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Hope and fear; Paxlovid for COVID-19 treatment: A Letter to the Editor

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Paxlovid is an effective oral treatment for COVID-19 patients that reduces mortality and can be administered in an outpatient setting, but it cannot substitute COVID-19 immunizations.

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Dear Editor,

The epidemic of COVID-19 has sparked a scientific revolution. Since the first reports of overburdened health systems and hospitals, outpatient treatments for symptomatic patients, especially for the high-risk group, have been developed. The two novel oral medications for COVID-19 treatment, including Molnupiravir and Paxlovid, can easily be administered at home and are significantly less expensive to manufacture than previous options that were discussed earlier in the pandemic. These medications are beneficial for nations with low vaccination coverage. This mini-review aims to investigate the therapeutically significant aspects of Paxlovid, its efficacy, metabolism, as well as application limitations. Paxlovid, a drug made by Pfizer company, is accessible for the treatment of COVID-19 patients with mild-to-moderate symptoms. It can also be used in people who were in contact with COVID-19 patients. Paxlovid is only available by prescription and should be taken within the first five days of COVID-19 symptoms(1). Paxlovid is a combination of two medications, including nirmatrelvir and ritonavir, that work together to prevent the spread of SARS-CoV-2. Paxlovid is administered as a five-day course taken orally twice daily for five days. It is forbidden

to take Paxlovid for more than five days in a row (1).

Paxlovid (ritonavir and nirmatrelvir)

Ritonavir is utilized as a pharmacokinetic enhancer for nirmatrelvir, which results in a higher nirmatrelvir systemic concentration. In the lab, nirmatrelvir works very well against SARS-CoV-2(2). Inhibition of SARS-CoV-2 viral replication was achieved by treating differentiated normal human bronchial epithelial cells with varying doses of nirmatrelvir (2). This was accomplished without evident cytotoxicity. Ritonavir is a CYP3A inhibitor that increases plasma levels of the medications with significant CYP3A metabolism such as pethidine, piroxicam, amiodarone, colchicine, clozapine, quetiapine, lovastatin, simvastatin, sildenafil, vardenafil, carbamazepine, and rifampin, which can lead to an elevated risk of serious or life-threatening side effects (3). Several HIV protease inhibitors that are commercially available and metabolized by CYP3A4 have been administered with ritonavir as a pharmacokinetic enhancer (4). Ritonavir's most common side effects are nausea, vomiting, diarrhea, changes in taste, tiredness, and rashes (5).

In addition, Paxlovid should not be taken by patients with severe hepatic impairment. Additionally, Paxlovid requires

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dose adjustment when is administered to patients with significant renal impairment (1). Nirmatrelvir is mainly excreted through the kidneys, whereas ritonavir is mainly eliminated through the liver (6). The recommended dose reduction for patients with an estimated glomerular filtration rate of $60 > \text{eGFR} \geq 30 \text{ mL/min}$ is 150 mg nirmatrelvir and 100 mg ritonavir twice daily for five days (7). Patients with an eGFR of less than 30 mL/min or significant hepatic impairment (7) should avoid taking Paxlovid. The T_{max} and $t_{1/2}$ of Nirmatrelvir and ritonavir in healthy persons following a single dose of 300 mg nirmatrelvir and a 100 mg ritonavir tablet were 3.00 hours and 3.98 hours, respectively(7).

According to the findings of a recent study, participants were placed into two groups: half received Paxlovid, and the other half received a placebo, both of which were administered orally every 12 hours for five days. On the 28th day after randomization, 0.8% of patients who received Paxlovid were admitted to the hospital, with no deaths among those who were treated within three days of symptom onset. In comparison, the placebo group had 7% (27/385) hospitalization and ended up with seven death cases. These findings were extremely statistically significant ($P= 0.0001$). Until the 28th day, there were no deaths in the Paxlovid group, compared to ten deaths (1.6%) in the placebo group (8).

Conclusion

Even though Nirmatrelvir is still effective against the mutated SARS-CoV-2 virus (9-11), it is not a substitute for vaccination. By increasing worldwide vaccination coverage, the risk of emerging new variants of coronavirus will be reduced. Medical treatment with Paxlovid can be used as a backup treatment for patients who do not have access to vaccination.

Authors' contribution

AP, MF and FK were the principal investigators of the study. MK, SB and FRJ revisited the manuscript and critically evaluated the intellectual contents. PP and NL conducted the secondary edit. All authors participated in preparing the final draft of the manuscript, revised the manuscript, and critically assessed the intellectual contents. All authors have read and approved the manuscript's content and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The authors have completely observed ethical issues (including plagiarism, data fabrication, and double publication).

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