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Short Article

COVID-19 Clearance with Favipiravir - A Retrospective Study

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I N F O

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A B S T R A C T

Background: Pharmacotherapy of Severe Acute Respiratory Corona Virus-2 (SARS-CoV-2), also denoted as COVID-19 is evolving. Many antivirals were found to be ineffective. Antiviral therapy used in 2020 was not originally developed for COVID-19. The effectiveness of favipiravir (an original drug for influenza) in COVID-19 pneumonia is questionable.

Methods: A small sample retrospective study was conducted to indicate if favipiravir is effective in COVID-19 clearance. It was conducted in a tertiary-level care hospital in the United Arab Emirates. COVID-19 pneumonia patients were admitted to the hospital from January to December 2020 were studied. SPSS version 26 was used for the data analysis.

Results: The average day of COVID-19 clearance for those who received favipiravir alone or favipiravir and hydroxychloroquine together were 12 days. Those who received no antivirals had COVID-19 clearance in an average of 11 days. Independent-Samples Kruskal-Wallis Test shows no statistically significant difference (p-value 0.663) in the length of COVID-19 clearance between these three treatment groups.

Conclusion: Favipiravir was not effective in mild COVID-19 pneumonia for achieving COVID-19 clearance. The effectiveness of favipiravir on COVID-19 clearance needs to be studied further.

Keywords: Drug use Evaluation, COVID-19, Antivirals, Favipiravir

Introduction

Pneumonia is a complication of COVID-19 (Severe Acute Respiratory Corona Virus-2). COVID-19 patients are screened for categorising the severity of their disease.[1] Having many patients to be treated and not having specific medications made for COVID-19 in 2020, the pharmacotherapy was more of a trial and error. Drugs that specifically treat SARS-CoV-2 infection are being developed.[2]

Favipiravir is an antiviral drug used in COVID-19, which was originally developed for influenza. As per the UAE national guidelines for clinical management and treatment of COVID-19, the favipiravir dose may need to be adjusted based on the clinical condition.[3] There was a decrease in the median period to viral clearance with favipiravir when compared with lopinavir/ ritonavir. Favipiravir has a relatively lower rate of adverse events in patients receiving lopinavir/ ritonavir.[4]

Many antiviral drugs tried for COVID-19 are being stopped from routine practice. As per World Health Organization

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(WHO) interim solidarity trial reports, remdesivir, hydroxychloroquine, lopinavir, and interferon antiviral regimens are not beneficial among hospitalised patients with COVID-19.[5,6]

Our study objective was to find a research direction on the effectiveness of favipiravir alone or in combination compared to no antivirals for COVID-19 clearance in hospitalised mild COVID-19 pneumonia patients.

Materials and Method

A retrospective study from January to December 2020 was conducted to follow-up mild COVID-19 pneumonia patients who received no antivirals, favipiravir alone, or in combination for COVID-19 clearance. The sample size was 120. The COVID-19 in-patients with mild pneumonia treated at the study site were included for follow-up until reverse transcription-polymerase chain reaction (RT-PCR) for COVID-19 became negative. The patients with moderate to severe pneumonia and those who received other antivirals without favipiravir were excluded. Informed consent from study participants were not obtained as it was a retrospective study, and the data was collected from the medical records. COVID-19 clearance is defined as RT-PCR negative. Every 10th mild COVID-19 patient was screened for their antiviral use.

The study was conducted in a tertiary-level care military hospital in the United Arab Emirates. Being a military hospital, the majority of patients being treated were adult males. RT-PCR is performed for COVID-19 pneumonia patients every 72 hours (3 days). If a patient becomes negative, the test is repeated in 24 hours. Institutional review board approval was obtained before data collection.

Statistical Analysis

Data were collected from medical records, diagnosis of COVID-19 pneumonia with severity status was mentioned on the medical records. Patient confidentiality was maintained. The test used was Independent-Samples Kruskal-Wallis to compare COVID-19 clearance among the study groups. The software used in calculating the results was SPSS Version 26.

Results

Simple random sampling was used to select 10% of the patients to create a pilot data analysis. From 140 hospitalised COVID-19 patients screened, 9 moderate to severe pneumonia cases were excluded. Data of second COVID-19 cases for the same patients (3 cases) and 3 patients who received remdisivir were also excluded. Those who received favipiravir alone were 22, hydroxychloroquine alone were 6, favipiravir and hydroxychloroquine together were 34 and the rest of the 63 patients among the total 125 did not receive any antiviral (Figure 1).

Fifty per cent of the study population stayed in the hospital for 1–2 weeks, while 24% stayed less than a week and 26% stayed more than 2 weeks. The patient demographics of the study population are shown in Table 1.

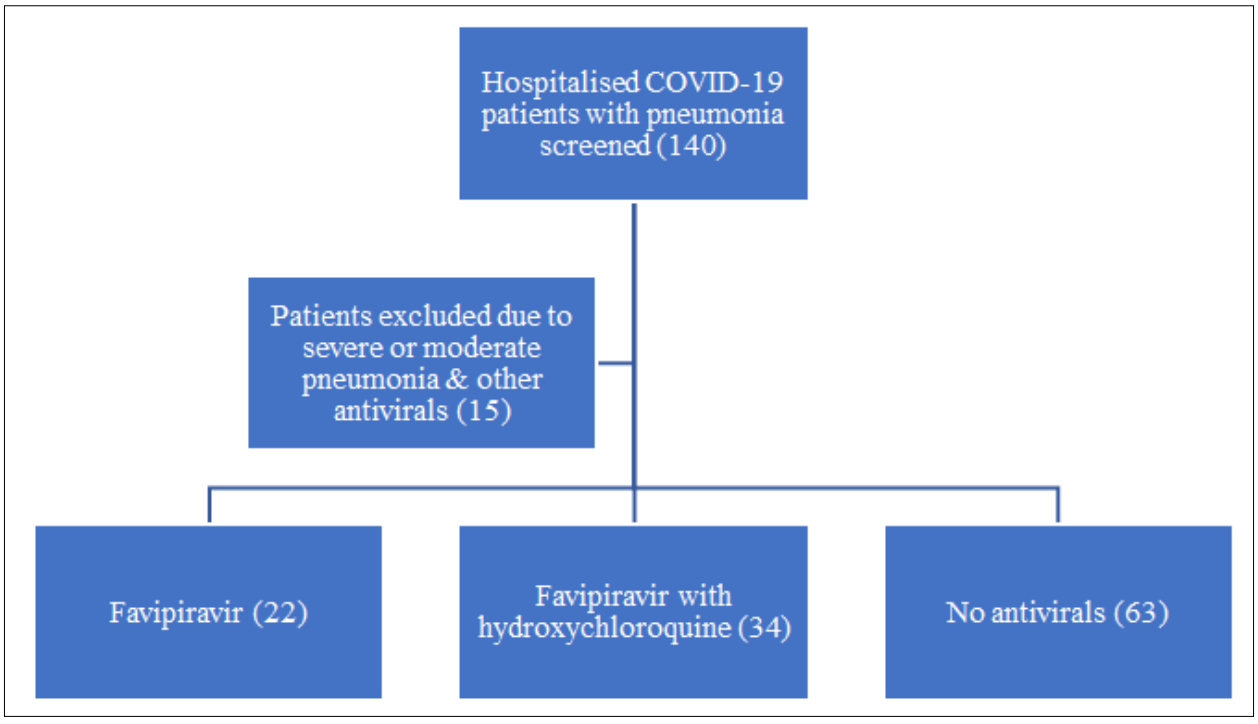

Figure 1.Study Flowchart

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Table 1.Patient Demographics (N = 125)

	Demographics	Number of Patients n (%)
Gender	Female	7 (6)
	Male	118 (94)
Body mass index	Obese (≥ 30 kg/m^2)	42 (35)
	Overweight (25-29 kg/m^2)	52 (40)
	Normal (18.5-24.9 kg/m^2)	29 (23)
	Underweight (≤ 18 kg/m^2)	2 (2)
Comorbidities	Hypertension	29 (22)
	DM	26 (20)

Table 2.Medications used in Mild COVID-19 Pneumonia Patients (Other than Antivirals)

Other Medications and Supplements Used	Number of Patients n (%)
Dexamethasone	7 (6)
Prednisolone	1 (1)
Anticoagulants	116 (93)
Vitamin C	115 (92)
Zinc	28 (22)
Antibiotics	15 (12)

Table 3.Comparison of Favipiravir Use and COVID-19 Clearance**

Antiviral Therapy		Number of Patients (%)	COVID-19 Clearance			P-value
			Median	Minimum	Maximum	
Mild COVID-19 Pneumonia	Favipiravir + hydroxychloroquine	34 (27)	10.0	3	40	0.66
	Hydroxychloroquine*	6 (5)	12.0	4	30	
	Only favipiravir	22 (18)	12.0	6	19	
	No antivirals	63 (50)	10.0	3	31	

*Not compared with other groups statistically **COVID-19 clearance is defined as becoming RT-PCR negative.

Anticoagulants and Vitamin C were commonly used in the study population. Few of the patients received corticosteroids and antibiotics. The viral clearance time was slightly higher (ranged from 10 to 29 days) in the corticosteroid group compared to 8 to 24 days in the non-steroid group. More details of the drug use are provided in Table 2.

The main antiviral drug used in the study population was favipiravir. Hydroxychloroquine was used in many patients with favipiravir. Patients with other antivirals were not included in this study. Hydroxychloroquine was a drug of choice in COVID-19 patients in the first few months of 2020 till the clinical guidelines update that recommend against its use. Favipiravir dosing was 1600 mg bid for one day, then 600 mg bid for 6 days. In some patients, favipiravir was given for 10 days, the first dose 1600 and then 600 every day for 9 days. Hydroxychloroquine was administered 400 mg bid for one day, then 200 bid for 6 days. Table 3 shows differences in the COVID-19 clearance among patients treated with favipiravir alone or in combination.

Independent-Samples Kruskal-Wallis test shows no statistically significant difference (p-value 0.663) in the length of COVID-19 clearance using favipiravir or favipiravir with hydroxychloroquine compared to no antivirals in mild COVID-19 pneumonia patients. The length of COVID-19 clearance is the duration for which a patient is RT-PCR positive. Hydroxychloroquine used alone was not compared with other groups as the focus was on favipiravir.

Discussion

The study population was mostly adult males as the study site is a military hospital. Other studies show, in general, that male patients have more complications than female patients.[7,8] Most hospitalised COVID-19 patients were older than our study.[9,10] Corticosteroid treatment is associated with prolonged viral RNA shedding and should

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be used cautiously.[11,12] In our study, very few patients have used dexamethasone because the cases were mild. In addition to that, the available evidence suggests that chloroquine or hydroxychloroquine does not improve clinical outcomes in COVID-19.[13] Data on the benefits and risks of hydroxychloroquine or chloroquine in the treatment of COVID-19 is poor and debatable.[14]

Many studies support the usage of vitamin C and zinc during the COVID pandemic. Vitamin C and zinc are part of the supportive care of COVID-19 patients. Vitamins C and zinc when used in high doses may be beneficial to COVID-19 patients. The associations of benefits of such nutrients in COVID-19 is evolving.[15] Association of early anticoagulation prophylaxis among hospitalised COVID-19 patients show a decreased risk of mortality.[16]

According to our findings, favipiravir in mild COVID-19 pneumonia did not affect the length of the clearance of the diseases. Compared to lopinavir/ ritonavir, favipiravir showed faster viral clearance and a better recovery rate compared to umifenovir.[17] In addition, adverse effects of favipiravir were significantly lower.[4,18]

There is mixed data that favipiravir alone or in combination could be beneficial for COVID-19 clearance or not.[19-22] Effectiveness data on favipiravir in COVID-19 pneumonia is evolving.

Like many current reports on COVID-19, the limitations of this study were primarily its retrospective design and patients from a single site. The study was only an exploratory data analysis.

Conclusion

Extensive studies are indicated to prove if favipiravir is effective for COVID-19 clearance among patients with mild COVID-19 pneumonia. Favipiravir might be beneficial for other outcome measures in COVID-19; further research is required.

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Conflict of Interest: None

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