ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 10, 2022

Online - 2455-3891
Print - 0974-2441

Research Article

EVALUATION OF OSELTAMIVIR AND FAVIPIRAVIR ON CLINICAL OUTCOMES AND LENGTH OF STAY IN COVID-19 PATIENTS AT FATMAWATI GENERAL HOSPITAL JAKARTA

MAREOZA AYUTRI[1]*, RETNOSARI ANDRAJATI[1], AHMAD SUBHAN[2]

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, University of Indonesia, Depok, West Java, Indonesia. [2]Department of Pharmacy, Fatmawati General Hospital, Jakarta, Indonesia. Email: mareoza20@gmail.com

Received: 02 August 2022, Revised and Accepted: 23 September 2022

ABSTRACT

Objectives: This study aimed to evaluate the effect of oseltamivir and favipiravir in patients with confirmed COVID-19 on clinical outcomes and length of stay at Farmawati General Hospital, Jakarta.

Methods: The cross-sectional study was conducted at Fatmawati General Hospital, Jakarta. The study sample consisted of 114 patients who met the inclusion and exclusion criteria from March to October 2020. Data were collected retrospectively using medical record data.

Results: The result showed that 98 patients (86.0%) received oseltamivir, while 16 patients (14.0%) received favipiravir in this study. The mortality rate was 11.4% (13 patients), while the recovered was 88.6% (103 patients). Patients who had LoS (Length of Stay) of ≤14 days were 58.8%, while patients with LoS >14 days were 41.2%. In bivariate analysis, antivirals (oseltamivir and favipiravir) effect on clinical outcome was not statistically significant (p=0.690; OR=0.478; CI 95%=0.058–3.950). Likewise, the association between antivirals and LoS was also not statistically significant (p=0.852; OR=0.767; CI 95%=0.251–2.342).

Conclusion: Antivirals were not significantly associated with clinical outcomes and length of stays in COVID-19 patients.

Keywords: Clinical outcome, COVID-19, Favipiravir, Oseltamivir, Length of stay.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i10.45801. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

COVID-19 is an infectious disease caused by a new type of coronavirus. This disease has become a pandemic that occurs in many countries around the world, including in Indonesia. China reported a case of pneumonia of unknown cause in December 2019. It showed that the number of patients had reached 44 patients within 3 days, and the number of cases continued to increase. Epidemiological data state that 66% of patients are related to a market in Wuhan, Hubei, China. The isolated sample showed a new type of beta coronavirus, named novel coronavirus (2019-nCoV). The WHO then gave the name of this new type of virus as COVID-19 (Coronavirus Disease 2019) on February 11, 2020 [1,2].

The rapidity with which clinical trials investigating potential COVID-19 therapeutics were begun demonstrates both the need for and possibility of producing high-quality evidence even in the midst of a pandemic. So far, there are no definitive therapies for this SARS-CoV-2 [3]. The study results show varying results of antiviral effectiveness against confirmed COVID-19 patients. Therefore, it is necessary to analyze to determine the effect of therapy on clinical outcomes and length of stay for patients with confirmed COVID-19.

METHODS

The study used a cross-sectional research design. This study is a retrospective study with consecutive sampling method. Data were collected retrospectively to evaluate the effect of using standard combination therapy on clinical outcomes and length of stay. The data used are secondary data, patient medical records from March to October 2020 that meet the inclusion and exclusion criteria. Patients with a confirmed primary diagnosis of COVID-19 will then be given antiviral therapy following the guidelines for managing COVID-19 patients issued by the Ministry of Health in 2020. The independent variable in this study is antiviral, while the dependent variable is clinical outcome and length of stay.

The inclusion criteria in this study were patients who were >18 years, patients receiving antivirus (oseltamivir or favipiravir), and patients with confirmed positive COVID-19 that showed by reverse transcription-polymerase chain reaction (RT-PCR). The exclusion criteria in this study were patients who changed antivirals during treatment and patients diagnosed with other infections at the time of hospital admission. Descriptive data show a number (n) and proportion (%). In addition, a bivariate test is the main independent variables on each dependent variable — this test is to determine the relationship between antivirals on clinical outcomes and antivirals to the length of stay. The analysis used the Chi-square test, but if it did not meet the requirements of the Chi-square test, then use Fisher's exact test.

RESULTS AND DISCUSSION

The characteristics of the research subjects consisted of age, gender, length of stay, clinical outcomes, severity, and comorbidities. The data are presented in the frequency distribution and the percentage of the variables studied. The demographic and clinical characteristics of the patients are shown in Table 1.

This study showed that cases mainly in the age range of 18–59 years at 82.4%, compared to those aged 60 years at 17.5%. It shows that the majority of inpatients with confirmed COVID-19 are patients of productive age. The more significant number of cases in this group could be due to a lack of compliance with recommendations for washing hands, using masks, and physical distance.

In this study, there were more female patients than male patients, with 58.8% in female patients and 41.2% in male patients. The expression of the angiotensin-converting enzyme 2 (ACE2) receptor that facilitates the entry of the SARS-CoV-2 virus and its human-to-human transmission differs between sexes. Oestradiol can affect ACE2 expression and the gene for ACE2 on the X chromosome, making it susceptible to escape X inactivation in females [4]. The length of treatment was mainly in

the ≤14-day group (58.8%) compared to the >14 days group (41.2%). A retrospective cohort study showed that the length of stay was associated with several risk factors, such as being male, having a fever at the time of hospital admission, having a history of chronic kidney or liver disease [5].

The recovery rate of the COVID-19 patients at Fatmawati Jakarta Hospital was 88.6% compared to 11.4% of patients who died of the total 114 patients. The national cure rate is 91.9%, with a mortality rate of 2.8% and the remaining 5.4% active cases. Based on data in Jakarta, the proportion of cures is 95.8%, and the mortality rate is 1.7%. It shows that the COVID-19 case has a high recovery rate compared to the mortality rate [6]. A study showed that mortality is associated with age >70 years [7].

Older age and specific comorbidities are associated with higher infection severity and mortality in patients with COVID-19 infection. The severity and death of cases of COVID-19 infection were higher in men, with a ratio of 2 times more likely to die from COVID-19 than women. Men generally have a higher prevalence of high-risk behaviors, including smoking and alcohol consumption, working in high-risk occupations that increase their risk of exposure to infection [8].

Data on the use of antiviral in the entire sample are depicted in Table 2. Patients taking oseltamivir with clinical outcomes recovered were 86 patients (87.8%), while the number of patients who died was 12 patients (12.2%). Patients who received favipiravir with clinical outcomes recovered were 15 patients (93.8%) and one patient (6.2%) who died. It indicates that the proportion of recoveries who received antivirals was higher than the number of patients who died.

Table 1: Demographic and clinical characteristics of patients from March to October 2020

Characteristics	Frequency (n)	Percentage (%)
Age group		
18–59 years	94	82.4
≥60 years	20	17.5
Gender		
Female	67	58.8
Male	47	41.2
Length of Stay (LoS)		
≤14 days	67	58.8
>14 days	47	41.2
Clinical outcomes		
Recovered	101	88.6
Death	13	11.4
Severity		
Non-severe	107	93.9
Severe	7	6.1
Comorbidity		
No	67	58.8
Yes	47	41.2

The significance value of p>0.05 is 0.690. It indicates that the effect of antiviral therapy on clinical outcomes is not statistically significant. The odds ratio (OR) of antiviral therapy to clinical outcomes in this study was 0.478. A low OR value indicates a negative association, which means that therapy has a more negligible effect on clinical outcomes. The 95% confidence interval is 0.058≤OR≤3.950. It indicates no significant association between the administration of antiviral therapy and the clinical outcome.

Based on a cohort study by Ramatillah and Isnani stated that the clinical outcome of patients receiving oseltamivir therapy was relatively high, 81.3% of the total patients receiving therapy as many as 16 patients. Oseltamivir is recommended because it is available in Indonesia and has been produced domestically. An analysis of the survival of COVID-19 patients using the Kaplan–Meier method showed that patients receiving Oseltamivir+Hydroxychloroquine had an average survival rate of about 83% after undergoing treatment for about 10 days (p=0.027). However, the large sample size and multicenter study will help find the most effective antiviral agents for COVID-19 [9].

In a third phase clinical trial, it was found that early administration of oral favipiravir reduced the duration of clinical signs and symptoms in patients with mild-to-moderate severity. However, the lack of statistical significance at the primary endpoint was due to the limitations of the RT-PCR assay. The primer endpoint in the test was the median time to reach a negative RT-PCR [10]. A study in Egypt stated that favipiravir could be a safe and effective alternative to hydroxychloroquine in patients with mild or moderate COVID-19. Favipiravir can be used safely during home isolation for mild-to-moderate cases, while the safety of hydroxychloroquine for self-isolation at home still needs to be investigated further [11].

In our study, the bivariate analysis also evaluates the association between antivirals to a length of stay. Table 3 shows that the proportion of subjects receiving oseltamivir with the length of stay ≤14 days was 46 patients (53.5%), while in the group with the length of stay >14 days was 40 patients (46.5%). In the group, receiving favipiravir with the length of stay ≤14 days was 9 patients (69.2%), while in the group with the length of stay >14 days was 6 patients (84.6%). It indicates that the majority of patients have a length of stay of ≤14 days.

The significance value of p on the two variables is 0.852. p>0.05 indicated that the effect of antiviral therapy on the length of treatment was not statistically significant. The OR value is 0.767, which indicates

Table 2: The association of antiviral on clinical outcome of COVID-19 patients on March–October 2020

No.	Antiviral	Clinical outcomes		Total	P	OR	CI 95%
		Recovered	Death				
1.	Oseltamivir	86 (87.8%)	12 (12.2%)	98 (100%)	0.690	0.478	0.058–3.950
2.	Favipiravir	15 (93.8%)	1 (6.2%)	16 (100%)			
Total		101	13	114			

Table 3: The association of antiviral on length of stay of recovered COVID-19 patients on March–October 2020

No.	Antivirus	Length of stay		Total	p	OR	CI 95%
		≤ 14 days	> 14 day				
1.	Oseltamivir	46 (53.5%)	40 (46.5%)	86 (100%)	0.852	0.767	0.251–2.342
2.	Favipiravir	9 (15.4%)	6 (84.6%)	15 (100%)			
Total		55	46	101			

CI: Confidence interval

that antiviral therapy does not affect the length of stay. The 95% confidence interval is 0.251≤OR≤2.342. It indicates no significant association between the administration of antiviral therapy and the clinical outcome.

The average length of stay in hospital is 14 (IQR=10–19) days for China, while outside China, the average length of stay is 5 (IQR=3–9) days. Patients discharged from the hospital recovery tend to have a more extended stay than patients who die in the hospital [12]. There are very few studies on the effect of oseltamivir or favipiravir on length of stay. The WHO Solidarity Trial study did not use these two antivirals but used remdesivir, hydrocycloroquine, lopinavir, and interferon beta-1a to affect patient mortality. The results showed that all four drugs had little or no effect on hospitalized patients. There are no drugs that can reduce mortality, use of ventilation, or length of stay [13].

CONCLUSION

The study's results indicate that antivirals were not significantly associated with clinical outcomes and length of stays in COVID-19 patients. The bivariate analysis between antivirals on clinical outcomes shows that the significance value of p>0.05 (p=0.690) Likewise, the bivariate analysis between antivirals on the length of stay shows that the p-value > 0.05 (p=0,852). In addition, further research is needed.

ACKNOWLEDGMENT

The authors thank to Fatmawati General Hospital Jakarta for allowing and facilitating authors in data collection.

AUTHORS' CONTRIBUTION

Mareoza Ayutri and Ahmad Subhan discussed the study design with Retnosari Andrajati to arrange the concept of the study. Mareoza Ayutri collected and analyzed the data. All authors discussed the final manuscript.

CONFLICTS OF INTEREST

All authors declared no conflict of interest related to this research and publication of this article.

AUTHOR'S FUNDING

Any grant sources did not fund this research.

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