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The Comparison of The Use of Antiviral Drugs Favipiravir and Remdesivir on The Outcome of Covid-19 Patients at RSM Ahmad Dahlan

Fendy Prasetyawan[1*], Lisa Savitri[2], Yuneka Saristiana[3], Shinta Mayasari[4], Novyananda Salmasfattah[5]
[1,2,3,5]Program Studi Pendidikan Profesi Apoteker, Fakultas Ilmu Kesehatan, Universitas Kadiri
[4]Program Studi Farmasi, Fakultas Ilmu Kesehatan, Universitas dr Soebandi
E-mail: fendy.pra@gmail.com[1], lisasavitri@unik-kediri.ac.id[2], yunekasaristiana@gmail.com[4], shintamayasari@uds.ac.id[4], salmasfattah@gmail.com[5]

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Abstract: *This study aims to compare the usage patterns, effectiveness, and therapy outcomes of two antiviral drugs, Favipiravir and Remdesivir, in the treatment of COVID-19 at Muhammadiyah Ahmad Dahlan Hospital, Kediri City. A total of 71 medical records of patients treated with Favipiravir and 50 treated with Remdesivir were analyzed, focusing on patient demographics, drug usage, and therapy outcomes. The patient characteristics reveal that Favipiravir was more commonly used in older patients (aged >65 years), while Remdesivir was more frequent in younger patients (aged 0-5 years). In terms of drug usage, Favipiravir was prescribed to 58.7% of patients, compared to 41.3% for Remdesivir. Both antivirals demonstrated high recovery rates, with Favipiravir achieving a 100% recovery rate and Remdesivir 98%. Evaluation of drug effectiveness showed that Favipiravir was superior in reducing CRP levels (34.78) compared to Remdesivir (7.74), while Remdesivir had a shorter average length of stay (5.68 days) than Favipiravir (8.67 days). These findings suggest that while Favipiravir is more effective in reducing inflammation, Remdesivir is more efficient in accelerating patient recovery. Both drugs play significant roles in COVID-19 management, with their use tailored to patient needs.*

INTRODUCTION

At the end of 2019, the world was shocked by reports of mysterious pneumonia cases with unknown causes in Wuhan, Hubei Province, China. Within three days, the number of cases reached 44 patients and continued to rise, now amounting to millions of cases worldwide (PDPI, 2020). Most of the early cases were linked to exposure at a seafood market in Wuhan, and specimens isolated identified an infection caused by a novel coronavirus, later named the 2019

novel coronavirus (2019-nCoV). This virus became globally recognized as SARS-CoV-2, the causative agent of Coronavirus Disease 2019 (COVID-19) (PDPI, 2020).

The common symptoms of COVID-19 infection include fever, cough, and shortness of breath, all of which are associated with respiratory tract disturbances. The longest incubation period is up to 14 days, with an average incubation period of approximately 5-6 days (Ministry of Health RI, 2020). As of November 2020, the World Health Organization (WHO) reported over 58 million confirmed cases and more than 1.3 million deaths globally. The United States had the highest number of cases, followed by other countries, including Indonesia. In Indonesia, the first cases were reported on March 2, 2020, and by November 2020, there were 502,110 confirmed cases and 16,002 deaths (PHEOC Ministry of Health RI, 2020).

COVID-19 has a spectrum of symptoms ranging from mild to severe cases. In mild cases, the symptoms are often nonspecific, such as fever, fatigue, and dry cough. Meanwhile, severe cases can result in pneumonia, acute respiratory syndrome, kidney failure, and even death (Ministry of Health RI, 2020). According to WHO, about 80% of COVID-19 patients experience mild to moderate symptoms, 13.8% develop severe symptoms, and 6.1% are in critical condition (WHO, 2020).

The management of COVID-19 varies depending on the severity of the disease. Primary therapy involves the use of antiviral drugs such as Remdesivir and Favipiravir, accompanied by supportive therapies such as antibiotics, corticosteroids, and multivitamin supplements (BPOM RI, 2020). Remdesivir is a broad-spectrum antiviral molecule initially developed for treating the Ebola virus. It works by inhibiting RNA-dependent RNA polymerase (RdRp), an essential enzyme in the replication process of the SARS-CoV-2 genome. Meanwhile, Favipiravir, first developed by Fujifilm Toyama Chemical, is an RNA polymerase inhibitor with activity against various RNA viruses, including SARS-CoV-2 (Holshue et al., 2020; Youzuke, 2017).

Studies have shown that Remdesivir provides clinical benefits for patients with severe COVID-19, such as reducing hospitalization duration and improving oxygen saturation. Favipiravir has also been proven effective in vitro against SARS-CoV-2, demonstrating strong antiviral activity against various strains of influenza viruses and SARS-CoV-2 (Wang M, 2019). However, the effectiveness of these two drugs in clinical practice often depends on factors such as the patient's condition, dosage, and individual immune response.

The Muhammadiyah Ahmad Dahlan Hospital, as one of the COVID-19 referral hospitals in Kediri, has utilized both drugs in patient management. Therefore, it is essential to conduct a comparative evaluation of the use of Remdesivir and Favipiravir regarding the therapeutic effectiveness for COVID-19 patients. This research is expected to contribute to clinical decision-making and the management of COVID-19 therapy, particularly in Indonesia.

LITERATRE REVIEW

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which had not been previously identified in humans (Kemenkes RI, 2020). SARS-CoV-2 differs from two other zoonotic coronaviruses, namely SARS-CoV and MERS-CoV, which emerged in the early 21st century. Previously, the Coronavirus Study Group (CSG) designated these two viruses as prototypes of a new species in the informal subgroup of the Betacoronavirus genus. However, the situation with SARS-CoV-2 is different because this virus has been classified into an existing species that includes hundreds of other viruses, most of which were isolated from humans and bats. All viruses within this species are named after SARS-CoV, although only human isolates

have been collected (Gorbalenya et al., 2020).

Antiviral drugs are a group of medications designed to treat viral infections specifically. These drugs work by preventing viral replication through the inhibition of one stage of replication, thereby preventing the virus from reproducing (Joyce L, 1996). Antiviral drugs are used to treat infections caused by viruses such as the Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), herpes viruses (HSV, VZV, CMV), Orthomyxoviruses (influenza), Paramyxoviruses (RSV), and Hepaciviruses (HCV). Research continues to develop new antiviral strategies, particularly against these viruses (Elsevier, 2007).

Remdesivir is a broad-spectrum antiviral molecule initially developed for the treatment of the Ebola virus. The first patient in the United States reported to be infected with SARS-CoV-2 showed clinical improvement after receiving intravenous Remdesivir, including a reduction in body temperature and improved oxygen saturation (Holshue et al., 2020). Remdesivir works by inhibiting SARS-CoV-2 replication through RNA-dependent RNA polymerase (RdRp), with a dosing regimen of 200 mg IV as an initial dose, followed by 100 mg IV daily for up to 10 days. Common side effects include gastrointestinal intolerance and hepatotoxicity (International Pulmonologist's Consensus, 2020). The FDA has approved Remdesivir for the treatment of COVID-19 in hospitalized adult and pediatric patients meeting specific criteria (NIH, 2020). Monitoring liver and kidney function is essential during treatment, and concomitant use with chloroquine or hydroxychloroquine is not recommended as it may reduce its antiviral activity (NIH, 2020).

Favipiravir is a broad-spectrum antiviral that also demonstrates in vitro activity against SARS-CoV-2. The drug has been approved in Japan and China for influenza therapy and has also been used in emergency settings for COVID-19, although its efficacy and safety are not fully established. Favipiravir is associated with side effects such as prolonged QT interval and is contraindicated in pregnant women or those planning to conceive (Johan, 2020). In Indonesia, the National Agency of Drug and Food Control (Badan POM) granted emergency use authorization for adult patients with mild to moderate COVID-19. Favipiravir dosing for COVID-19 varies based on the patient's body weight, with regimens tailored for each weight category (PDPI, 2020).

This study utilizes indicators for evaluating the effectiveness of Remdesivir and Favipiravir treatments, with parameters such as improvement in C-Reactive Protein (CRP) levels and the length of hospital stay (LOS). Normal CRP levels are < 0.5 mg/dL, which typically increase within 8-15 hours during inflammation (Hermawan et al., 2019). According to previous studies, the average length of hospitalization for patients treated with Favipiravir is 8.8 days, while for Remdesivir, it is 9.3 days (Riptasari et al., 2022).

METHODS

This study employed a descriptive design with a non-experimental cross-sectional approach. Descriptive research aims to present, describe, and report the condition of the research object as it exists without applying specific treatments to the subjects. The cross-sectional design is a type of observational study that analyzes variable data collected at a specific point in time from a predefined population or sample. The research data were collected retrospectively through medical records of COVID-19 patients at Muhammadiyah Ahmad Dahlan Hospital in Kediri City from April to June 2021 to evaluate the effectiveness of Favipiravir and Remdesivir usage.

The research subjects were medical records of patients confirmed positive for COVID-19 who received Favipiravir or Remdesivir therapy at Muhammadiyah Ahmad Dahlan Hospital

during the specified period. The study population consisted of all medical records of COVID-19 inpatients at the hospital, totaling 221 records. The research sample was determined using purposive sampling techniques with specific inclusion and exclusion criteria, resulting in 143 medical records based on calculations using the Slovin formula.

The inclusion criteria included COVID-19 inpatients treated with Favipiravir or Remdesivir, patients with a positive SWAB test upon hospital admission, and medical records containing complete data on demographics, clinical conditions, laboratory results, medication usage, and CRP values at hospital admission and discharge. The exclusion criteria included asymptomatic patients (OTG), patients hospitalized for less than one day, deceased patients, and incomplete or damaged medical records.

The research material comprised COVID-19 patient medical records, while the research tools included data collection sheets containing information on demographics, clinical data, laboratory results, and antiviral therapy. The independent variable in this study was the usage pattern of Favipiravir and Remdesivir, while the dependent variables were the therapy effectiveness measured by CRP improvement, length of stay (LOS), and patient outcomes. Operational definitions included measuring drug usage patterns, comparing the effectiveness of the two drugs, and therapy outcomes.

The data collection instrument was the medical records, which were analyzed and transferred to data collection sheets to document information on patient demographics, clinical data, laboratory results, and therapy details. The research process included preparation (obtaining research permits), implementation (identifying and reviewing patient data), and report preparation (data processing and analysis). Data analysis was conducted to determine drug usage patterns, compare effectiveness based on CRP and LOS, and evaluate therapy outcomes of Favipiravir and Remdesivir usage. The research findings will be presented descriptively to illustrate the patterns and effectiveness of these two antiviral drugs.

RESULTS AND DISCUSSION

Patient Demographics

This study was conducted at Muhammadiyah Ahmad Dahlan Hospital, Kediri City, with data obtained from 71 medical records of patients treated with Favipiravir antiviral therapy and 50 medical records of patients treated with Remdesivir antiviral therapy. Patient characteristics include gender, age, comorbidities, and domicile, as shown in Table 4.1 below:

Table 1. Patient Characteristics

Characteristics	Favipiravir (n=71)	Remdesivir (n=50)
Gender		
Female	38 (53.5%)	21 (42%)
Male	33 (46.5%)	29 (58%)
Age		
0-5 years	–	28 (56%)
6-11 years	–	17 (34%)
12-16 years	–	5 (10%)
17-25 years	6 (8.5%)	–
26-35 years	9 (12.7%)	–
36-45 years	12 (16.9%)	–

46-55 years	11 (15.5%)	–
56-65 years	16 (22.5%)	–
>65 years	17 (23.9%)	–
Comorbidities		
0 Comorbidities	35 (49.3%)	–
1 Comorbidity	31 (43.7%)	–
2 Comorbidities	5 (7.0%)	–
Domicile		
Kediri	46 (64.8%)	45 (90%)
Outside Kediri	25 (35.2%)	5 (10%)

The gender characteristic indicates that among patients treated with Favipiravir, females were more dominant (53.5%) than males (46.5%), whereas for patients treated with Remdesivir, males were more dominant (58%) than females (42%). This difference may relate to males' more active movement patterns outside the home, making them more susceptible to COVID-19 exposure (BPS, 2020). Additionally, biological factors such as the X chromosome and progesterone hormones in females contribute to stronger immunity against infections (Susilo et al., 2020).

Regarding age, the use of Favipiravir was most common in the >65 years age group (23.9%) and the 56-65 years age group (22.5%), while the use of Remdesivir was dominant in the 0-5 years age group (56%) and the 6-11 years age group (34%). This shows that older individuals are more vulnerable to COVID-19 due to declining immunity, whereas children are at higher risk due to their immature immune systems, making them prone to respiratory infections (Hidayani, 2020; Huang et al., 2020).

Drug Usage Patterns

The drug usage patterns at Muhammadiyah Ahmad Dahlan Hospital include two types of antivirals: Favipiravir and Remdesivir. The data on drug usage are presented in Table 4.2 below:

Table 2. Drug Usage Patterns

Antiviral	N (121)	Persentace (%)
Favipiravir	71	58.7%
Remdesivir	50	41.3%

Based on the table above, Favipiravir was used more frequently (58.7%) compared to Remdesivir (41.3%). Both antivirals are the primary choices for COVID-19 treatment at Muhammadiyah Ahmad Dahlan Hospital due to their proven efficacy. The dominance of Favipiravir usage may be attributed to the patient characteristics, particularly the elderly group, who are more susceptible to severe COVID-19 and often require antiviral therapy to prevent further complications.

Therapy Outcomes

The therapy outcomes from using Favipiravir and Remdesivir are shown in Table 4.3 below:

Table 3. Therapy Outcomes

General Condition	Favipiravir (n=71)	Remdesivir (n=50)
Recovered	71 (100%)	49 (98%)

Referred	–	1 (2%)
Deceased	–	–

From the table above, all patients treated with Favipiravir (100%) were declared recovered, while among patients treated with Remdesivir, 98% recovered, and 2% were referred for further treatment. These high recovery rates indicate that both antivirals are effective in managing COVID-19. However, the 2% referral rate in the Remdesivir group highlights the need for specialized care in certain critical cases or those with comorbidities.

Drug Effectiveness

The effectiveness of drug usage was evaluated based on CRP improvement and length of stay (LOS). The results are presented in two tables below.

Table 4. CRP Improvement Results

Antiviral	N	Total CRP Reduction	Average (ΔCRP)
Favipiravir	71	2470.01	34.78
Remdesivir	50	387.2	7.74

The results indicate that Favipiravir had a greater average CRP reduction (34.78) compared to Remdesivir (7.74). The significant decrease in CRP among Favipiravir patients suggests that this drug is more effective in reducing inflammation than Remdesivir.

Table 5. LOS Results

Antiviral	N	Total LOS	Average LOS
Favipiravir	71	616	8.67
Remdesivir	50	284	5.68

Regarding length of stay, patients treated with Remdesivir had a shorter average LOS (5.68 days) compared to those treated with Favipiravir (8.67 days). This indicates that while Favipiravir is more effective in reducing inflammation, Remdesivir is more efficient in accelerating patient recovery.

Comparison of Drug Usage

The comparison of effectiveness between Favipiravir and Remdesivir demonstrates distinct advantages for each. Favipiravir is more effective in reducing inflammation (CRP), while Remdesivir is more efficient in shortening the recovery time (LOS). Therefore, the choice of antiviral can be adjusted based on the clinical needs of the patient, such as reducing inflammation or achieving faster recovery. This study confirms that both antivirals play a significant role in managing COVID-19, with their effectiveness optimized according to patient characteristics.

CONCLUSION

Based on the results of the study, it can be concluded that Favipiravir and Remdesivir are both effective in the treatment of COVID-19, with specific advantages depending on the clinical indicators used. Favipiravir was more frequently used in therapy, with 71 patients (58.7%) receiving it, compared to 50 patients (41.3%) treated with Remdesivir at Muhammadiyah Ahmad Dahlan Hospital in Kediri City. When comparing the effectiveness of the two antivirals,

Favipiravir demonstrated better results in reducing inflammation based on the improvement in C-Reactive Protein (CRP) levels. In contrast, Remdesivir showed superior performance in reducing the length of stay (LOS), indicating a faster recovery process. Therefore, both drugs are equally efficient and can be utilized effectively in COVID-19 treatment, depending on the clinical needs of the patient.

Therapy outcomes also revealed a high recovery rate for both antivirals. All patients (100%) treated with Favipiravir recovered, while 98% of patients treated with Remdesivir recovered, and 1 patient (2%) was referred for further treatment. This indicates that both Favipiravir and Remdesivir contribute significantly to successful outcomes in COVID-19 management, with each drug offering specific benefits tailored to different patient conditions and therapeutic goals.

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