e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(6); 708-709

Original Research Article

Conversion from Calcineurin Inhibitors to mTOR Inhibitors in Renal Allograft Recipients: A Single Center Experience

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Received: 01-03-2026 / Revised: 15-04-2026 / Accepted: 21-05-2026
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Conflict of interest: Nil

Abstract

Background: Calcineurin inhibitors (CNIs) are the standard of care for maintenance immunosuppression in renal transplantation but are associated with long-term nephrotoxicity and other systemic complications. Mammalian target of rapamycin (mTOR) inhibitors offer a non-nephrotoxic alternative.

Methods: We conducted a retrospective analysis of 151 renal transplant recipients between February 2022 and June 2024 to evaluate the outcomes of patients converted from CNIs to mTOR inhibitors.

Results: Eight patients required conversion. Indications included drug-induced nephrotoxicity, Posterior Reversible Encephalopathy Syndrome (PRES), and Hemolytic Uremic Syndrome (HUS). Following conversion to everolimus, serum creatinine levels returned to baseline, and neurological symptoms resolved without recurrence.

Conclusion: Early conversion to mTOR inhibitors is an effective strategy for managing CNI-related complications while preserving graft function.

Keywords: mTOR inhibitor, Calcineurin inhibitors, renal allograft transplant.

DOI: 10.25258/ijcpr.18.6.117

Introduction

For over four decades, calcineurin inhibitors (CNIs), specifically cyclosporine A (CsA) and tacrolimus (TAC), have remained the cornerstone of maintenance immunosuppressive therapy in renal transplantation [1,2]. While highly effective at preventing acute rejection, prolonged exposure often leads to chronic nephrotoxicity and various extra-renal adverse effects. The advent of potent mammalian target of rapamycin (mTOR) inhibitors, such as everolimus, provides a clinical pathway to reduce or withdraw CNI therapy early post-transplantation, thereby mitigating these risks [1].

Material and Methods

A retrospective study was conducted at a single center (Apollo Multispeciality Hospital, Kolkata) involving all renal transplant recipients between February 2022 and June 2024. All patients underwent ABO-compatible transplants. Initial induction therapy consisted of antithymocyte globulin (ATG) or methylprednisolone (MPS), combined with tacrolimus and mycophenolate mofetil (MMF). Maintenance therapy was initially standardized to a triple regimen of tacrolimus, MMF, and steroids.

Results

Out of 151 patients, 8 (5.3%) required conversion from tacrolimus to the mTOR inhibitor everolimus due to adverse clinical indications.

Patient Characteristics: The cohort included five males and three females, with ages ranging from 10 to 60 years.

Indications for Conversion:

- **Drug-induced Nephrotoxicity:** 4 patients (one associated with hyponatremia and another with anemia/loose motion).
- **Posterior Reversible Encephalopathy Syndrome (PRES):** 2 patients (occurring 5 days post-transplant).
- **Atypical Hemolytic Uremic Syndrome (HUS):** 2 patients.

Clinical Outcomes:

The mean creatinine at discharge was approximately 1.0 mg/dl. At the time of

conversion, creatinine levels had risen (up to 2.4 mg/dl in HUS cases). Post-conversion, creatinine levels returned to baseline in all 8 patients. Notably, no new episodes of PRES were recorded following the switch. Additionally, two patients showed significant improvement in hemoglobin levels post-conversion.

Discussion

Our findings align with the growing body of evidence suggesting that mTOR inhibitors can successfully replace CNIs when toxicity occurs.

In this series, conversion was not only effective for nephrotoxicity but also served as a critical intervention for rare but severe neurological and hematological complications like PRES and HUS.

The restoration of baseline creatinine suggests that the renal impairment was reversible upon removal of the CNI.

Conclusion

Conversion from tacrolimus to everolimus is a viable and effective strategy for renal transplant recipients experiencing CNI-related complications. This approach preserves allograft function and manages systemic toxicities without compromising the immunosuppressive efficacy.

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