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Use of Anti-T- Lymphocyte Globulin as an Induction Agent in Kidney Transplantation

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Abstract

Aim: Anti-T-lymphocyte globulins (ATG) are most commonly used as induction agents in kidney transplantation (KT). In our study, we investigated the outcomes of ATG induction in kidney transplantation.

Material and Method: Between April 2014 and April 2019 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 100 patients with kidney transplantation after ATG induction were studied retrospectively.

Results: The mean age was 38.3±15.6 years. 68 (68%) patients were male and 32 (32%) patients were female. Mean ATG dosages per kilogram were 1.57±0.17 mg/kg. Mean cumulative ATG dosages per patient were 370±140 mg. Mean follow-up was 29.1±15 months. During follow-up, there were 4 graft loss, and 5 patients died.

Conclusions: Short-term and low-dose ATG induction appears to be successful and most favorable in kidney transplantation.

Keywords: Kidney transplantation; Anti-t- lymphocyte globülin; Induction

Introduction

Kidney transplantation is the treatment of choice in patients with end-stage renal disease when compared with chronic dialysis therapy in relevant to patient survival and quality of life [1]. Rejection is most important complications in kidney transplantation. Immunosuppressive and induction treatment are used to avoid rejection. Induction during the perioperative period lowers acute rejection [2]. Anti-interleukin (IL) 2 receptor antagonists and anti-lymphocyte antibodies are the most frequent induction therapies [3]. If the rejection episode is defined as steroid-resistant, used the ATG [4,5]. The aim of our study was to evaluate the outcomes of ATG induction in kidney transplantation.

Material and Method

Between April 2014 and April 2019 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 100 patients with kidney transplantation after ATG induction were studied retrospectively.

Immunosuppression

All patients received quadruple sequential immunosuppression consisting of induction with ATG, followed by triple immunosuppressive therapy.

All this patients were given ATG at the intraoperative period and continues postoperative 2 days.The ATG was administered intravenously and premedication with steroid, paracetamol and antihistamine drugs.The dosage was adjusted according to platelet and lymphocyte count. 2 mg/kg dosage was administered if the platelet and lymphocyte counts were >100,000 and 100/mm^3, respectively. 1.5 mg/kg dosage was administered if the platelet and leukocyte counts were <100,000 and 100/mm^3, respectively.

The patient will be used as a standard immunosuppressive therapy for life-long calcineurin inhibitors (tacrolimus or cyclosporine). Mycophenolate Mofetil or Mycophenolate Sodium to be used in the first year, Prednisolone to be used in the first third months.

All rejection episodes were diagnosed by renal biopsy confirmed or were characterised by an increase in serum creatinine levels by 30% or more from the baseline. All episodes were initially treated with intravenous methyl prednisolone (MP) at a dose of 500 mg for 3 consecutive days. The rejection episode was defined as steroid resistant and was treated with ATG. In patients whose creatinine levels are increasing, additional 5 daily doses (1.5-2 mg/kg) of ATG was administered.

Opportunistic ınfection prophylaxis

In our clinic, patients were given the 900 mg/day Valganciclovir for the first 100 days in CMV prophylaxis. Patients were given the 400 mg/day Sulfamethoxazole/trimethoprim prophylaxis for Pneumocystis Pneumonia and urinary tract infection was administered for 6 months. Patients were given the 100 mg/day Flukonazole prophylaxis for candida prophylaxis.

Patients received control once a week for the first month after discharge, and once every 15 days for the second month and monthly for the following months.

Statistical analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Continuous variables which have normal distribution were presented as mean ± Standard deviation. Statistical analysis for the parametric variables was performed by the Student's

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Table 1: Comparison of our results with literature results.

	ATG Dose (mg/kg/day)	Acute Rejection Rate (%)	CMV Infection Rate (%)	Malignancies Rate (%)	Graft Survival Rate (1 Years) (%)	Patient Survival Rate (1 Years) (%)
Gaber et al.	5.29±1.88	6.5	4.2	0.4	98.4	98.2
Yilmaz et al.	5.1± 2.7	29.1	12	1	97.6	98.3
Our Study	1.57±0.17	9	-	-	98	98

T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as $p<0.05$.

Results

Mean age was 38.3±15.6 years, 68 (68%) patients were male and 32 (32%) patients were female. Twelve patients were younger than 18 years. The mean body mass index was 25.2±5.6 kg/m^2, preoperative creatinine level was 7.1±1.5 mg/dL, postoperative first month creatinine level was 0.89±0.26 mg/dL. The 27 (27%) patients were done preemptive transplantation. Ten (10%) deceased donor and ninety (90%) living donors were used.

The indications for kidney transplantation were; 37 (37%) patients had no cause, 32 (32%) had diabetes mellitus, 14 (14%) had hypertension, 12 (12%) had chronic glomerulonephritis, 3 (3%) patient had polycystic kidney disease and 2 (2%) other causes (Alport syndrome, vesicoureteral reflux, etc.).

Mean Warm ischemia time was 90.5 ± 21 second, Mean Cold ischemia time was 53.5±14 minutes, Class I and class II panel reactive antibody (PRA) positive patients were numbered as 4 (4%) and 5 (5%), respectively. Within the first year of transplantation, acute rejection rate was 9% (9 patients).

Mean ATG dosages per kilogram were 1.57±0.17 mg/kg. Mean cumulative ATG dosages per patient were 370±140 mg.

Mean follow-up was 29.1±15 months. There was not detected tumor or infections, due to ATG induction in follow up.

During follow-up, there was 4 grafts loss, and 5 patients died. Graft survival rates for 1 and 5 years were 98% and 96%, respectively. Patient survival rates for 1 and 5 years were 98% and 95%, respectively. There was four grafts loss due to humoral rejection. Five patients died with cardiovascular disease.

Discussion

Kidney transplantation is the treatment of choice in patients with end-stage renal disease [1]. Immunological and non-immunological factors influence the graft and patient survival in kidney transplantations. Rejection is the most important immunological complication in kidney transplantation. Immunosuppressive and induction treatments are used to avoid rejection [2]. The primary aim is to reduce the risk of acute rejection [6]. The incidence of acute rejection rates were reported by 5-45% [7,8]. Hardinger et al. [9] reported that the incidence of acute rejection rate was 5%, Gaber et al [10] reported that the incidence of acute rejection rate was 6.5%, Yilmaz et al. [11] reported that the incidence of acute rejection rate was 29.1% and in our study, the incidence of acute rejection rate was 9%.

T lymphocyte depleting agents have been used in kidney transplantation since the 1980s [12]. ATG is the most important from these agents [2]. Currently, lymphocyte depleting agents (ATG) are used in the majority (60%) of kidney transplantations [7].

Intraoperative ATG induction decrease delayed graft function by blocking adhesion molecules and decrease ischemia reperfusion injury by T cell depleting [13].

In our clinic, all patients received quadruple sequential immunosuppression consisting of induction with ATG, followed by triple immunosuppressive therapy. In our protocol, the ATG induction begins in the intraoperative period and continues postoperative 2 days. In patients whose creatinine levels are increasing, additional 5 daily doses (1.5-2 mg/kg) of ATG was administered.

ATG induction must be careful while. Long-term and high-dose ATG induction can increase the incidence of bacterial-viral-fungal infections rates and malignancy rates [14-17].

In our study, there was no increase in bacterial-viral- fungal infections and malignancies.

Gaber et al (10) had reported a 4.2% incidence for Cytomegalovirus (CMV) infections. Yilmaz et al (11) had reported a 12% incidence for CMV infections. In our study, 4% patients had CMV infection diagnosed with CMV DNA positivity.

Polyomavirus infection diagnosed with blood BK DNA positivity was 7% in our study, similar to results from Schenker et al. [18] (5%), but in our study 1 patient had biopsy confirmed polyoma nephropathy.

Posttransplant lymphoproliferative disorders (PTLD) ad lymphoma are a rare but life threating complication after solid organ transplantation. Immunosuppression and Epstein Barr virus (EBV) are the risk factors (29) Hardinger et al. [9] showed that there is no increase in the incidence of PTLD in a prospective, randomized trial with a follow-up of 10 years. Opelz at al. [16] reported a higher cumulative 3-year incidence of lymphoma with ATG 1%. In our study, there was no PTLD or Lymphoma.

Gaber et al. [10] had reported low post-transplant complications with ATG induction patient and graft survival rates at 1 year were 98.4% and 98.2%, respectively.

Yilmaz et al. [11] had reported graft survival rates at 1 year were 97.6% and 98.3%, respectively.

In our study, the graft survival rates were 98% and 91% for 1 and 5 years, respectively. The patient survival rates were 98% and 95% for 1 and 5 years,respectively,

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

Conclusion

Despite the limitations described in discussion, in this study, graft loss and mortality results, concerning are proper the results in literature. Short-term and low-dose ATG induction appears to be successful and most favorable in kidney transplantation.

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