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Clinical Experiences in Patients Treated with the Diagnosis of COVID-19

COVİD-19 Tanısıyla Tedavi Edilen Hastalarda Klinik Deneyimler

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ABSTRACT

Objective: *All over the world, a specific antiviral and immunomodulatory treatment method that can affect COVID-19 infection has not been found, and research is ongoing. Our goal is to share our clinical experience in patients receiving in patient treatment in our clinic.*

Materials and Methods: *Patients whose symptoms were compatible with COVID-19 and whose microbiological findings and/or tomography findings were compatible between March 11 and May 31, 2020 were included in the study.*

Results: *Among 180 patients included in the study; It was found that favipiravir treatment was added to 45 (25.0%) patients after HCQ treatment. A significant difference was found between treatment groups concerning; age, occupation, oxygen saturation, presence of diabetes mellitus, hypertansion and lung disease, and CT findings (p <0.05).*

Conclusion: *In patient groups; Switching to favipiravir treatment and getting a response in patients aged 65 and over, with comorbidities, widespread CT involvement at admission, and Sat O2≤94 may be predictive in treatment selection.*

ÖZET

Amaç: *Tüm dünyada COVID-19 enfeksiyonunu etkileyebilecek spesifik bir antiviral ve immünomodülatör tedavi yöntemi bulunamamıştır ve araştırmalar devam etmektedir. Amacımız kliniğimizde tedavi gören COVID-19 hastalarındaki klinik deneyimlerimizi paylaşmaktır.*

Gereç ve Yöntem: *11 Mart – 31 Mayıs 2020 tarihleri arasında semptomları COVID-19 ile uyumlu olan ve mikrobiyolojik bulguları/ tomografi bulguları uyumlu olan hastalar çalışmaya alındı.*

Bulgular: *Çalışmaya dahil edilen 180 hasta arasında; 45 (%25.0) hastaya HCQ tedavisi sonrası favipiravir tedavisi eklendiği saptandı. Tedavi grupları arasında; yaş, meslek, oksijen satürasyonu, diabetes mellitus, hipertansiyon ve akciğer hastalığı varlığı ve BT bulguları arasındaki ilişki bu idi. (p <0.05).*

Sonuç: *Hasta gruplarında; 65 yaş ve üzeri, komorbiditesi olan, başvuruda yaygın BT tutulumu olan, Sat O2≤94 olan hastalarda favipiravir tedavisine geçilmesi ve yanıt alınması tedavi seçiminde belirleyici olabilir.*

Keywords:
COVID-19
Treatment
Favipiravir
Hydroxychloroquine

Anahtar Kelimeler:
COVID-19
Tedavi
Favipiravir;
Hydroxychloroquine;

INTRODUCTION

Coronavirus Disease (COVID-19) continues to be widely seen worldwide as a cause of a serious and severe pandemic (1-4). Currently, there is noeffective and eliable therapeutic agent in the treatment of COVID-19. Various antimicrobial agents have been used as emergency treatment options in the treatment experience of variousc ountries (4,-8). However, the evidence for the efficacy and safety of these drugs is limited and research on the subject continues (7,9).

In Türkiye, hydroxychloroquine (HCQ), favipiravir, combination of lopinavir and ritonovirarere commended molecules in the treatment of COVID-19 disease by the Ministry of Health (10). Countriesusing HCQ among these drugs have different clinical experiences.In some of the studies, it has been reported that this drug may be preferred in thetreatment and prophylaxis of COVID-19 infection because it is thought to have antiviral, anti-inflammatory and immunomodulatory properties against the virus and it is cheaper (7,9,11). In addition, there are studies showing that it has no effect, and information confusion about the use of the drug continues (12). In COVID-19 infection, which needs to be treated urgently all over the world, it is thought that countries sharing their own clinical experiences may be beneficial for COVID-19 infection studies, which are still in search of specific and reliable antimicrobial agents. Our aim is to contribute to the literature by presenting our clinical experiences of our patients for whom HCQ and-or favipiravir therapy was initiated.

MATERIALS AND METHODS

This retrospective, descriptive study was carried out by the inclusion of patients treated and followed up using the COVID-19 Clinical and Therapeutic Assessment Form at the Infectious Disease and Clinical Microbiology Departments of Rize Research and Training Hospital and Rize State Hospital between 11 March and 31 May 2020.

Inclusion criteria: Patients aged > 18 years hospitalized due to PCR or CT findings consistent with COVID-19 infection were included if they did not have critical clinical course, received HCQ and/or favipiravir, and completed their prescribed treatment at the infectious disease unit. In

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addition, patients with clinical symptoms, PCR and/or CT findings compatible with COVID-19, who were initiated HCQ and/or favirapir treatment, hospitalized, followed by the infectious diseases clinic, aged 18 years and older were included.

Patients classification: Patients were classified into subgroups based on clinical, microbiological, and radiological findings.

Symptomatic classification: Clinical classification of the patients based on symptoms at presentation was performed according to the COVID-19 Diagnostic and Therapeutic Guidelines issued by the Turkish Ministry of Health (10). In this guidelines, patients are divided into three groups as follows: 1) Uncomplicated disease (high fever, muscle and joint pain, cough, sore throat without shortness of breath; respiration rate < 24/min, SpO2 > 93%) without lung involvement; 2) mild-to-moderate pneumonia (high fever, muscle and joint pain, cough, sore throat together with a respiration rate of < 30/min and SpO2 > 90%, plus lung involvement); and 3) severe pneumonia (high fever, muscle and joint pain, cough, sore throat with SpO2 < 90, respiration rate ≥ 30/min, and widespread lung involvement).

Radiologic Classification: Based on computed tomography images, 4 patient groups were defined: 1) no specific signs or atypical signs; 2) unilateral involvement consistent with COVID-19 disease; 3) bilateral involvement consistent with COVID-19 disease; and 4) bilateral diffuse involvement consistent and presence of consolidations.

Clinical classification: Patients were classified into three groups based on clinical, microbiological, and radiological findings: 1) negative PCR at admission, but clinical symptoms or tomographic findings consistent with COVID-19; 2) positive PCR at admission, with clinical symptoms and tomographic findings inconsistent with COVID-19; and 3) positive PCR at admission with clinical symptoms and tomographic findings consistent with COVID-19.

Treatment Protocol: Treatments were administered following the Diagnostic and Therapeutic Guidelines for COVID-19 issued by the Turkish Ministry of Health (10). Initially, treatment with HCQ was started in uncomplicated patients with mild to moderate pneumonia, and the primary endpoint was negative PCR at 6 days. The second endpoint consisted of drug side effects, lack of clinical improvement

Table 1: Demographic characteristics and risk factors for COVID-19 disease of patients (n=180)

		n	%			n	%
Sex	Female	89	49.4	**Occupation**	Healthcare worker	37	20.6
	Male	91	50.6		Non-healthcare worker	143	79.4
PCR	Positive	91	50.6	**Contact with COVID**	Present	104	57.8
	Negative	89	49.4		Absent	76	42.2
Group	PCR(+)/ BT(+)	62	34.4	**Travel history**	Absent	94	52.2
	PCR(+) / BT(-)	29	16.1		Present	42	23.3
	PCR(-) / BT(+)	89	49.4		Contact individuals	44	24.4
Preferred treatment group	1	12	6.7	**CT findings**	1	28	15.6
	2	48	26.7		2	49	27.2
	3	75	41.7		3	49	27.2
	4	45	25.0		4	54	30.0
Smoking	Yes	33	18.3	**Anticoagulant use**	Yes	142	78.9
	No	147	81.7		No	38	21.1
Alcohol use	Yes	4	2.2	**C vit use**	Yes	92	51.1
	No	176	97.8		No	88	48.9
Diabetes	Yes	38	21.1	**CT progression**	Present	29	16.1
	No	142	78.9		Absent	151	83.9
HT	Yes	76	42.2	**Antibacterial use**	Present	25	13.9
	No	104	57.8		Absent	155	86.1
Pulmonary findings	Yes	33	18.3				
	No	147	81.7				

Based on CT findings: 1) CT normal or no typical involvement; 2) unilateral involvement; 3) bilateral involvement; 4) bilateral involvement and consolidation (diffuse involvement)

Based on treatment groups: Hydroxychloroquine (1), Hydroxychloroquine- Azithromycin (2), Hydroxychloroquine- Oseltamivir-Azithromycin (3), Hydroxychloroquine-Azithromycin-Favipiravir (4)

despite 48 to 72 hours of treatment, or switch in therapy due to worsening condition. On the other hand, favipiravir was given to patients with severe pneumonia at admission, prolonged QT at or after admission, no improvement or worsening in symptoms despite 48-72 hours of treatment with HCQ, and congenital long QT syndrome (basal QTc > 480 msec). HCQ treatment consisted of an initial 800 mg dose on the first day of treatment, continued with 400 mg/day for 5 days, with the total dose not exceeding 2400 mg, while favirapir was given at a dose of 3200 mg on the first day, followed by 1200 mg for the next 4 day, for a total treatment duration of 5 days. Treatment groups: for statistical evaluation, treatment groups divided into two parts according to the drug which have been used: Non-favipiravir group (Groups 1, 2, and 3) and Favipiravir group (Group 4)

Data Analysis: Study data were analyzed using IBM SPSS 21.0 software pack (Chicago, US). The level of significance was set at < 0.05. Descriptive statistics (percentage, frequency, mean, standard deviation) were used for data assessment. To evaluate CT findings and treatment groups (more than 2) ANOVA test was used for numerical values, and the Kruskal-Wallis test was used for non-numerical values.

Ethical considerations: The study protocol was approved by the Scientific Research Committee, General Directorate of Health Services, Turkish Ministry of Health (Permission no: 2020-05-17T01_18_25)and Ethics Committee for Non-Interventional Research, Recep Tayyip Erdogan University (Permission no: 2020/129).

RESULTS

A total of 180 patients were included with a mean age of 55.5 ± 19.8 years (range: 18-89 y). There were 91 male patients (50.6%), and 86 (47.7%) with a history of travel. One-hundred and four patients (57.8%) had a positive history for contact with an individual with COVID-19 diagnosis, 18.3% (n=33) were smokers. The most frequent comorbidity was hypertansion (HT) in 42.2% (n=76). Table 1 summarizes the sociodemographic characteristics and COVID-19 risk factors in the patient group. Rates of PCR positivity, 81.1% (n=158) Table 1). PCR positivity rate was 50.6% (n = 91), and CT involvement rate was 81.1% (n = 158). In our study population, which consisted of patients with mild to moderate and severe pneumonia, oxygen saturation at admission was 95.4% ± 2.9 (90-99), 138 patients (76.7%) had a SatO2 of > 93%, the QTc at admission was 408.1 ± 19.4 msec (357-480), and the mean duration of hospital stay was 10.7 ± 3.9 days (7-21). Two patients required intensive care during the subsequent course of their illness, and one of these subjects died. A comparison of sociodemographic characteristics among treatment groups showed significant differences (p<0.05)

Table 2: Distribution of demographic characteristics and risk factors according to treatment groups

		Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Group 4 n (%)	Test and p value
Age (y)		34.8±4.2 (26-53)	53.8±2.9 (20-89)	54.6±2.2 (22-88)	63.0±2.9 (23-88)	KW=18.95 p=0.000
Sex	Female	8 (9)	23 (25.8)	42 (47.2)	16 (18)	$\chi2$=6.23 p=0.101
	Male	4 (4.4)	25 (27.5)	33 (36.3)	29 (31.9)	
Occupation	Healthcare worker	9 (24.3)	5 (13.5)	15 (40.5)	8 (21.6)	$\chi2$=25.03 p=0.000
	Non-healthcare worker	3 (2.1)	43 (30.1)	60 (42)	37 (25.9)	
Travel history	Absent	6 (6.4)	31 (33)	36 (38.3)	21 (22.3)	$\chi2$=4.06 p=0.256
	Present	6 (6.4)	17 (19.8)	39 (45.3)	24 (27.9)	
Contact individuals	Absent	2 (1.1)	32 (30.8)	44 (42.3)	26 (25)	$\chi2$=9.89 p=0.020
	Present	10 (13.2)	16 (21.1)	31 (40.8)	19 (25)	
Diabetes	Yes	0 (0)	8 (21.1)	19 (50)	11 (28.9)	$\chi2$=4.88 p=0.181
	No	12 (8.5)	40 (28.2)	56 (39.4)	34 (23.9)	
HT	Yes	0 (0)	18 (23.7)	32 (42.1)	26 (34.2)	$\chi2$=13.68 p=0.003
	No	12 (11.5)	30 (28.8)	43 (41.3)	19 (18.3)	
Pulmonary disease	Yes	0 (0)	7 (21.2)	11 (33.3)	15 (45.5)	$\chi2$=10.58 p=0.014
	No	12 (8.2)	41 (27.9)	64 (43.5)	30 (20.4)	
Smoking	Yes	4 (12.1)	9 (27.3)	9 (27.3)	11 (33.3)	$\chi2$=4.94 p=0.176
	No	8 (5.4)	39 (26.5)	66 (44.9)	34 (23.1)	
Sat O2 (%)	> 93	11 (33.3)	38 (21.1)	66 (36.7)	23 (25.8)	KW=23.36 p=0.000
	≥ 90-93	1 (0.6)	10 (13.2)	9 (27.3)	22 (12.2)	
Treatment duration(d)		7.2±0.2 (7-10)	8.5±0.4 (7-21)	10.1±0.3 (7-14)	14.9±0.6 (10-21)	$\chi2$=78.03 p=0.000

Treatment groups: Group 1. Hydroxychloroquine, Group 2. Hydroxychloroquine- Azithromycin, Group 3. Hydroxychloroquine- Oseltamivir-Azithromycin, Group 4. Hydroxychloroquine-Azithromycin-Favipirav

in terms of age, history of contact with a COVID-19 positive subject, oxygen saturation, duration of treatment, presence/absence of HT, presence/absence of pulmonary conditions, and treatment types according to CT findings. The mean duration of hospital stay was 10.7 ± 3.9 days (7-21), and the longest mean duration of hospital stay was recorded in Group 4, with 14.9 ± 0.6 days (10-21) (r=0.528, p < 0.001). Table 2 shows the sociodemographic characteristics and risk factor distribution in the study population. Examination of the pre-admission clinical data showed significant (p<0.05) differences in terms of baseline lymphocyte count, neutrophil count, lymphocyte/neutrophil ratio, CRP, D-dimer, and Troponin values. Lymphocyte count (1372 ± 72; 300-3430) and lymphocyte/neutrophil ratio (0.35 ± 0.06; 0.03-2.47) were lowest in Group 4, patients with more severe CT findings were more likely to be in Group 4. Table 3 shows a comparison of patients in terms of CT and laboratory findings according to the treatment group. A linear regression analysis for the association between clinical parameters and treatment duration showed significant positive correlation between age and the duration of treatment (R2=0.274, p=0.003). Also, HT, diabetes mellitus (DM), and pulmonary conditions were found to be significantly correlated with the treatment duration and treatment type (R=.246, R2= 0.60, p < 0.05; and R=.298, R2=.089, p<0.05, respectively).

The t test for the significance of regression coefficients did not confirm a significant association between the duration of treatment and HT, DM, and pulmonary disease, while the significant correlation with the type of treatment was retained. Also, there was a significant correlation between treatment duration and administration of treatment containing favipiravir (R=.336. R2=.113. p<0.05). Two groups of patients were defined on the basis of favipiravir use (favipiravir group vs. non-favipiravir group), and a regression analysis was performed to examine the relationship between treatment groups and epidemiologic data as well as comorbidity. When significance (p<0.05) was found in the initial univariate analysis, a multivariate analysis performed (although p was 0.224 for smoking, it was still included in the analysis due to its importance as a risk factor). Accordingly, no significant correlations were found between favipiravir use and smoking, being a healthcare worker, travel history, and history of COVID-19 contact. However, favipiravir treatment was associated with age, gender, CT findings, low saturation, HT, and pulmonary disease. A multivariate analysis, on the other hand, showed an association only between low saturation and having favipiravir treatment (p<0.001) (Table 4). When a ROC analysis was performed for the low saturation values in the favipiravir treatment group, the sensitivity and specificity of a SatO2 of ≤ 94% for receiving favipiravir containing treatment were 60% and 76.3%, respectively (p < 0.01, 95% CI=0.638-0.775).

During the 3 month follow up of patients receiving

Table 3: Comparison of treatment groups according to laboratory and CT findings

	Group 1 (n=12)	Group 2 (n=48)	Group 3 (n=75)	Group 4 (n=25)	Test value p value
Lymphocyte count (/uL)	2344±450 (1000-4700)	1378±91 (370-2900)	1518±78 (290-3070)	1372±72 (300-3430)	KW=10.54 p=0.015
Neutrophil count (/uL)	3248±336 (1500-6090)	6037±486 (770-14800)	4748±330 (1330-14300)	5495±468 (720-18000)	KW=12.69 p=0.005
Lymphocyte/Neutrophil ratio	0.83±0.18 (0.19-2.28)	0.35±0.04 (0.05-1.38)	0.41±0.03 (0.2-1.0)	0.35±0.06 (0.03-2.47)	KW=18.42 p=0.000
CRP (mg/L)	5.6±4.7 (1-15)	51.4±18.5 (1-462)	73.7±24.4 (2-358)	50.9±8.6 (10-113)	KW=19.33 p=0.000
D-Dimer (mg/L)	0.33±0.15 (0.1-0.6)	1.33±0.43 (0.1-11.5)	1.53±0.67 (0.1-12.0)	0.77±0.19 (0.2-2.5)	KW=12.53 p=0.006
Troponin (pg/ml)	4.67±3.67 (1-12)	50.3±22.7 (2-600)	194.4±95.9 (1-1447)	44.7±10.1 (1-135)	KW=7.79 p=0.050
CT findings n (%)					
1	12 (6.7)	1 (0.6)	1 (0.6)	1 (0.6)	
2	0 (0)	27 (15.0)	16 (8.9)	6 (3.4)	χ^2=192.7 p=0.000
3	0 (0)	12 (6.7)	23 (12.8)	14 (7.8)	
4	0 (0)	8 (4.5)	22 (12.2)	24 (13.4)	
PCR and CT positivity n (%)					
PCR(+)-BT(+)	0 (0)	5 (2.8)	31 (17.2)	26 (14.4)	
PCR(+)-BT(-)	10 (5.6)	3 (1.7)	15 (8.3)	1 (0.6)	χ^2=28.53 p=0.000
PCR(-)-BT(+)	2 (1.1)	40 (22.2)	29 (16.1)	18 (10.0)	

Based on CT findings: 1) CT normal or no typical involvement; 2) unilateral involvement; 3) bilateral involvement; 4) bilateral involvement and consolidation (diffuse involvement)

Treatment Groups: Group 1. Hydroxychloroquinine, Group 2. Hydroxychloroquinine- Azithromycin, Group 3. Hydroxychloroquinine- Oseltamivir-Azithromycin, Group 4. Hydroxychloroquinine-Azithromycin-Favipiravir

Table 4: Regression analysis of epidemiological data for favipiravir containing treatment group

	Univariate Analyses			Multivariate Analyses		
Variable	**p value**	**Logistic Regression**	**95% Cl**	**p value**	**Logistic Regression**	**95% Cl**
Sex (male)	0.033	2.134	1.062-4.289	0.064	2.065	0.957-4.452
Age	0.003	1.029	1.010-1.048	0.867	0.998	0.973-1.024
Presence of CT findings	0.020	11.000	1.450-83.460	0.110	5.396	0.682-42.684
Smoking	0.224	1.662	0.733-3.769	0 .787	0.868	0.311-2.423
Healthcare worker	0.595	1.265	0.531-3.013	-	-	-
Travel history	0.390	1.346	0.684-2.647	-	-	-
Contact individual	1.000	1.000	0.505-1.980	-	-	-
Presence of DM	0.528	0.773	0.347-1.720	-	-	-
Presence of HT	0.016	0.430	0.216-0.854	0.315	0.626	0.251-1.559
Presence of pulmonary disease	0.004	0.308	0.139-0.681	0.057	2.358	0.974-5.709
Low oxygen saturation	0.000	0.759	0.673-0.856	0.000	0.799	0.706-0.904

HCQ treatment, bradycardia was observed in two, and arrhythmia with QT prolongation in one patient, requiring discontinuation of HCQ treatment. Although gastrointestinal complaints such as nausea, vomiting, and/or diarrhea was the most common side effect of HCQ, treatment was continued due to improvement of symptoms with subsequently better drug tolerance. Following the initiation of favipiravir treatment, three patients had rash, four had mild elevation of liver function tests, two had diarrhea, and five had hypomagnesemia, all of which improved with replacement therapy.

DISCUSSION

The global search for effective and safe treatments for COVID-19 infection continues, with no specific treatments with confirmed efficiency currently available. Clinical experience is being continuously reported from different countries (4,7,8). It is thought that sharing experiences by exchanging ideas can be useful in fighting the COVID-19 pandemic. In our research, which we think may contribute to the fight against pandemic, our clinical experiences with our patients treated have been shared. We observed no life-threatening side effects occurred in patients receiving HCQ or favipiravir during their hospital stay. Although initial reports on HCQ use described some benefits, the need for in vivo and randomized controlled studies was also underscored. Also, HCQ is thought to be ineffective in those with persistently elevated viremia (4,7,8,13-15). In Cortegiani et al.'s review involving studies from China, France, Italy, Holland, and Guandong, it was reported that HCQ could be used for the treatment of COVID-19 infection, with therapeutic effects such as reduced body temperature, improved CT signs, and delayed disease progression (9).

However several limitations of these studies have also been emphasized, including the limited sample size, preliminary nature of the data, and absence of randomization and control groups. On the other hand, in a multi-center observational study across Belgium, supportive therapy alone was compared with HCQ + supportive therapy in terms of mortality, and the latter treatment was associated with reduced mortality rates (4). In the first results of the studies on the use of HCQ, which is one of the drugs recommended at the beginning of the pandemic, although the drug was reported to be beneficial, it was reported that its effectiveness was not sufficient in studies published afterwards and it was not effective in patients with persistently high viremia (4,7,8,13,14,15). In the review of Cortegiani et al., It was reported that COVID-19 treatment reduced fever, improved tomography findings, and showed theropathic effects such as delaying the progression of the disease (9). In these studies, various limitations such as limited number of data and presenting them as preliminary data, and lack of non-randomized controlled studies were also mentioned. However, in a multi-center observational study conducted in Belgium, patients who received only supportive treatment and HCQ + supportive treatment were compared in terms of mortality and mortality was found to be lower in the group using HCQ (4). Conversely, in the SOLIDARITY study endorsed by UK-based Recovery and WHO, HCQ was administered at a high dose (9200-9600 mg) for 10 days, but the treatment was halted due to cardiotoxic effects. However, it should be noted that the doses utilized in that study were much higher compared to the generally recommended dose of 2400 mg, possibly causing the observed side effects. Similarly, in a publication by Catteau et al., another study was mentioned that was withdrawn from publication due to side effects associated with high doses. These authors observed no significant cardiotoxic side effects at a dose of 2400 mg in their study (4). The doses used in our study were similar to those reported by Catteau et al., and except for three patients (1.6%) no significant side effects occurred. These findings support the view that HCQ with a long history of use as safe antimalarial and anti-rheumatic agent may also be used in appropriately selected COVID-19 patients. Also presence clinical, laboratory, and radiologic responses to HCQ among mildly ill patients as well as the low rate of cardiotoxic effects and complications suggest that HCQ should not be disregarded in the first place. When one

also considers the low cost of the drug, HCQ may also be used as an emergency treatment option in selected patients, particularly in developing countries where drug availability is low (4,8,12). Reporting of clinical experience with HCQ treatment in real-life conditions may also assist in eliminating some of the confusion surrounding HCQ use.In the recent WHO-led SOLIDARITY and UK- based Recovery study, HCQ therapy was given a high dose of 9200-9600 mg for 10 days, and the study was stopped due to cardio toxiceffects. administering at a dose much above there commended weekly dose of 2400 mg in the treatment of COVID-19 may be associated with side effects due to the high dose. They also reported that they did not experience any significant cardiotoxicside effects at a dose of 2400 mg given weekly in their studies (4). In our study, the weekly dose given was similar to the study of Catteau et al. No significant cardiotoxic side effects were observed excep for three patients (1.6%). Although favipiravir is another recommended agent for the treatment of COVID-19 infection, literature data regarding this agent is relatively scarce. In one study comparing favipiravir and a combination of lopinavir-ritonavir in these patients, favipiravir was associated with more rapid viral clearance, earlier improvement in CT signs, and lower rate of side effects (15). On the other hand, pre-clinical animal models have not yielded clear-cut results, and further and larger double blind studies are warranted. Furthermore, despite pharmacokinetic concerns such as low serum concentrations, it was also reported that this agent may be used as a safe treatment option (7,16). Although it was found effective in our study, it should be supported by long-term data that more patients were followed up.

Studies reported that both agents were used in this study have a relatively good safety profile, with no significant side effects when used in appropriate dose and duration in selected patients (7). While favipiravir could be associated with elevation in liver enzymes, HCQ may lead to gastrointestinal side effects such as nausea, vomiting, and diarrhea; on the other hand longer treatment with higher doses may result in retinopathy or cardiomyopathy (4). In multi-center nationwide studies in China and Belgium, the most frequently reported side effect was diarrhea, and no life-threatening or cardiotoxic complications were observed (4,17). In our study, the most common side effects were found to be gastrointestinal symptoms in patients who were treated similarly, and nosignificant cardiotoxic sideeffects were observed. This situation may be related to the administration of the treatment in the appropriate patient group at the appropriate dose. However, it is thought that it may be more beneficial to monitor the long-term sideeffects of the patients and to share the results.

It is very important to determine how the clinical course of a disease will develop, in which conditions the prognosis may be poor, and to determine the prognostic factors at the time of application in order to take precautions against these situations. When the laboratory data and treatment groups of the patients were examined at the time of first application; the fact that parameters such as low lymphocyte counts (KW = 10.54 and p = 0.015), high neutrophil count (KW = 12.69 and p = 0.005), low lymphocyte / neutrophilratio (KW = 18.42 and p = 0.000), CRP, D –Dimer and troponin elevation (KW = 19.33 and p = 0.000, KW = 12.53 and p = 0.006 and KW = 7.79 and p = 0.050, respectively.) show statistical significance to wards Group 4 (thegroupreceiving Favipiravir). This may provide an idea for the treatment selection in patients. A similar situation can be stated for CT involvement at the time of admission (2 = 192.7 and p = 0.000).

When examined which parameter showed the strongest correlation with clinical progression among thepatients comorbidity conditions; Multivariate Analysis was applied and it was found that there is a significant relationship between low oxygen saturation. In the Roc Analysis performed after wards, it was determined that the SatO2≤94 value was 60% sensitive and 76.3% specific for starting the treatment group containing favipiravir. These parameters are thought to be useful in determining the treatment method of the patient at the time of application.

In conclusion, response to favipiravir treatment observed in elderly patients (≥ 65 y), in those with comorbid conditions, or in those with diffuse CT involvement at presentation may provide insights for the clinician regarding the choice of therapy. In this context, we believe that appropriate treatments may be administered to carefully selected patients by considering physical examination and laboratory findings as well as comorbid conditions prior to initiation of therapy. However, our results should be corroborated with larger and randomized, controlled studies. As a result; responseto favipiravir treatment in patients aged 65 and over, with comorbidities, and extensive involvement in CT at hospitalization, especially Sat O2≤94, may provide an idea for treatment selection. The prominence of favipiravir treatment in our patient group has concluded that the treatment should be initiated in the appropriate patient group ands electively

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