Drug Interaction Between Co-packaged Nirmatrelvir-ritonavir and Tacrolimus might cause Hyponatremia and Tacrolimus Intoxication in Lung Transplant Recipients

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Case Report

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Abstract

COVID-19 infection in recipients of lung transplants could be lethal owing to the immunosuppressant agents. Antiviral agents should be administered to these patients. Co-packaged nirmatrelvir-ritonavir is a new agent that is used in combination with antiviral medications. Here, we report a case of high serum tacrolimus concentration and hyponatremia after co-packaged nirmatrelvir-ritonavir administration.

Introduction

The outcomes of lung transplant recipients infected with COVID-19 (Coronavirus disease 2019) are poor (1). As of yet, the appropriate treatment of COVID-19 infection in lung transplant recipients has not been established (2). Antiviral agents should be considered for lung transplant recipients.

Paxlovid is a new co-package that combines 300 mg of nirmatrelvir (two 150 mg tablets) with 100 mg of ritonavir (one 100 mg tablet). It passed the emergency use authorization by the Food and Drug Administration in December 2021. (3). The usage of paxlovid in lung transplant recipients is not a contraindication but requires close follow-up due to immunosuppressant agents such as tacrolimus. We present the case of a lung transplant recipient in whom combined paxlovid and tacrolimus caused severe hyponatremia. This study was approved by the institutional review board of Chang Gung Memorial Hospital with IRB No. 202201455B0.

Case Description

A 64-year-old woman underwent bilateral lung transplantation on 2021-10-07 due to bronchiolitis obliterans organizing pneumonia in Kaohsiung Chang Gung Memorial Hospital. She had received oral prednisolone (10 mg every 12 hours), mycophenolate mofetil (500 mg every 12 hours), and tacrolimus (4 mg every 12 hours) for the past 3 months. She confirmed COVID-19 infection on 2022-07-05 by rapid antigen testing with mild sore throat symptoms and visited clinics around her home receiving paxlovid treatment. She experienced weakness and was easily fatigued two days after receiving the treatment. She visited the emergency department. She was admitted to a separate ward containing all COVID-19 patients who did not require critical care. The laboratory data showed hyponatremia (115 mEq/L) and elevated tacrolimus levels (> 60ng/mL). We stopped prescribing tacrolimus. After paxlovid treatment was completed on 2022-07-10, hyponatremia improved gradually and tacrolimus levels returned to the therapeutic level. On 2022-07-12, we resumed the tacrolimus prescription (2 mg every 12 hours), mycophenolate mofetil (500 mg every 12 hours), and prednisolone (10 mg every 12 hours). She was discharged without any neurologic deficits on 2022-07-14. Laboratory findings during the clinical course are shown in Fig. 1.

Discussion
The interaction between paxlovid and tacrolimus is not well known (4, 5). However, paxlovid is a strong inhibitor of CYP3A induced by ritonavir. Tacrolimus is not contraindicated in combination therapies.

In conclusion, paxlovid combined with tacrolimus causes high serum tacrolimus levels and intoxication. Hyponatremia and acute renal failure may develop following combination therapy. If combination therapy is necessary, serum tacrolimus level should be closely monitored. If hyponatremia develops due to tacrolimus intoxication, aggressive correction of hyponatremia may not be necessary. More experience and reports are needed to identify drug interactions between paxlovid and other agents to prevent severe adverse effects.

**Abbreviations**

COVID-19: Coronavirus disease 2019

**Declarations**

Ethics approval and consent to participate

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Institutional Review Board of Chang Gung Memorial Hospital. In the retrospective design, the requirement of informed consent was waived and the study protocol was approved by the Ethics Committee of Chang Gung Memorial Hospital (Institutional Review Board number: 202201455B0).

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References


Figures
Figure 1

Drug Interaction between Paxlovid and Tacrolimus might cause Tacrolimus Intoxication and Hyponatremia