Tacrolimus in Delayed Graft Function in Cadaveric Renal Transplantation

Mee Sook Lee, M.D.*, Jai Won Chang, M.D., Duck Jong Han, M.D.†
Eunsil Yu, M.D.†, Won Seok Yang, M.D. and Su-Kil Park, M.D.

Department of Internal Medicine*, Jeongseup Asan Hospital,
Department of Internal Medicine, General Surgery† and Pathology†,
College of Medicine, University of Ulsan, Seoul, Korea

Abstract

Background: In the presence of anticipated or established acute tubular necrosis (ATN) immediately after cadaveric kidney transplantation, induction with monoclonal or polyclonal antibody is recommended in preparation of increased risk of acute rejection caused by ATN. Tacrolimus is a potent immunosuppressive agent than cyclosporine. In this study, we analyzed retrospectively the clinical outcome of patients who had taken tacrolimus as a replacement of cyclosporine in the period of delayed graft function (DGF) to determine the eligibility of tacrolimus instead of antilymphocyte antibody in this situation.

Methods: Between March 1, 1991 and August 31, 2000, DGF developed in eighteen first cadaveric renal transplant recipients in our center. During DGF period, twelve patients received tacrolimus based immunosuppression without OKT3. We reviewed the complete clinical course of the 12 patients.

Results: Among the 12 patients, 1 patient underwent graft nephrectomy at postoperative 27 days, because of poor renal function and concomitant aspergillosis infection. In the remaining 11 patients, however, for whom tacrolimus was maintained continuously without OKT3 therapy, renal function was recovered successfully. One acute rejection developed at postoperative 15 months. One patient died at postoperative 5 months with functioning graft. One-year graft survival rate was 83%.

Conclusion: Tacrolimus could be used in replacement of cyclosporine for the prevention of acute rejection in DGF. This could provide a graft survival comparable to that by the monoclonal or polyclonal antibodies without the potential risk of life-threatening side effects in this situation. (Korean J Nephrol 2002;21(4):667–674)

Key Words: Tacrolimus, Acute tubular necrosis, Delayed graft function, Cadaveric renal transplantation, Nephrotoxicity

INTRODUCTION

Delayed graft function (DGF), the situation in which a newly transplanted kidney does not func-
tion well, is frequently encountered in cadaveric renal transplantation\(^1\). The major cause of it is acute tubular necrosis (ATN). Accelerated rejection and technical complications such as vascular thrombosis are the other rare causes of DGF\(^2\).

Due to the ischemic insults received before retrieval, during cold preservation or during the transplant procedure\(^3\), up to 8–50% of primary cadaveric renal transplant recipients suffer from ATN in early transplant periods\(^4\). Though most of the ATN will resolve spontaneously and needs only conservative management and dialysis, there are some problems in the administration of immunosuppressive agents to prevent rejection of the transplanted kidney. The triple immunosuppressive regimen of cyclosporine (CsA), azathioprine and prednisolone is usually sufficient for cadaveric renal transplant recipients whose renal allograft works well immediately after transplantation. In patients with ATN, CsA causes the delay in the recovery of renal function due to its nephrotoxicity\(^5\). In addition, ATN increases the risk of acute rejection in transplanted kidney\(^6\). Thus, in the presence of ATN, CsA administration should be avoided and immunosuppressive protocol needs to be modified, adopting a more potent and less nephrotoxic agent until the recovery of renal function. Some transplant centers routinely use monoclonal or polyclonal antibody induction therapy in the presence of anticipated or established ATN. In some patients, however, the administration of the OKT3 or ATGAM causes the serious side effects such as capillary leakage syndrome, severe infection and lymphoproliferative disorders\(^7,8\).

Tacrolimus is a macrolide compound isolated from Streptomyces tsukubaensis, a soil fungus that can be found in Northern Japan\(^9\). It is more potent in immunosuppressive activity than CsA, with similar nephrotoxicity.

In this study, we analyzed retrospectively the clinical outcome of patients who had taken tacrolimus as a replacement of CsA in the period of DGF to determine the eligibility of tacrolimus instead of antilymphocyte antibody in this situation.

**MATERIALS AND METHODS**

1. **Patient population**

Between March 1, 1991 and August 31, 2000, 316 cadaveric renal transplantations were performed in Asan Medical Center. Twenty-three second cadaveric renal transplant patients were excluded from this study. DGF was developed in eighteen renal transplant recipients among the 293 first cadaveric renal transplant recipients, whose etiology was identified as ATN.

2. **Delayed graft function and acute tubular necrosis**

DGF was defined as a lack of diuresis or the need for dialysis within the first 7 days after transplantation. Patients with pre- and post-rejection causes of graft dysfunction, which include dehydration, hypotension, bleeding, vascular thrombosis and urological complications, such as urinary leakages, were excluded.

ATN was defined by the following criteria: (1) failure of the serum creatinine level to decrease from baseline and (2) radionuclide scan within 24 to 48 hours of implantation demonstrating good perfusion of the allograft but poor function, without evidence of urine leak or obstruction and/or (3) the findings of ATN in transplanted kidney biopsy. ATN was diagnosed clinically by (1), (2), transplant ultrasound without evidence of urinary obstruction and renal arterial thrombosis and a requirement of at least one hemodialysis treatment during the first postoperative week. ATN was considered to have resolved as of the first day the serum creatinine level began to decrease in the absence of dialysis.

Graft loss was defined by a return to chronic dialysis or patient death, even if the allograft