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mTOR Inhibitors versus CNI in Kidney Transplant

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Abstract

Transplantation is the renal replacement therapy of choice for patients with end stage renal disease (ESRD). However, not all patients are suitable candidates for transplantation, and suitability is often determined by the risks of receiving graft versus the risks of not receiving a graft**.**

Keywords: mTOR; CNI; Kidney

Introduction

Immunosuppressive therapy after kidney transplantation is based on calcineurin inhibitors (CNI). **(1)**. In most cases CNI therapy is combined with mycophenolate and steroids. In spite of good short-term results this therapy is associated with long-term toxicities, graft loss and patient death. Therefore, alternative immunosuppressive strategies are needed that combine excellent efficacy with low incidences of long-term adverse outcome (**2).**

The mammalian target of rapamycin (mTOR) inhibitor class of immunosuppressive drugs were introduced more than 15 years ago as a new opportunity to create selective antirejection therapy in solid organ transplantation. In particular, absence of early nephrotoxicity seemed to provide an important opportunity to minimize or replace the calcineurin inhibitor (CNI) drugs, which were plagued by progressive nephrotoxicity when administered at doses needed to prevent rejection **(3)**

The post-transplant period is associated with a wide range of complications, including cardiovascular (CV), metabolic, oncologic, infectious, immunological, surgical, osseous, and hematologic complications **(4)**

The long-term graft survival in renal transplantation results is still controversial, the toxicity and adverse reactions of the immunosuppressive drugs are implicated, as well as cellular and humoral antigen-specific immune mechanisms; **(5)**therefore, different strategies for adapting immunosuppression are used to reduce the complications associated with the use of these drugs. Calcineurin inhibitors (CNI) require an adequate dose-dependent concentration leading to the appearance of drug-related adverse reactions. **(6)** The variability in the required dose of CNI leads to minimization strategies that do not result in a higher acute rejection (AR) incidence when compared to other immunosuppressive agents. **(7-8)** Early steroid withdrawal is another strategy, although with an increase in AR, but without an impact on the function and survival of the renal graft. **(9)**The reduction of mycophenolate mofetil to 1.5 g/day seems to be a therapeutic option, decreasing the infectious, hematological and gastrointestinal adverse reactions. **(10)**

All the study subjects will be subjected to the following:

- Complete clinical history taking.
  - Careful clinical evaluation
  - Laboratory investigations; they will include:
    - Complete blood count (CBC) Determined by automated cell counter SYSMEX KX-2iN (TAO Medical Incorporation, Japan).
    - Renal function tests (RFTs) Will be assayed using fully automated clinical chemistry autoanalyzer system Konelab 20i (Thermo-Electron Incorporation, Finland).

- Liver function tests (LFTs) Will be assayed using fully automated clinical chemistry auto analyzer system Konelab 20i (Thermo-Electron Incorporation, Finland).
- Fasting blood glucose (FBG) (fasting 8 hours).

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