A comparative study of Tacrolimus versus Cyclosporine as immunosuppression for kidney transplant recipients

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ABSTRACT

Kidney transplantation is the most common transplantation in the world. Annually, a large number of patients that have chronic renal failure are undergoing renal transplantation and the major subject about these patients is the rejection of graft that should be controlled by immunosuppressive agents. The aim of this study is investigation of the effect of Cyclosporin against Tacrolimus in patients with kidney transplantation. This study was performing between 2010 and 2012 on all patients who had kidney transplantation and refer to Imam Reza hospital from Kermanshah University of Medical Sciences. 100 patients, aged 18–60 years, with end-stage renal disease were administered either Tacrolimus (n=49) or Cyclosporine (n=51). In both groups, Cellept could be discontinued from day 92 onwards. Corticosteroid treatment comprised methylprednisolone boluses followed by a rapid prednisone taper from 20 mg (day 2) to 5 mg (day 43 and thereafter). Patients followed up 12 months.
In the Tacrolimus treatment group, 7 grafts (14%) were lost and 8 (16%) grafts were lost in the Cyclosporine treatment group between months 0 and 12 and there is no significant different between these groups (*P= 0.845*). No cases were diagnosed with biopsy-proven chronic rejection at months 0 and 12. Mean serum creatinine concentrations were 1.8 ± 1.5 mg/dl in the Tacrolimus group and 2.3 ±2.9 in the Cyclosporine group by month 12 (*P= 0.348*). these data are consistent with previously published observations and confirm that Tacrolim us is a highly efficacious baseline immunosuppressant for patients undergoing kidney transplantation. Tacrolimus-based immunosuppression may promote long-term benefits with regard to graft functio n and graft survival.

Key words: Kidney transplantation; Cyclosporine; Tacrolimus.

INTRODUCTION

Renal transplantation is the treatment of choice for most patients with end stage renal disease and the number of new patients requiring renal transplantation for permanent kidney failure is increasing worldwide [1]. Calcineurin inhibitors are considered the mainstay of immunosuppression in renal transplantation [2]. Much of the success in organ transplantation has been credited to the use of Cyclosporine; after its introduction renal graft survival at 1 year increased from 64% to 78%. Despite the improvement in early graft function, long term kidney graft survival has not changed dramatically since the introduction of Cyclosporine [3]. The chronic loss of transplanted kidneys and the potential toxicity of Cyclosporine have prompted the development of other immunosuppressant drugs. Tacrolimus (FK506), a drug which has a similar mode of action to Cyclosporine, was first used in clinical transplantation in 1989 [4]. Benefits of treatment with Tacrolimus have included a reduction in steroid dose, a decreased need for

antihypertensive drugs, and a lower serum cholesterol concentration [5, 6]. Pronounced global differences in use of Tacrolimus exist; 63% of new renal transplant recipients in the United States receive Tacrolimus for primary immunosuppression compared with only 22% in Australia [7, 8]. However, Cyclosporine and Tacrolimus are currently the most widely used baseline immunosuppressants for prevent ion of acute rejection following kidney transplantation. The aim of this study is compare the positive and negative effects of Tacrolimus and Cyclosporine as initial treatment for renal transplant recipients.

MATERIAL AND METHODS

This randomized, open study was conducted in Imam Reza hospital from Kermanshah University of Medical University, Iran between 2010 and 2012. 100 patients, aged 18–60 years, with end-stage renal disease were administered either Tacrolimus (n=49) or Cyclosporine (n=51). The initial dose of Tacrolimus was 0.2 mg/kg/day to achieve target whole-blood trough levels of 10–15 ng/ml in the first month post-transplant and 5–10 ng/ml thereafter. Cyclosporine microemulsion was given at an initial dose of 8 mg/ kg/day with target levels of 150–250 ng/ml in the first month post-transplant and 100–150 ng/ml thereafter. In both groups, Cellept (1–2 mg/kg/day) could be discontinued from day 92 onwards. Corticosteroid treatment comprised methylprednisolone boluses (day 0: 500 mg; day 1: 125 mg) followed by a rapid prednisone taper from 20 mg (day 2) to 5 mg (day 43 and thereafter). Adverse events, laboratory parameters and renal function (serum Creatinine) and GFR (glomerular filtration rate) were recorded throughout the study. All statistical analysis was performed by using SPSS software version 16.0. Frequency and percentage were computed for categorical variables and mean and standard deviation were estimated for quantitative variables.

RESULTS

Demographic and baseline characteristics were similar between the two treatment groups (Table 1). Of the original 100 patients randomized to treatment, 49 (49%) patients in the Tacrolimus treatment group and 51 (51%) patients in the Cyclosporine group were assessed at 1 year follow-up. In the Tacrolimus treatment group, 7 grafts (14%) were lost and 8 (16%) grafts were lost in the Cyclosporine treatment group between months 0 and 12 and there is no significant different between these groups (*P= 0.845*) (Table 2 and Figure 1). No cases were diagnosed with biopsy-proven chronic rejection at months 0 and 12. Mean serum creatinine concentrations were 1.7 ± 1.1 mg/dl in the Tacrolimus group and 1.7 ±1.3 mg/dl in the Cyclosporine group by month 6. Mean serum creatinine concentrations were 1.8 ± 1.5 mg/dl in the Tacrolimus group and 2.3 ±2.9 in the Cyclosporine group by month 12 (*P= 0.348*) (Figure 2). Also, there is no significant different in GFR between these two groups by month 12 (*P= 0.572*) (Table 3)

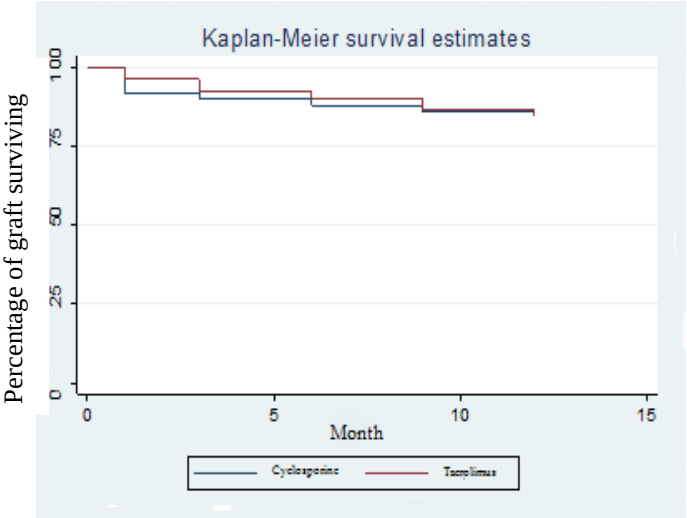

Figure 1. Graft survival rate

Table 1. Demographic data of the patients

	Gender		Age	Weight
	Male	**Female**		
Tacrolimus (n=49)	34 (69.3%)	15 (30.6%)	40.4 ± 15.6	58.1 ± 5.6
Cyclosporine (n=51)	35 (68.6%)	16 (31.3%)	37.1 ± 12.9	61.5 ± 5.8
***p* value**	0.935		0.247	0.123

Table 2. Incidence of acute rejection

Acute Rejection	Tacrolimus (n=49)	Cyclosporine (n=51)	P value
0-1 month	4 (8%)	2 (4%)	0.432
1-3 month	1 (2%)	2 (4%)	0.999
3-6 month	1 (2%)	1 (2%)	0.999
6-9 month	1 (2%)	2 (4%)	0.999
9-12 month	0 (0%)	1 (2%)	0.999
Total	7 (14%)	8 (16%)	0.845

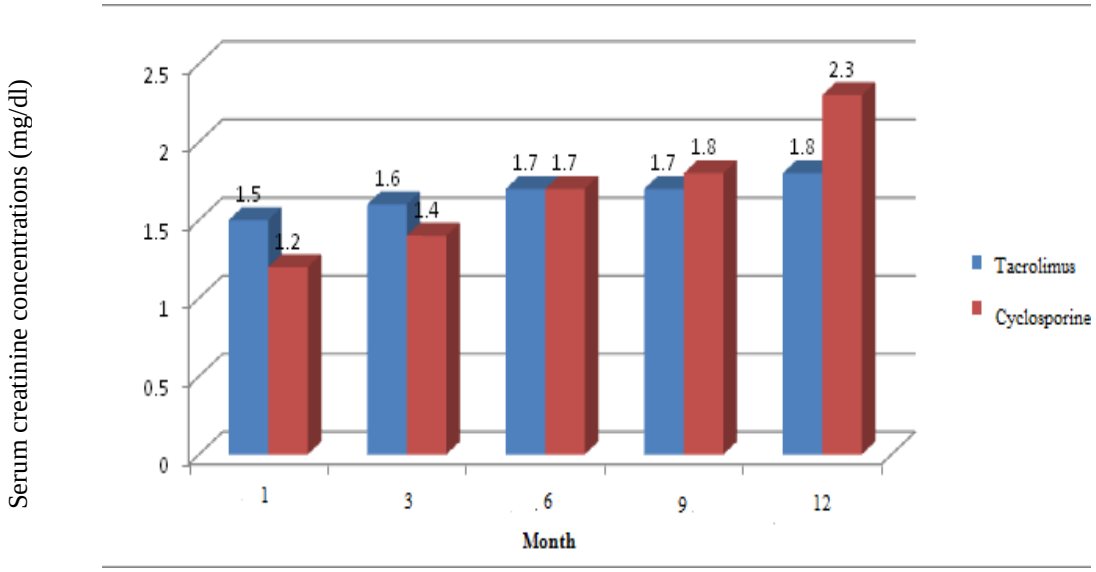

Figure 2. Serum creatinine concentrations in patients

Table 3. Renal function based on GFR measurement in 0-12 month

GFR	Tacrolimus (n=49)	Cyclosporine (n=51)	P value
0-1	51.6±28.1	68.8±15.4	0.158
1-3	47.8±25.2	59.3±18	0.304
3-6	45.3±21.9	49.6±26.8	0.806
6-9	44.7±25	46.2±32.3	0.915
9-12	41±28.5	35.2±39.1	0.572

DISCUSSION

In renal transplantation, a reduced incidence of acute rejection and improved 1-year graft survival in recent years ha s necessitated investigation of additional clinically relevant parameters to differentiate between immunosuppressive strategies. Our data showed there is no significant different between these two treatments. However, according to lower mean of serum creatinine concentration and lower total acute rejection in Tacrolimus group it seems to be this agent is better than Cyclosporine treatment. In compare to our study, two large, randomized, multicentre studies conducted in Europe and the US demonstrated that the incidence of acute rejection was significantly less in 508 renal transplant recipients receiving Tacrolimus-based immunosuppression compared with 355 receiving Cyclosporine-based immunosuppression [9, 10]. Projected graft half-life was longer and chronic rejection less frequent with Tacrolimus-based immunosuppression at 5 year follow-up [9]. Furthermore, renal function better after 5 years in patients receiving Tacrolimus-based immunosuppression compared with Cyclosporine-based immunosuppression [10]. In another long-term data from the Tacrolimus vs Cyclosporine Kidney Transplant Study (randomization of 232 patients to Tacrolimus or Cyclosporine microemulsion cornerstone immunotherapy)

demonstrated higher 6 year graft survival, longer estimated graft half-life and significantly better renal function (GFR) with Tacrolimus [11]. Gjertson *et al* reported a significant improvement in long term renal graft survival for recipients of Tacrolimus based immunosuppression. Patients who received Tacrolimus had a renal allograft half life of 13.8 years compared with 8.8 years for recipients of Cyclosporine based treatment [3]. Further, Kramer *et al* concluded Tacrolimus-based immunosuppression may induce long-term benefits with regard to graft function and graft survival [12]. Webster *et al* in his meta-analysis concluded, in compared with cyclosporine, treating kidney transplant recipients with Tacrolimus resulted in a substantial improvement in graft survival —a 44% reduction in graft loss (censored for death) within the first six months, an effect revealed for the first time by his meta-analysis and not evident when considering each trial in isolation. Treating with Tacrolimus led to 31% fewer patients having acute rejection and 51% fewer having severe rejection that needed treatment more intensive than steroids, within the first year [13]. In conclusion, these data are consistent with previously published observations and confirm that Tacrolim us is a highly efficacious baseline immunosuppressant for patients undergoing kidney transplantation. Tacrolimus-based immunosuppression may promote long-term benefits with regard to graft functio n and graft survival.

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