole study population. (Table 2). There were statistically significant correlations between the CRP and heart rate both at the pre-treatment stage and at the end of the treatment ($r_s=.364$, $p=0.009$ vs $r_s=.453$, $p=0.001$; respectively). There was not any significant correlation between pre-treatment Tpe and potassium levels ($rs=.002$, $p=0.988$); however, a significant correlation was observed on the 5th day of the treatment ($rs=-.284$, $p=0.043$) (Figure 1).

We also compared the demographic data, serum electrolytes and 12-derived ECG findings between the treatment groups (HCQ + AZM vs HCQ + LEV/MXF). cQT, Tpe and cTpe levels were statistically significantly increased on the 5th day of HCQ + AZM treatment ($p=0.018$, $p=0.007$ and $p=0.034$; respectively). Heart rate was statistically significantly decreased and Tpe was statistically significantly increased on the 5th day of HCQ + LEV/MXF group ($p=0.008$ and $p=0.046$;

respectively) (Table 3). Although Tpe was significantly increased in both treatment strategies on the 5th day of the treatment, rates of increase in Tpe values were similar between HCQ + AZM vs HCQ + LEV/MXF groups (p=0.508) (Figure 1).

Serum potassium levels were significantly increased in both treatment regimens after the 5th day of the treatment, however, rate of increase in potassium level was more prominent in HCQ + LEV/MXF group than HCQ + AZM group (p=0.018).

Table 1. Baseline characteristics according to the treatment regimens.

Variable	HCQ + azithromycin (n=35)	HCQ + LEV/MXF (n=16)	*p* value
Age (years)	42 (31-57)	47.5 (42-59)	0.141
Male gender n (%)	27 (77.1%)	14 (87.5%)	0.387
Chronic diseases n (%)	7 (20.0%)	6 (37.5%)	0.183
Use of QTc-prolonging medications n (%)	4 (11.4%)	2 (12.5%)	0.912
Severe Disease n (%)	6 (17.1%)	10 (62.5%)	0.002
Sodium (mmol/L)	140 (138.0-141.5)	138 (134.5-140.5)	0.076
Potassium (mmol/L)	4.2 (4.1-4.4)	4.1 (3.7-4.3)	0.042
Calcium (mg/dL)	9.03 (8.83-9.36)	8.67 (8.59-9.03)	0.001
Magnesium (mg/dL)	2.00 (1.98-2.11)	2.00 (1.77-2.00)	0.028
CRP (mg/L)	4.74 (3.11-14.80)	49.80 (10.65-78.20)	0.001
Procalcitonin (µg/L)	0.030 (0.01-0.05)	0.70 (0.03-0.25)	0.003
Fibrinogen (mg/dL)	345.00 (295.00-447.50)	438.46 (413.93-568.50)	0.015
D-dimer (ng/mL)	471.88 (194.34-925.48)	1383.05 (740.31-2893.90)	0.003

The categorical data are expressed as n (%) and the continuous data are expressed as median with q1-q3 (25th and 75th percentiles). P values that statistically significant are shown in bold. CRP: C-reactive protein; HCQ: hydroxychloroquine; LEV: levofloxacin; MXF: moxifloxacin

Table 2. Changes in 12-derived electrocardiographic and laboratory parameters among whole treatment regimens

	Pre-treatment	5th day of treatment	*p*
Heart rate (per min)	80 (53-107)	76.3 (53-101)	0.019
Tpe (ms)	80 (55-120)	90 (60-150)	0.005
cTpe (ms)	94 (62-192)	101 (68-165)	0.031
CRP (mg/L)	9.91 (3.1-199.0)	3.76 (3.1-148.0)	0.001
Potassium (mmol/L)	4.2 (3.5-5.3)	4.62 (3.7-5.8)	<0.001
D-dimer (ng/mL)	534.9 (115.5-9035.3)	420.8 (75.1-7467.9)	0.005
Procalcitonin (µg/L)	0.04 (0.01-8.52)	0.02 (0.00-0.26)	0.001

The continuous data are expressed as median with q1-q3 (25th and 75th percentiles). P values that statistically significant are shown in bold. CRP: C-reactive protein

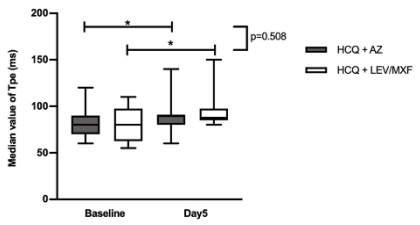

Figure 1. Comparison of median Tpe value at baseline and after 5 days of therapy for each treatment regimen.

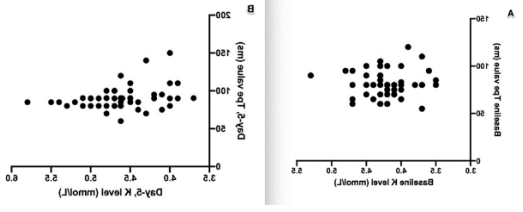

Figure 2. Correlation between Tpe and K levels in patients at baseline (A) (rs=.002, p=0.988) and after 5 days of therapy (B) (rs=-.284, p=0.043).

Table 3. Changes in 12-derived electrocardiographic and biochemical parameters by either treatment regimen.

	HCQ + azithromycin (n=35)			**HCQ + LEV/MXF (n=16)**		
	Baseline	Day 5	*P* Value (z Scores)	Baseline	Day 5	*P* Value (z Scores)
Heart rate (per min)	78.00 (70-87)	77.00 (73-81)	0.446 (-0.762)	85.0 (77.0-95.0)	75.6 (67.0-80.0)	0.008 (-2.638)
QRS (ms)	80.00 (68.00-90.0)	82.00 (74.00-85.00)	0.393 (-0.854)	85.0 (80.0-89.5)	82.0 (64.5-90.0)	0.509 (-0.660)
cQT (ms)	413.00 (389.00-433.00)	421.20 (413.0-426.0)	0.018 (-2.376)	413.5 (386.0-446.0)	410.0 (384.5-422.5)	0.255 (-1.138)
Tpe (ms)	80.0 (70-90)	90.0 (80-90.34)	0.007 (-2.686)	80.0 (62.5-97.5)	87.5 (85.0-97.5)	0.046 (-1.996)
cTpe(ms)	92.00 (80.00-102.00)	101.40 (92.00-103.00)	0.034 (-2.122)	97.5 (71.7-124.7)	100.0 (91.2-108.0)	0.756 (-0.310)
cTpe/ cQT	0.22 (0.19-0.25)	0.24 (0.21-0.25)	0.140 (-1.474)	0.22 (0.18-0.28)	0.24 (0.23-0.25)	0.535 (-0.621)
Sodium (mmol/L)	140.00 (138.00-142.00)	140.00 (139-141)	0.910 -0.114)	138.00 (134.25-140.75)	139.50 (139.00-141.75)	0.098 (-1.656)
Potassium (mmol/L)	4.20 (4.10-4.40)	4.62 (4.30-4.80)	0.002 (-3.159)	4.10 (3.70-4.30)	4.75 (4.25-5.15)	0.001 (-3.241)
Calcium (mg/dL)	9.03 (8.82-9.37)	9.10 (8.96-9.25)	0.824 (-0.222)	8.67 (8.58-9.03)	9.10 (8.93-9.10)	0.004 (-2.898)
Magnesium (mg/dL)	2.00 (1.98-2.13)	1.97 (1.97-1.97)	0.003 (-3.004)	2.00 (1.75-2.00)	1.97 (1.97-1.98)	0.195 (-1.297)
CRP (mg/L)	4.74 (3.11-14.80)	3.33 (3.11-11.14)	0.142 (-1.467)	49.8 (10.37-83.40)	4.28 (3.11-7.18)	0.001 (-3.351)
Procalcitonin (µg/L)	0.03 (0.01-0.05)	0.02 (0.02-0.02)	0.012 (-2.510)	0.07 (0.03-0.25)	0.02 (0.02-0.04)	0.001 (-3.300)
Fibrinogen (mg/dL)	345.00 (294.00-458.00)	386.55 (304.00-386.55)	0.544 (-0.606)	438.46 (413.93-578.75)	386.55 (386.55-456.75)	0.047 (-1.988)
D-dimer (ng/mL)	471.88 (191.37-940.85)	420.87 (211.89-847.33)	0.295 (-1.297)	1383.05 (730.15-3315.17)	459.15 (327.76-847.33)	0.002 (-3.103)

The categorical data are expressed as n (%) and the continuous data are expressed as median with q1-q3 (25th and 75th percentiles). P values that statistically significant are shown in bold. CRP: C-reactive protein; HCQ: hydroxychloroquine; LEV: levofloxacin; MXF: moxifloxacin

DISCUSSION

In this study, we reported the cardiac safety of off-label drugs (HCQ and AZM) in COVID-19 disease, at least during the initial 5 days of hospitalization. We showed our results via novel parameters of 12-derived ECG (Tpe, cTpe and cTpe/cQT) as distinct from previous COVID-19 related studies. cQT, Tpe and cTpe levels were statistically significantly increased on the 5th day of HCQ + AZM arm when compared to HCQ + LEV/MXF arm. However, rates of increase in repolarization alterations were similar between treatment arms. All patients were successfully discharged as PCR negative and without moderate-severe symptoms.

Heart rhythm problems were described as the most common pathological findings in patients with COVID-19. Although arrhythmias could be seen in a wide range in patients with COVID-19 disease, from feeling palpitations to the wide QRS complex tachycardias, in case of acute respiratory distress arrhythmia prevalence may increase in up to half of the patients[15]. Arrhythmias were more common and lethal in critically ill patients. Wang et al. reported

16% severe arrhythmia in their study and arrhythmias were twice-fold higher in patients in the intensive care unit (ICU) than in patients hospitalized in non-ICU and half of them received invasive mechanical ventilation support[2]. They also showed that coagulation factors and troponin were significantly higher in patients with severe symptoms and suffered from more arrhythmias. In our study, patients neither suffered from invasive mechanical ventilation nor from apparent arrhythmia. Another study reported that in both critically severe and severe COVID-19 patients, atrial fibrillation and Q wave progression were the most significant determinants for the prognosis. However, they did not detail repolarization indices except for QT prolongation[16]. Lazzerini et al. reported the potential risk of arrhythmias in case of serious infection milieu[17]. Life-threatening arrhythmias and progressive heart diseases were reported as case reports in patients with COVID-19 to identify the underlying mechanism[18]. Although ventricular arrhythmias are evocative for myocardial ischemia, they may be attributable to hypoxia, electrolyte disarrays, inflammatory response, cardiomyopathies secondary to the COVID-19, myocarditis and therapies used for COVID-19[19,20]. For this reason routine ECG surveillance has been suggested for patients with COVID-19[21]. Sarayani et al. reported the cQT prolongation risk in patients using HCQ alone, azithromycin alone, and HCQ + azithromycin group[9]. Their study population did not include COVID-19 pandemic. They elucidated the comprehensive results from the public data between 1969-2019. Their results indicated the safety signals in azithromycin alone group, however, not in HCQ alone and HCQ + azithromycin groups. Their reports were based on 500 mg azithromycin dose which was higher than our treatment dose. Chorin et al. reported that 64 COVID-19 patients' median cQT results reflected an increase from 435 ± 24 ms to 463 ± 32 ms ($P < 0.001$) during the median surveillance of 3.6 ± 1.6 days[22]. They treated their patients by HCQ (400 mg 2x1->200 mg 2x1) similar to our treatment dose and a higher dose of azithromycin (500 mg 1x1) with a longer duration (10 days). They also reported an excessive increased level of QT (>500 msn) in about 11% of all cases without a lethal arrhythmia (TdP, ventricular fibrillation etc.) during hospitalization. We reported only 1 patient, suffering from previous myocardial infarction, who experienced an excessive cQT prolongation (>500 ms). Similarly, our patients neither experienced an obvious arrhythmia, nor clinical decompensation secondary to cardiac involvement during hospitalization. Our cQT results were also similar for all three visits (pre-treatment, 2nd and 5th days of treatment). Roden et al. reported the risk of combination therapy (Hydroxychloroquine and azithromycin) on QT prolongation and polymorphic ventricular tachycardia in COVID-19 patients[23]. O'Connell et al. recently reported the risk association of QT prolongation in patients using AZM/HCQ in COVID-19 disease[24]. Their baseline cQT interval was 443 ms, and progressively increased with administration of HCQ/AZM to the value of 473 ms. However, during the treatment period no life threating arrhythmia was observed.

As repolarization alterations may provoke arrhythmogenicity, in addition to traditional electrocardiographic parameters, we investigated some repolarization indices (Tpe, cTpe, cTpe/cQT)[25]. Repolarization durations vary from the different layers of ventricle (the shortest one is in the epicardium, and the longest one is in the myocardium), and the difference of nadir and peak points of T wave reflects "Tpeak-Tend interval" that was proposed for measuring the global repolarization dispersion of ventriculum. Prolonged Tpe interval reveals the vulnerable period of repolarization and facilitates being captured by ventricular extrasystoles which can ultimately result in life threatening arrhythmias (torsade de pointes (TdP), ventricular tachycardia/fibrillation)[26].

However, novel ECG parameters (Tpe, cTpe etc.) which were reported as more valuable in predicting future lethal ventricular arrhythmias than traditional ECG parameters have not been yet reported in patients with COVID-19 patients[27,28].

In our study, while Tpe and cTpe levels were statistically increased at the end of our therapy, findings were not concluded as a major adverse cardiovascular event (myocardial infarction, ventricular arrhythmia, death etc.). Although there was already a potential risk for delayed repolarization and ventricular arrhythmia in patients with prolonged QT or prolonged Tpe/cTpe, precautions and situations requiring dose reduction were described in the literature (additional QT prolongation drug usage, CrCl < 10 mL/min, congenital QT syndrome, hypokalemia, hypomagnesemia, hypocalcemia). However, as COVID-19 is a highly mortal disease, these situations are not essential to discontinuation of the COVID-19 drugs. Close surveillance and treatment of underlying pathology (electrolyte

disturbance, ischemia etc.) is the main target during COVID-19 treatment[29].

Only hospitalization period was the limitations in terms of interpreting the results of the current study. Other limitations were the LEV/MXF combination which was the another potential risk of cQT prolongation and the small patients population, complicated the interpretation of drug safety, however it has been shown that the arrhythmia risk markers have been shown to be similar between the groups. However these results were preliminary as we planned the post-discharge ambulatory holter ECG interpretations of patients.

These results showed that, electrocardiographic and laboratory parameters were similar between severe and moderate COVID-19 patients. Although there was a potential risk for ventricular arrhythmia, the mentioned treatments we have applied did not increase the risk of a lethal arrythmia or cardiac death during hospitalization within the scope of the current treatment period and doses.

Yazar Katkıları: Çalışma konsepti/Tasarımı: TB, HY, ÖB; Veri toplama: ÖB, HY, TB, OA; Veri analizi ve yorumlama: ÖB, MÇ; Yazı taslağı: GA, TB, OA; İçeriğin eleştirel incelenmesi: GA, MÇ, HY, TB, ÖB; Son onay ve sorumluluk: GA, OA, TB, HY, ÖB, MÇ; Teknik ve malzeme desteği: OA, ÖB, MÇ; Süpervizyon: GA, ÖB, OA; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma Hatay Mustafa Kemal Üniversitesi Girişimsel Olmayan Klinik Araştırmalar yerel etik kurul tarafından onaylanmıştır (no.32 , tarih: 06.07.2020).
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.
Author Contributions: Concept/Design : TB, HY, ÖB; Data acquisition: ÖB, HY, TB, OA; Data analysis and interpretation: ÖB, MÇ; Drafting manuscript: GA, TB, OA; Critical revision of manuscript: GA, MÇ, HY, TB, ÖB; Final approval and accountability: GA, OA, TB, HY, ÖB, MÇ; Technical or material support: OA, ÖB, MÇ; Supervision: GA, ÖB, OA; Securing funding (if available): n/a.
Ethical Approval: Hatay Mustafa Kemal University Non Interventional Clinical Research Ethics Committee (no.32, date: 06.07.2020) approved the current study.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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