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The Efficacy of Antiviral Medications in Managing Blood Oxygen Levels in Covid-19 Patients Afflicted by Chronic Kidney Conditions

Fendy Prasetyawan[1]*, Faisal Akhmal Muslikh[2], Anis Akhwan Dhafin[3], Elsa Mahardika Putri[4], Yuneka Saristiana[5], Susilo Margining Raharjo[6]
[1,3,4,5,6]Universitas Kadiri, [2]Institut Ilmu Kesehatan Bhakti Wiyata
Corresponding Author: Fendy Prasetyawan fendy.pra@gmail.com

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A B S T R A C T

This research assesses the efficacy and safety of employing antiviral drugs in individuals with COVID-19 and chronic kidney disease. The study results reveal a reduced effectiveness of the drug in enhancing oxygen saturation in patients, as indicated by a p-value of 0.026 for SpO2. Consequently, the administration of antiviral drugs to individuals with chronic kidney disease warrants careful consideration. Moreover, there is a need to pay attention to the safety aspects of antiviral drug utilization, particularly with a p-value of 0.026 for Clcr. It is advisable to refrain from using specific antiviral drugs, such as favipiravir, in COVID-19 patients with chronic kidney conditions. However, contemplating the use of remdesivir at an appropriate dosage may be viable if the patient's glomerular filtration rate (GFR) exceeds 30 ml/minute. The study's conclusion underscores the significance of meticulous and personalized management when employing antiviral drugs in COVID-19 patients with chronic kidney disease. A comprehensive consideration of factors such as effectiveness, safety, and the patient's renal health is imperative to ensure an optimal and tailored treatment approach

INTRODUCTION

In 2020, the world was shaken by the spread of a new virus, namely SARS-CoV-2, and the associated disease named COVID-19. COVID-19 is considered a health crisis that requires serious control measures (Prasetyawn, F. et al. 2023). As of December 19, 2021, more than 273 million people had been infected with COVID-19, and over 5.3 million people had died. The first case of COVID-19 in Indonesia was announced on March 2, 2020, approximately 4 months after the first cases were detected in Wuhan, China. Since the first reported case of COVID-19 in Indonesia, the number has continued to increase over time, necessitating serious attention. Additionally, various variants have been found circulating in different regions of Indonesia, increasing the risk of infection and reducing vaccine effectiveness.

Although all age groups can be affected, the clinical effects on children are generally milder compared to adults. With the progression of the pandemic, the rates of infection, hospitalization, and death vary between countries and regions, raising questions about the risk factors and protection against COVID-19. Key risk factors influencing the severity and mortality of COVID-19 include laboratory values, proinflammatory cytokine levels, and other comorbidities (Yıldırım et al., 2022).

The novel coronavirus infection (COVID-19) is classified into several categories based on severity: asymptomatic, mild, moderate, severe, and critical. One exacerbating factor for COVID-19 is the presence of chronic kidney disease, which generally makes the immune system more vulnerable than in individuals without comorbidities. Therefore, the COVID-19 pandemic is a significant issue requiring serious attention, given its potential for a significant increase in global mortality (Sherina et al., 2023).

Patients with chronic kidney failure are more likely to be at higher risk of severe COVID-19 infection. Therefore, it is recommended for patients with chronic kidney failure to take stricter preventive measures to reduce the risk of contracting the virus. To minimize the risk of COVID-19 spread, chronic kidney failure patients exposed to COVID-19 need to undergo hemodialysis with stricter protocols (Rudiansyah et al., 2020).

As of now, there are no specific recommendations for preventing or treating COVID-19. The treatments used are still based on in-vivo, in-vitro, and randomized controlled trial results. Available options include the use of broad-spectrum antiviral drugs such as nucleoside analogs, neuraminidase inhibitors, SARS-CoV-2 RNA polymerase analog nucleotide inhibitors, RNA-dependent RNA polymerase (RdRp) inhibitors, and HIV protease inhibitors that can weaken the virus until specific antivirals are available (Lu H, 2020). The use of antivirals for COVID-19 patients in Indonesia is based on the severity of symptoms (PAPDI, 2020). Antivirals used for COVID-19 patients in several countries include lopinavir or ritonavir, remdesivir, Oseltamivir, chloroquine, hydroxychloroquine, and Favipiravir (Zhong et al., 2020).

Based on the circular letter from the director of RSUD dr. Soedomo Kabupaten Trenggalek number 445/1593/406.010.001/2020 regarding the alertness and prevention of COVID-19, it is stated that RSUD dr. Soedomo

actively participates in preventing COVID-19 and implements preventive measures. One of these preventive measures is providing treatment to patients diagnosed with COVID-19. Researchers are interested in conducting research at RSUD dr. Soedomo because it is the best hospital in Kabupaten Trenggalek in handling COVID-19 cases. Therefore, the research aims to determine the effectiveness of antiviral drugs in treating COVID-19 patients and assess their safety when given to COVID-19 patients with Chronic Kidney Disease.

LITERATURE REVIEW

This study is a cross-sectional (non-experimental) research. The sample was obtained using purposive sampling method. The data source for the study is primary data obtained from the medical records of patients. The data used is in the form of retrospective data. This research was conducted on COVID-19 patients with Chronic Kidney Disease (CKD) who received antiviral therapy to observe the reduction in the severity of the disease in COVID-19 patients with CKD after receiving antiviral treatment, the duration of treatment for COVID-19 patients with CKD after receiving antiviral treatment, the mortality rate in COVID-19 patients with CKD after receiving antiviral treatment, and the side effects of antiviral drugs in COVID-19 patients with CKD.

METHODOLOGY

This research is a cross-sectional analysis without experimental intervention, using a deliberate selection method from the medical records of COVID-19 patients who also suffer from Chronic Kidney Disease (CKD). The research aims to understand the reduction in the severity of the disease, treatment periods, mortality rates, as well as the side effects of antiviral drugs on patients with the same condition after undergoing treatment.

The research was conducted at the RSUD Dr. Soedomo Trenggalek located at Jl. dr. Sutomo No.2, Cengkong, Tamanan, Kec. Trenggalek, Kabupaten Trenggalek, East Java 66311. The study took place during the month of August 2023. The instruments used in data collection from Medical Records include patient demographic data, records of antiviral drug usage, oxygen saturation examination results, ClCr examination, and Covid-19 tests. Data analysis consists of two parts, namely Descriptive and Inferential. Descriptive analysis uses percentages to explain the variables of antiviral drugs (independent) and COVID-19 patients with chronic kidney disease.

The data analysis in this research includes descriptive analysis and inferential analysis. In univariate analysis, descriptive methods are employed to depict the independent variable of antiviral drugs and the dependent variable of COVID-19 patients with chronic kidney disease. In the process of this data analysis, percentages are used as a descriptive method, utilizing the percentage formula to present information regarding the relationship between antiviral drug variables and the condition of COVID-19 patients with chronic kidney disease.

P=n : (Total Sampel) x 100%

P" stands for percentage, "n" represents the number of parts, and these values are incorporated into the criteria for calculating the percentage. Differential analysis using the chi-square test is conducted to assess the impact of the effectiveness and safety of antiviral drugs on COVID-19 patients with chronic kidney disease. The decision-making criteria for hypothesis testing in this research are as follows: if the P-value is less than α (0.05), then the null hypothesis (H0) is rejected, and the alternative hypothesis (H1) is accepted; if the P-value is greater than α, then H0 is accepted, and H1 is rejected.

RESEARCH RESULT

Translate the following into English: "P = There were 50 patients treated at RSUD dr. Soedomo during the year 2022 with a diagnosis of Coronavirus Disease 2019 (COVID-19) who also suffered from chronic kidney disease. Demographic information about the patients can be found in Table 1 below:"

Table 1. Patient Demographic Data

Characteristics of Respondents	Total	
	Frekuensi	Persentase (%)
Age		
<15 year	4	8
16-35 year	7	14
36- 50 year	9	18
> 50 year	30	60
Gender		
Man	37	74
Woman	13	26
length of hospital stay		
<3 days	12	24
4-7 days	36	72
>7 days **Outcome**	2	4
Recovered		
Died	36	72
	14	28
Total	**50**	**100**

Based on demographic data of confirmed COVID-19 patients with chronic kidney disease at RSUD dr. Soedomo Trenggalek, the majority of patients are above 50 years old, reaching 60%. Males dominate at 74%, while the average length of hospitalization ranges from 4 to 7 days, reaching 72%, and the final outcome shows a recovery rate of 72%. Demographic factors related to the severity of COVID-19 involve age and gender. Elderly patients tend to be more vulnerable to various diseases due to a decline in physiological function, including the immune system regulated by B and T cells (Fitriani, NI. 2020). Differences in the expression of ACE2 and TMPRSS2 receptors based on gender

may explain variations in the severity and mortality rates of COVID-19 (Di Gennaro et al., 2020).

The number of patients recovering is attributed to their clearance from the critical period after undergoing treatment for 4 to 7 days, significantly reducing the risk of death. In patients with kidney disease, the risk of contracting COVID-19 is three times higher compared to those without chronic kidney disease. This is due to a weakened immune system and the routine hospital visits of patients for hemodialysis, which increases the risk of transmission if health protocols are not strictly followed during hospital treatment.

Name drug	Frekuensi (n)	Persentase (%)
Favipirafir	32	64
Remdesivir	18	36
Total	**50**	**100**

In Dr. Soetomo Hospital, two types of antiviral drugs are used, namely favipiravir and remdesivir. The use of favipiravir reaches 64%, while remdesivir is used by 36%. Favipiravir, a broad-spectrum antiviral drug, has proven effective in clinical trials in COVID-19 patients. The valid maintenance dose ranges from 200 to 600 mg, twice a day, for 10 to 14 days, with initial doses varying between 1600, 1800, and 2400 mg. In patients with chronic kidney disease, monitoring favipiravir administration is necessary as it can accumulate, increasing the potential risk of toxicity (Chen et al., 2020).

From the above data, there is a 68% increase in leukocyte examination, supported by a p-value of 0.068, higher than 0.05. This indicates that antiviral drugs are effective in reducing and improving leukocyte levels in COVID-19 patients with chronic kidney disease. The normal range of leukocytes is 4,800-10,800/µL. Leukocytes are an indicator of inflammation in COVID-19 patients. Inflammation itself is an essential mechanism in protecting the body from foreign substances, where SARS-CoV-2 has a specific receptor in the body, namely ACE-2. If the virus binds to this receptor, the virus replication process will occur, triggering an inflammatory response as part of the body's defense mechanism (M. Surip, Elly Prihasti W, 2020).

SpO2 examination shows that only 12% of patients experienced improvement, with a p-value of 0.026, indicating that antiviral drugs are not effective in reducing or improving the condition of COVID-19 patients who also suffer from kidney failure. This result can be seen from the oxygen saturation examination, where the normal value should be above 95%. Oxygen saturation refers to the amount of oxygen bound to hemoglobin in the blood. Decreased oxygen saturation can occur due to Diffuse Alveolar Damage (DAD), which causes the formation of hyaline membranes due to inflammation and accumulation of dead lung cells. This condition hampers gas exchange and results in decreased oxygen saturation. Research related to oxygen saturation in COVID-19 patients shows that saturation below 95% can cause oxygen deficiency in the body, leading to Hypoxemia or Hypoxia. Oxygen deficiency can cause sudden consciousness decline in patients due to increased intracranial pressure.

If this condition is not detected, it can end in respiratory failure and death (M. Surip, Elly Prihasti W, 2020).

Clcr examination does not show significant improvement at 88%, supported by a p-value of 0.026. This indicates that the antiviral drugs used in this study are not safe for COVID-19 patients with chronic kidney disease. Some patients experienced improvement due to hemodialysis treatment and previous vaccination. It was found that patients who died were generally over 50 years old and had not received the vaccine. Remdesivir, as an example of an antiviral drug, is not recommended for patients with a GFR below 30 ml/min and creatinine >1mg/dl unless its benefits are considered greater than its potential risks. Meanwhile, favipiravir, if given after 48 hours, can worsen kidney damage in patients with normal creatinine. However, kidney improvement can occur 24 to 48 hours after therapy discontinuation.

DISCUSSION

The research results indicate that the drug is less effective in increasing oxygen saturation in patients, as evidenced by a p-value of 0.026 for SpO2. The safety of using antiviral drugs needs to be considered, especially with a p-value of 0.026 for Clcr. It is recommended not to use certain antiviral drugs in patients with chronic kidney conditions, such as favipiravir in COVID-19 patients.

CONCLUSIONS AND RECOMMENDATIONS

The conclusion of this research is that the drug is less effective in improving oxygen saturation in patients, as evidenced by a p-value of 0.026 for SpO2. Therefore, the use of antiviral drugs in patients with chronic kidney disease should be carefully considered.

Furthermore, the research results indicate that the safety of using antiviral drugs in patients with chronic kidney disease should be taken into account, especially with a p-value of 0.026 for Clcr. It is recommended not to use specific antiviral drugs in patients with chronic kidney conditions. For example, the use of favipiravir in COVID-19 patients with chronic kidney disease should be done with caution while continuously monitoring the Clcr value.

Thus, the conclusion of this research highlights the importance of careful and personalized management of antiviral drug use in COVID-19 patients with chronic kidney disease, considering effectiveness, safety, and the patient's kidney condition.

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