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Analysis of Adverse Drug Reaction of Favipiravir in COVID-19 Patients in Dr. Mohammad Hoesin General Hospital Palembang

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ABSTRACT

The coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Due to its heterogeneous disease severity and rapid transmission, the use of antiviral and immunomodulator drugs is crucial. Favipiravir, an antivirus, can treat SARS-CoV-2 due to its action on RNA Genome ACE2 receptor, therefore halting the viral replication. However, Adverse Drug Reactions (ADRs) monitoring of Favipiravir is recommended. The study design is a descriptive cross-sectional approach with prospective sampling. The study was held in May-July 2021 and aimed to determine the adverse effects of Favipiravir in confirmed COVID-19 patients in Dr. Mohammad Hoesin General Hospital Palembang. Adverse events such as gastrointestinal symptoms (nausea, vomiting, and decreased appetite) occurred in 2 of 170 patients (1.18%). Several side effects, such as an elevated liver enzyme, leukopenia, neutropenia, hyperuricemia, and increased triglyceride levels, cannot be assessed due to a lack of laboratory results before and after Favipiravir administration. Other side effects such as skin rash, asthma, rhinitis, nasopharyngeal pain, and oropharyngeal pain, were not found in the study.

1. Introduction

COVID-19 is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). High human mobilization enables rapid transmission of the virus. SARS-CoV-2 has infected several age groups and instigated a wide spectrum of clinical manifestations. COVID-19 demonstrated various disease severity, ranging from asymptomatic or mild symptoms to critical state. COVID-19 can rapidly progress to severe pneumonia, acute respiratory distress syndrome (ARDS), respiratory failure, multiorgan dysfunction syndrome, and death. Eighty percent of COVID-19 cases were asymptomatic, mild, and moderate cases; 15% were severe cases, and 5% were critical cases.[1-3]

Expanding treatment choices for COVID-19 is crucial. Repurposing existing antiviral and immunomodulatory drugs is an important strategy. Unfortunately, the clinical efficacy and safety of the proposed drugs have not been established due to discordance in timing, treatment duration, and study endpoints between studies. A good clinical study should specifically elaborate and examine the drug type, doses, and treatment duration, as well as the type of patients who qualify for the inclusion criteria. The choice of antiviral drugs being evaluated should also be based on scientific evidence from both in vitro and in vivo studies.

The antiviral action of Favipiravir lies in its selective inhibition of the RNA Genome ACE2 receptor, thereby terminating SARS-CoV-2 replication. Favipiravir has been approved in Japan as an antiviral drug for influenza treatment. In 2016, Fujifilm granted a license to Zhejiang Hisun Pharmaceutical Co for Favipiravir distribution in China. In 2020, China investigated the use of Favipiravir for emergency cases of COVID-19. Compared with influenza treatment, the dose and duration of Favipiravir therapy for COVID-19 are higher and longer, augmenting the risk of unwanted side effects. Therefore, close monitoring of its adverse events is recommended.[4-8]

To date, there is no strong evidence about the efficacy of repurposing antiviral drugs for the treatment of COVID-19. The clinical trials of antiviral drug administration in COVID-19 provide were unsatisfactory. Therefore, caution during antiviral drug administration in COVID-19 patients and close monitoring of the side effects are compulsory. Favipiravir was evaluated in this study because this drug is recommended as the drug of choice for COVID-19 patients by the World Health Organization and is a part of the treatment protocol for hospitalized COVID-19 patients in Dr. Mohammad Hoesin General Hospital, Palembang.

2. Methods

The study design utilized a descriptive cross-sectional approach with prospective sampling. The study was carried out at Mohammad Hoesin General Hospital, Palembang from May to July 2021. The study incorporated all hospitalized patients with confirmed cases of COVID-19 in Dr. Mohammad Hoesin General Hospital, Palembang.

Meanwhile, exclusion criteria involved pregnant women, chemotherapy patients, and patients with drug allergies, traced through medical records and direct interviews with patients or their families.

The research instrument for data collection used Adverse Drug Reaction monitoring and the research form. Adverse drug reaction monitoring was performed through drug reconciliation and education by pharmacists to patients via phone calls.

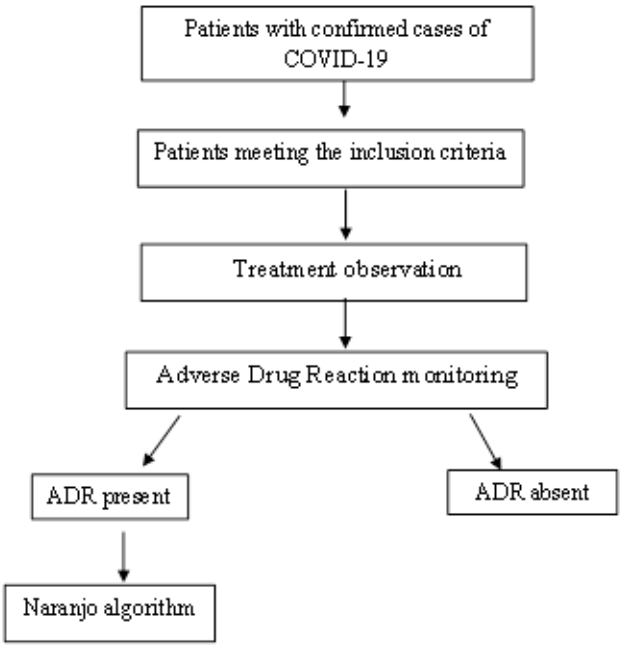

Figure 1. Research flow.

3. Results

The study was performed on hospitalized patients with confirmed COVID-19 cases in Dr. Mohammad Hoesin General Hospital, Palembang from May to July 2021. The steps of the data processing was demonstrated in Figure 2.

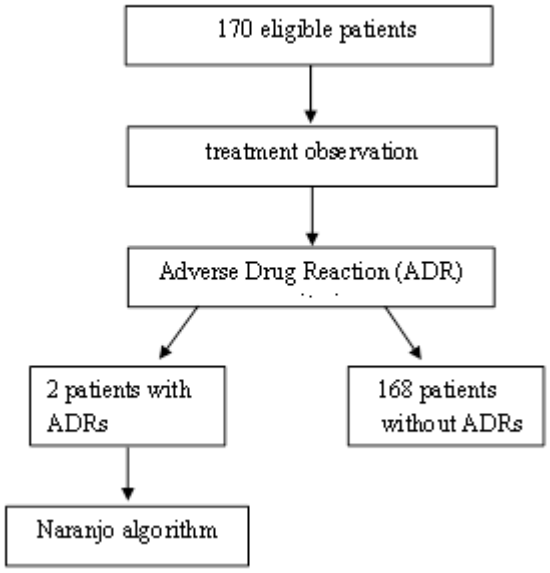

Figure 2. Data processing.

Adverse drug reaction of favipiravir

In the study, 2 patients reported side effects and scored 4 on Naranjo analysis, which mean that there was a possibility that the side effects were due to Favipiravir administration.

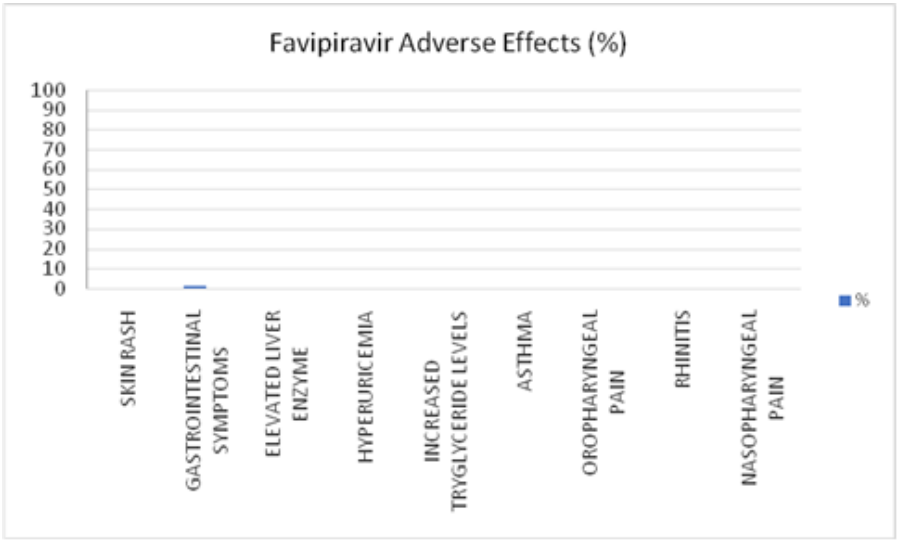

Figure 3. Side effects of favipiravir.

According to Figure 3, of 11 adverse drug reactions determined before data collection, the side effects found in the study were gastrointestinal symptoms (nausea, vomiting, decreased appetite), which were reported by 1.18% of patients (Table 1).

Table 1. Reported adverse events.

No	Side effects	Drug Culprit	Number of patients (%) (n=170)
1	Nausea, vomiting, decreased appetite	Favipiravir	2 (1.18%)

4. Discussion

The study of Adverse Drug Reaction monitoring in patients with confirmed cases of COVID-19 in RSUP Dr. Mohammad Hoesin General Hospital, Palembang, was done in May until July 2021. Adverse drug reactions described by confirmed cases of COVID-19 patients were gastrointestinal symptoms (1.18%). Two patients suffered from nausea, vomiting, and decreased appetite.

The first patient (ME) consumed Favipiravir on July 16-20, 2021. On the first day (July 16), the patient developed nausea and vomiting. The patient was then given domperidone 10 mg every 8 hours. The second patient (AD) consumed Favipiravir on July 3-7, 2021. Decreased appetite was reported on July 4, 2021, and he was treated with 1 tablet of Curcuma every 8 hours.

The adverse effects reported by the two patients were consequently analyzed with the Naranjo algorithm and score 4 was obtained, which means that the occurrence of the side effects was likely to be caused by Favipiravir. Score 4 was acquired because there were a few questions in the Naranjo algorithm that could not be confirmed, i.e drug concentration in the blood, no intervention regarding adding or subtractingFavipiravir doses, and no placebo was administered.

Some adverse effects could not be evaluated, such as an elevated liver enzyme, leukopenia, neutropenia, hyperuricemia, and increased triglyceride levels due to lack of laboratory assessment before and after Favipiravir usage. Moreover, several side effects were not found, such as skin rash, asthma, rhinitis, nasopharyngeal pain, and oropharyngeal pain.[9-10]

5. Conclusion

In our study, the adverse drug reaction of favipiravir in confirmed cases of COVID-19 patients were gastrointestinal symptoms. Two patients (1.18%) reported nausea, vomiting, and decreased appetite. The reported side effects were subsequently analyzed and scored 4 by the Naranjo algorithm, meaning that the side effects were likely to be caused by favipiravir.

6. References

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