Letters to the Editor

Case Report: Nirmatrelvir/Ritonavir and Tacrolimus in a Kidney Transplant Recipient With COVID-19

Published online April 19, 2022.

To the Editor: A 41-year-old female patient with a history of renal transplant presented to the emergency department with nausea, vomiting, and tremors. The patient had been prescribed nirmatrelvir/ritonavir (Paxlovid) for COVID-19 and had taken five of the 10 total doses. The patient was also taking 4 mg of extended-release tacrolimus (Envarsus) per day. Initial laboratory results showed an acute renal injury and hyperkalemia. The tacrolimus level was more than 60 ng per mL (therapeutic range is 4 to 10 ng per mL); therefore, tacrolimus and nirmatrelvir/ritonavir were held.

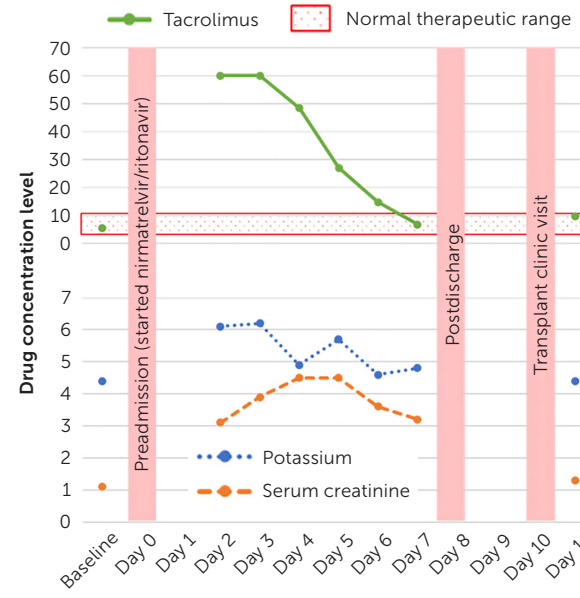
Figure 1 shows the patient's tacrolimus, potassium, and serum creatinine levels. The tacrolimus level decreased on day 3 of hospitalization. The patient was discharged on day 7 with tacrolimus and potassium returned to normal levels; the serum creatinine was elevated but returned to baseline three days after discharge.

In December 2021, the U.S. Food and Drug Administration granted emergency use authorization for the first oral antiviral drug treatment for COVID-19 (Paxlovid).[1] Nirmatrelvir/ritonavir is a combination of nirmatrelvir, a SARS-CoV-2 main protease inhibitor, and ritonavir, a potent cytochrome P-450 3A and P-glycoprotein inhibitor.[2] The emergency use authorization is for patients who have mild to moderate COVID-19 who are at high risk of progression to severe COVID-19.[2]

Solid organ transplant recipients are an at-risk population because they are prescribed immunosuppressant medications from the calcineurin inhibitor class (e.g., tacrolimus, cyclosporine) or mammalian target of rapamycin inhibitor class (e.g., everolimus, sirolimus).[3,4] All are substrates of cytochrome P-450 3A and P-glycoprotein. Concomitant administration of tacrolimus and ritonavir can slow the rate of tacrolimus metabolism, increasing its blood concentration to toxic levels.

Published recommendations can help clinicians avoid drug-drug interactions when prescribing nirmatrelvir/ritonavir.[5,6] It is recommended to hold all doses of calcineurin inhibitors during nirmatrelvir/ritonavir therapy. Prescribers should contact appropriate care team members (e.g., transplant coordinator) to schedule patient monitoring and follow-up.

FIGURE 1



Tacrolimus, potassium, and serum creatinine levels in a kidney transplant recipient who was prescribed nirmatrelvir/ritonavir for the treatment of COVID-19.

Note: Tacrolimus reference range is 4 to 10 ng per mL, potassium reference range is 3.5 to 5.5 mEq per L (3.50 to 5.50 mmol per L), and serum creatinine reference range is 0.5 to 1.2 mg per dL (44.20 to 106.08 mmol per L).

Kristen E. Lindauer, PharmD
Norfolk, Va.
Email: k_ingold2@yahoo.com

Ashlee G. Hamel, PharmD, BCPS
Norfolk, Va.

Author disclosure: No relevant financial relationships.

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This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

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Reevaluating the Measurement of Potency of Topical Corticosteroids

Original Article: Topical Corticosteroids: Choice and Application

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To the Editor: The article by Drs. Stacey and McEleney references the traditional use of vasoconstriction assays to determine potency. These assays were originally described in 1962 and have evolved only minimally since then.[1] It was hypothesized that the degree of skin blanching correlated with the degree of cutaneous absorption of topical corticosteroids and clinical effectiveness. Although advances in quantification have been developed, vasoconstriction still determines the potency of topical corticosteroids.[2]

However, the vasoconstriction assay lacks standardization and is limited in its ability to correlate potency to clinical effectiveness. The mechanisms of action of topical corticosteroids are hypothesized to be multifactorial, including antiproliferation, antipruritic, immunomodulation, and vasoconstriction. Vasoconstriction assays may not be the ideal measurement of potency and clinical effectiveness.[3-5]

Data on vasoconstriction assays of the skin of people of color are extremely limited, and most studies measuring the effects of medications on the skin are predominately in White patients.[1,6] Aging affects skin characteristics, including thinning of the epidermis and decreased vascularity of the dermis. Although older adults have not traditionally been included in vasoconstriction assay studies, physiologically, changes attributed to aging are likely to affect these assays and may alter the pharmacokinetics of topical corticosteroids in older adults. This variable is not accounted for in the current classification of the potency of topical steroids.

Family physicians should recognize the significant limitations of current standards of measurements of topical corticosteroid potency because these may not reflect the variety of skin colors and ages of our patients.

Alyssa D'Addezio, MD
Pittsburgh, Pa.
Email: daddezioas@upmc.edu

Gretchen Shelesky, MD
Pittsburgh, Pa.

Author disclosure: No relevant financial relationships.

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In Reply: Thank you for highlighting these significant limitations of the vasoconstriction assay. Some studies support ordering the clinical potency of topical corticosteroids as determined by the vasoconstriction assay.[1-4] Current practice is to prescribe topical corticosteroids according to potency charts, which were created using data gathered from their performance on the vasoconstriction assay. No alternative model has been widely adopted as an acceptable replacement.

Despite its disadvantages, the vasoconstriction assay has several advantages. It assesses how effectively the corticosteroid is absorbed and how the compound activates steroid receptors.[5] It is relatively inexpensive and easy to perform in a standardized setting. Data exist for each steroid preparation's performance on the vasoconstriction assay. There are relatively sparse data comparing the numerous preparations for pathologies, ages, and the skin types you describe.

Stephen K. Stacey, DO
La Crosse, Wis.
Email: Stacey.stephen@mayo.edu

Mark McEleney, MD, MME, CAQSM
La Crosse, Wis.

Author disclosure: No relevant financial relationships.

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