LETTER TO THE EDITOR

Tacrolimus-associated Pruritus: Role of a Clinical Pharmacologist in the Management

Saibal Das[1], Saptarshi Bishnu[2]

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Sir,

We read the case report on tacrolimus-associated pruritus by Sen et al. and was intrigued by the suggestions by the authors of clinical pharmacological consultation in cases of suspected drug-related problems.[1] A 46-year-old male with comorbidities like type 2 diabetes and hypertension underwent ABO-incompatible liver transplantation in January 2020. He was on multiple drugs, such as basal-bolus insulin (long-acting glargine insulin and rapid-acting insulin aspart), tacrolimus 3 mg twice daily, prednisolone 10 mg twice daily, mycophenolate mofetil 250 mg once daily, amlodipine 10 mg once daily, and ursodeoxycholic acid 300 mg twice daily. The patient visited a dermatologist with a complaint of generalized itching since March 2020. He was managed conservatively with anti-allergic drugs and emollient. However, the clinical condition did not improve. Liver function test showed normal serum bilirubin, alanine transaminase, aspartate transaminase, and alkaline phosphatase levels. Magnetic resonance cholangiopancreatography did not reveal any significant dilatation of the intrahepatic bile ducts, although small perihepatic fluid pockets were seen. Besides, the blood glucose level was fluctuating, and there were several episodes of postprandial hyperglycemia (glucose level, 350–400 mg/dL) with evening and night-time hypoglycemic episodes (glucose levels, 40–70 mg/dL). Itching intensified with localized skin swelling around the insulin administration site since early June 2020. The liver function test was found to be within the normal limit during that time period.

The patient went for a consultation with a clinical pharmacologist via telemedicine. The occurrence of an error in insulin dosing and administration time was noted—the patient took glargine insulin thrice daily instead of rapid-acting aspart insulin. The same was rectified; however, the itching persisted. The blood level of tacrolimus was towards the higher therapeutic range (14 mg/dL). The liver and renal functions were within normal limits. The clinical pharmacological advisory suggested replacing tacrolimus with everolimus, along with a consultation with the liver transplantation physician. Compliance with the advice was rewarded with the resolution of symptoms and resumption of glycemic control in 2 weeks.

The success of solid organ transplantation (SOT) depends, in part, on immunosuppressive therapy.[2,3] Tacrolimus is a calcineurin inhibitor (CNI) and macrolide antibiotic that is frequently used as an immunosuppressant following solid organ transplantation. It inhibits interleukin-2-mediated cell proliferation. Its therapeutic window is narrow.[4,5] CNIs lead to long-term complications, such as nephrotoxicity and increased risk for hepatocellular carcinoma recurrence.[6–8] This warrants an alternative approach to minimize chronic CNI exposure, for example, the use of mammalian target of rapamycin (mTOR) inhibitor, such as everolimus.[8]

The problems associated with this case were of two types. One was drug administration error related to both long- and rapid-acting insulin, which was promptly solved. The other problem of generalized itching was solved with the discontinuation of tacrolimus and switching to everolimus. Although everolimus is structurally similar to tacrolimus, it has a different mechanism of action (mTOR inhibitor).[9] This case highlights the importance of a clinical pharmacologist consultation in managing drug-related problems in routine patient care. The opinion of a clinical pharmacologist can be routinely used to ensure a favorable clinical outcome.

[1]Independent Clinical Pharmacology Consultant, Kolkata, West Bengal, India

[2]Consultant Hepatologist and Liver Transplant Physician, Apollo Hospital, Chennai, Tamil Nadu, India

Corresponding Author: Saibal Das, Independent Clinical Pharmacology Consultant, Kolkata, West Bengal, India, Phone: +91 9433429401, e-mail: saibaldas123@gmail.com

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