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Original Research Article

Efficacy and Safety of Favipiravir in COVID 19 Patients- A Retrospective Analysis in a Tertiary Care Hospital from South Gujarat

Riya Ashokbhai Patel[1], Krishnakant N Bhatt[2], Priyanka Patel[3], Uttam Jitendrabhai Gondalia[4], Jaswantbhai Manharbhai Rathwa[5], Yatri Nareshkumar Patel[6], Subalakshmi R[7].

[1]Senior Resident, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

[2]Professor and HOD, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

[3]Assistant Professor, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

[4]3rd Year Resident, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

[5]2nd Year Resident, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

[6]2nd Year Resident, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

[7]1st Year Resident, Department of General Medicine, Government Medical College, Surat, Gujarat, India.

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Corresponding Author: Dr. Priyanka Patel
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Abstract:

Background: Favipiravir inhibits the viral RNA polymerase and has been shown to be effective against other RNA viruses. This study was conducted to evaluate the efficacy and safety of Favipiravir in moderate to severe cases of COVID-19.

Materials and Methods: This single-center retrospective observational study was conducted to evaluate the efficacy and safety of Favipiravir in terms of length of hospital stay and in-hospital mortality. Data of adult patients, who were diagnosed with moderate to severe COVID-19 disease, and were admitted in the hospital till 31st July 2022, was collected from the medical record section. Study included two groups: Study group: COVID-19 positive patients who received Favipiravir (n=100) and Control group (COVID-19 positive patients who did not receive Favipiravir)

Results: Patients with moderate-to-severe COVID-19 patients who received Faviparavir showed shorter hospital stay, higher rate of transfer out of ICU, and decreased mortality rate when compared to patients who did not receive Faviparavir.

Conclusion: Faviparavir is a safe and efficient drug in treating hospitalized patients with moderate-to-severe COVID-19 patients.

Keywords: Covid-19, Efficacy, Favipiravir, Safety

Introduction

More than 275 million individuals have been infected with the 2019 corona virus (COVID-19) and approximately five million have died as of December 20, 2021. [1] Since the World Health Organization classified COVID-19 a pandemic, scientistshave looked into treatments that might be beneficial. [2,3] It has been linked to a wide range of symptoms and diseases, from asymptomatic sickness to deadly pneumonia. The virus responsible for COVID-19 is an enveloped positive-sense RNA virus that primarily uses RNA-dependent RNA polymerase (RdRp) for viral genetranscription and replication. [4] Antiviral medication favipiravir was initially created to combat influenza and is now also utilized in COVID-19. It inhibits the viral RNA polymerase and has been shown to be effective against influenza. Antiviral activity against other RNA viruses has been demonstrated. [5] Since SARS-CoV-2 is a positive-sense single-strand RNA virus, favipiravir may be effective against it since it inhibits RNA-dependent RNA polymerase. [6] Various health regulators and organizations have

included favipiravir as a potential treatment in different regimens for mild to moderate COVID19 because to the good results seen in individuals in earlier studies. [7,8] The progression of moderate COVID-19 to a more severe form of the disease may be halted by starting treatment early, but some of the clinical trials on COVID-19 have shown conflicting outcomes. [5-7] Thus, we have conducted this study to evaluate the efficacy and safety of favipiravir in moderate to severe cases of COVID-19.

Materials and Methods

This retrospective study was conducted for a period of one year in a tertiary care Hospital. Ethical clearance was obtained from the Institutional Review Board prior to the commencement of the study. Data of adult patients, who were diagnosed with moderate to severe COVID-19 disease, as confirmed by reverse transcriptase-polymerase-chain reaction (RT-PCR), and were admitted in the hospital till 31st July 2022, was collected from the medical record section. 100 COVID-19 positive patients who received Favipiravir were included in the study group, while 100 patients who did not receive Favipiravir constituted the control group. In the study group, patients had received Tablet Favipiravir as a part of their treatment protocol according to the guidelines given by ICMR and government of Gujarat: Tablet Favipiravir1800 mg BD (9 tablets of 200 mg each BD) on day 1, followed by 800 mg BD(4 tablets of 200 mg each BD) for a total duration of 7 days. Data thus collected was analyzed for the efficacy and safety of this drug in terms of length of hospital stay and in-hospital mortality.

The diagnosis of severity was defined as follows:

Clinical severity	Clinical presentation	Clinical parameters
Mild	Patients with uncomplicated upper respiratory tract infection, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache	Without shortness of breath or hypoxia (normal saturation)
Moderate	Pneumonia with no signs of severe disease	Adults with features of dyspnoea or hypoxia, fever, cough, including SpO2 90 to ≤93% on room air, Respiratory rate ≥24/min
Severe	Severe pneumonia	Adults with clinical signs of pneumonia in combination with one of the following: respiratory rate >30/min, severe respiratory distress, SpO2 <90 on room air.

Statistical Analysis:

Categorical variables were analyzed using either the chi square test or Fisher's exact test. One way ANOVA was used to compared the mean. Person correlation was performed to establish the correlation between two continuous variables. P<0.05 was considered statistically significant.

Results

Majority of the patients with Covid-19 belonged to 41-50 years of age in our study, followed by 31-40 years. (p>0.31). Male were predominant in our study as compared to female, suggesting that males are at a higher risk of COVID-19 infection than female, but it was not statistically significant (p>0.064). Most commonly observed co-morbidity was hypertension (HTN), followed by Diabetes Mellitus (DM). (Table 1)

Table 1: Characteristics of Study Patients

Patient Characteristics		Control Group	Study Group	Total	p value
Age (years)	**≤30**	11	8	19	0.312
	31-40	28	20	48	
	41-50	33	30	63	
	51-60	11	22	33	
	61-70	15	17	32	
	>70	2	3	5	
Gender	**Female**	37	50	87	0.064
	Male	63	50	113	
Co-morbidities	**COPD**	5	5	10	0.682
	DM	12	11	23	
	HTN	16	15	31	
	Psychosis	1	1	2	
	Thyroid	5	3	8	

*COPD: Chronic obstructive Pulmonary Disease; DM: Diabetes Mellitus; HTN: Hypertension

There was statistically significant difference in level of s. ALT (p=0.029) and s. Uric acid (p=0.0001) between the two groups. (Table 2)

Table 2: Comparing Clinical and Laboratory parameters

Parameters	Control Group		Study Group		p value
	Mean	SD	Mean	SD	
BMI (kg/m2)	24.035	2.1031	23.966	2.0958	0.816
Duration of thesymptom (days)	6.09	1.741	6.01	1.642	0.739
C-reactive protein (mg/dL)	18.3046	6.21908	17.7268	6.49258	0.521
Ferritin (ug/L)	234.657	108.5260	233.925	107.6398	0.962
Lymphocyte (k/uL)	1.4825	.40743	1.6904	1.43610	0.165
LDH (U/L)	312.50	74.810	313.36	77.991	0.937
Serum creatinine(mg/dL)	1.0452	.32286	1.0385	.34493	0.887
Haemoglobin (g/dL)	11.097	1.5505	11.152	1.5607	0.803
WBC counts/permicroliter	8678.37	2619.345	8735.87	2668.302	0.878
D-dimer (ug/ml)	.394	.2131	.387	.2102	0.815
Serum ALT(U/L)	26.49	20.17	33.05	21.9698	0.029
Serum Uric acid	3.7	0.92	4.91	1.8	0.0001

Time to symptoms resolution was significantly lower in Study group (5.96+1.44 days), when compared to Control group (6.44+1.70 days) (p<0.033). However, there was no significant difference in the duration of hospital stay between Study group (11.11±2.46 days) and Control group (11.71+2.71 days) (p=0.103). (Table 3)

Table 3: Comparison of post-operative parameters between two groups

Post-Operative Parameters	Mean	Std. Deviation	p value
Time to symptom resolution			
Control Group	6.44	1.707	0.033
Study Group	5.96	1.442	
Time to hospital discharge (days)			
Control Group	11.71	2.713	0.103
Study Group	11.11	2.465	

In terms of outcome of disease, Study group patients had significantly lower rate of mortality, higher discharge rate and lower ICU shifting rate as compared to Control group patients (p<0.007). (Table 4)

Table 4: Comparing outcome between the two groups

Outcome	Control Group	Study Group	Total	p value
Death	4	1	5	0.007
Discharge	70	88	158	
ICU shift	26	11	37	

Discussion

Remdesivir, hydroxychloroquine, lopinavir-ritonavir, and interferon are some of the antiviral medicines that have been tested for their potential to cure SARSCoV-2 infection but have been shown to be ineffective in the solidarity trial and other trials. [9,10] Since the investigated drugs had no effect on COVID-19 mortality, other possible antivirals, such as favipiravir, needed to be tested in a prospective context. [11,12] By inhibiting the viral RNA polymerase enzyme selectively, favipiravir exerts broadantiviral efficacy against RNA viruses. This stops the viral genome from being replicated and transcribed. [13] It can now be used for the treatment of novel influenza viruses. The RNA viruses that cause viral hemorrhagic fever, including Ebola, have been proven to be susceptible to this treatment. [14] Several clinical trials on COVID-19 showed conflicting outcomes. [5-7] As a result, we thought it would be wise to look into Favipiravir's potential usefulness in treating COVID-19.

In our study both groups' Covid-19 patients skew middle-aged, with the median age falling between 41 and 50 years. Some researches have indicated that older age is the key risk factor for the severity of COVID-19 disease, particularly with those over the age of 50 being at increased risk. [15,16] Similar findings have been observed in other research conducted in India and elsewhere. [7,17,18] The majority of people who tested positive were between the ages of 20 and 50, according to research by Al-Mudhaffer et al [19] Our study included 113 males and 87 females, with the former being the clear majority. Another study who had reported 1153

confirmed cases of COVID-19 found that 64.4% of their study patients were male and 35.6% were female. [19] However, in another study, female patients accounted for 50.3% while male patients accounted for 49.7%. [20] Our study area is unique since it has a predominantly male population engaged in outdoor professions, accounting for the discrepancy we observe. Our research showed that among COVID-19 patients, HTN (n=31), DM (n=23), COPD (n=10), and thyroid disorders (n=8) were the most often occurring co-morbidities. As far as related illnesses go, there was no statistically significant difference between the two groups (p>0.84). Albanghali et al [20] analysed data from 811 patients admitted for COVID-19 treatment and found that the most common co-occurring illnesses were DM (31%) and HTN (24%). Because hypertension accounts for such a high percentage of deaths in India, we must maintain a constant state of vigilance. [21]

The results of clinical severity and laboratory examinations were similar across the two groups in our study (p>0.514). (Table 2) Duration of hospital stay was not significantly different between the Study group (11.11+2.46 days) and the Control group (11.71+2.71 days) in the current study (p>0.103). Udwadia et al [22] found that Favipiravir reduced the length of hospital stay by 1 day (95% CI: 7 days, 10 days) when compared to the control group patients (10 days, 95% CI: 8 days, 12 days). [23]Our findings showed that patients who were given faviparavir had a shorter time to symptom resolution (5.96+1.44 days) than those who were not given faviparavir (6.44+1.70 days; p=0.033). Thus, early beginning of faviparavir is associated with a greater reduction in COVID-19 symptoms such as fever, fatigue, sore throat, shortness of breath, and headache compared to those in Control group (p<0.05). Consistent with these findings, a meta-analysis by Hassanipour et al [24] found that patients treated with Favipiravir had significantly greater clinical improvement after 7 and 14 days in the hospital compared to those treated with other medicines. Similar observations were made by Udwadia et al [22] and Shrestha et al [25].

Our study found that patients in Favipiravir group had lower mortality rates from any cause compared to those in Control group. In the study by Dabbous et al, one patient in hydroxychloroquine group passed away, while in the Favipiravir group, no mortality was recorded. [14] A study by Alamer et al[7] showed that in the Favipiravir group, median time to discharge was 21 days, while in the control group it was 32 days, and the mortality rates were 46.2% in the Favipiravir group and 25.9% in the control group. Smaller sample size and use of retrospective data were the limitations of our study.

Conclusion

This single-center observational analysis showed that Faviparavir is a safe and efficient drug in treating hospitalized patients with moderate-to-severe COVID-19 which has shorter hospital stay, higher rate of transfer out of ICU, and improved survival rate when compared to patients who were not treated with Favipiravir.

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