Thymoglobulin Induction Therapy in Deceased Donor Kidney Transplantation: Single-Center Experience in Mexico

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ABSTRACT

Background. Induction therapy is used to reduce the incidence of graft rejection and delayed graft function. Thymoglobulin is the most used inductor agent in deceased donor kidney transplantation due to its lower rejection and delayed graft function rates.

Methods. Retrospective study of patients who underwent deceased donor kidney transplantation from 2011 to 2014. Efficacy and safety outcomes evaluated were primary graft nonfunction, delayed graft function, acute rejection episodes, the lowest leukocyte count during the induction, adverse effects, eGFR, and patient and graft survival. $P < .05$ was considered statistically significant.

Results. A total of 42 patients were registered. Of these, 51.7% were female, with a mean age of 36.4 ± 11.1 years. Mean dialysis time was 112.4 ± 365 months. Mean donor age was 33.7 ± 13.1 years. Of the registered patients, 14.3% were extended criteria donors and 23.8% high-risk. Mean thymoglobulin dose was 4.4 ± 0.8 mg/kg. Primary graft nonfunction was 2.4%. Nineteen percent presented with delayed graft function and 19% with acute rejection. Mean lowest leukocyte count was of 4.6 ± 1.5 × 10^3 cells/mm^3. Mean hospital stay was 11.3 ± 6.3 days. Adverse effects were seen in 59.5% of registered patients, whereas graft survival 1 year and 3 years after transplantation was 85.3% and 56.9%, respectively. Patient survival 1 year and 3 years after transplantation was 85.3% and 53.8%, respectively. Patients who received a higher dose (>4.4 mg/kg) had a shorter hospital stay (9.4 ± 4.6 and 8.1 ± 2.3) than those who received lower dose (13.6 ± 7.9 and 12.8 ± 7.4; $P < .05$).

Conclusion. Thymoglobulin induction at doses near 5 mg/kg in deceased donor kidney transplant is efficient and secure at our center.

INDUCTION therapy is utilized at the beginning of transplantation to reduce the incidence of graft rejection and delayed graft function [1]. Nowadays, thymoglobulin is the most used inductor agent in deceased donor kidney transplantation [2]. Previous studies have shown excellent results with thymoglobulin induction therapy in deceased donor kidney transplantation with low acute rejection rates, low delayed graft function, good patient and graft survival, and a tolerable safety profile [3–8]. The aim of this study was to evaluate the efficacy and security of thymoglobulin induction in patients who underwent deceased donor kidney transplant at our center.

METHODS

A retrospective study of patients who underwent deceased donor kidney transplantation from October 2011 to October 2014 and approved by the ethics and research committee was carried out at our institution. Donor and recipient sociodemographic and anthropometric data were recorded. Efficacy and safety outcomes evaluated were primary graft nonfunction, delayed graft function (DGF), dialysis during first week after transplantation, acute

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rejection episodes during the first year after transplantation (biopsy proven), lowest leukocyte count during the use of thymoglobulin, adverse effects, estimated glomerular filtration rate (eGFR) (using MDRD-4 formula), as well as patient and graft survival. $P < .05$ was considered statistically significant using SPSS software version 21 (IBM Corp., Armonk, N.Y., United States).

RESULTS

Forty-two patients were registered; of these, 51.7% were female, with a mean age of 36.4 years, and a mean BMI of 22.06 kg/m^2. Mean donor age was 33.7 years (9–54 years). Three patients had prior transplants, 14.3% of the organs corresponded to extended criteria donors and 23.8% of the transplants were considered high-risk (panel-reactive antibodies >30%, retransplant, extended criteria donors and cold ischemia time >24 hrs). Donor and recipient data are depicted in Table 1. Cold ischemia time (CIT) had a mean of 14 ± 6.1 hours (4–30). Mean dose of thymoglobulin was 4.4 ± 0.8 mg/kg (mode 5 mg/kg) (2.4–7.9). All patients received mycophenolate mofetil (MMF) and steroids as initial immunosuppression. Most common calcineurin inhibitor used was cyclosporine in 59.5% (n = 25). Primary graft nonfunction was 2.4%, and 19% had delayed graft function. The acute rejection rate during the first year was 19%. The lowest leukocyte count during induction had a mean of 4.6 ± 1.5 × 10^3 cells/mm^3 (2.5–9). None of the patients presented with leukopenia (<2.5 × 103 cells/mm^3). Mean hospital stay was 11.3 ± 6.3 days (2–31). In total, 59.5% of patients presented adverse effects, mostly infectious (n = 7) or immunological (rejection) (n = 8). There was no cytomegalovirus (CMV) disease in the population study. The mean eGFR at 1 year after transplant was 57.2 ± 20.6 mL/min (19–106.9), and at 2 years after transplant was 56.2 ± 26.2 ml/min (23.3–88.9). Current immunosuppression management in all patients was as follows: cyclosporine/MMF/steroids in 19 (45.2%) patients; tacrolimus/MMF/steroids in 16 (38.1%) patients, and sirolimus/MMF/steroids in 7 (16.7%) patients.

Death censored graft survival at 1 and 3 years after transplantation was 85.3% and 53.9% respectively (Fig 1A), and patient survival at 1 and 3 years after transplant was 85.3% and 56.8%, respectively. To determine the effect of the total dose of thymoglobulin (mg/kg), patients were divided into those who had a dose of thymoglobulin lower than the mean dose (4.4 mg/kg) (n = 17) or a dose lower than the mode (5 mg/kg) (n = 29). Patients with higher doses of thymoglobulin (>4.4 and 5 mg/kg) had shorter hospital stays (9.4 ± 4.6 and 8.1 ± 2.3, respectively) than patients with lower doses of thymoglobulin (<4.4 and 5 mg/kg) (13.6 ± 7.9 and 12.8 ± 7.4, respectively) ($P < .05$). There were no differences in mean graft survival between higher (>4.4 mg/kg: 33.12 ± 3.47 [95% CI 26.31–39.92]; >5 mg/kg: 30.83 ± 2.84 95% CI [25.26–36.40]) and lower doses (<4.4 mg/kg: 20.88 ± 2.16 95% CI [16.65–25.11]; <5 mg/kg: 34.13 ± 2.79 95% CI [28.66–39.60]) ($P = .62$ by log rank) (Figs 1B and 1C). No differences were noted in graft nonfunction, DGF, acute rejection episodes during the first year after transplantation, lowest leukocyte count during the use of thymoglobulin, adverse effects, and eGFR.

Table 1. Donor and Receptor Characteristics

	Mean ± SD (range)	Percentage (n)
Donors		
Age (y)	33.7 ± 13.1 (9–54)	
Sex		
Female		33.3% (14)
Male		66.7% (28)
BMI (kg/m^2)	26.7 ± 4.03 (20.8–36.6)	
Donor creatinine (mg/dL)	1.18 ± 0.41 (0.7–1.9)	
Donor cause of death		
Trauma		71.4% (30)
Stroke		28.6% (12)
Extended criteria donor		14.3% (6)
Recipients		
Age	36.4 ± 11.1 (12–59)	
Sex		
Female		51.7% (24)
Male		42.9% (18)
BMI	22.06 ± 3.05 (15.5–30)	
Diabetes		9.5% (4)
Time on dialysis	112.4 ± 36.3 (8–192)	
Retransplant		7.1% (3)
Mean PRA%	10.3 ± 7.3 (0–23)	
HLA match	1.02 ± 0.81 (0–3)	
High-risk transplant		23.8% (10)
PRA >30%		0%
ECD		14.3% (6)
Retransplant		7.1% (3)
Cold ischemia time > 24 hours		7.1% (3)
Immunosuppression		
At transplantation:		
Mycophenolate mofetil		100% (42)
Steroids		100% (42)
Cyclosporine		59.5% (25)
Tacrolimus		40.5% (17)
Current:		
Mycophenolate mofetil		100% (42)
Steroids		100% (42)
Cyclosporine		45.2% (19)
Tacrolimus		38.1% (16)
Sirolimus		16.7% (7)

Abbreviations: BMI, body mass index; ECD, extended criteria donors; HLA, human leukocyte antigen; PRA, panel reactive antibodies; SD, standard deviation.

DISCUSSION

The results of our study grows the body of evidence that good patient and graft survival and good efficacy and safety outcomes are obtained when thymoglobulin is used as an induction agent in southern Mexican kidney transplant recipients. Our study shows that total accumulated recommended thymoglobulin dose (5 mg/kg approximately) is effective as previously recommended by other studies [3–7].

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