

Basiliximab as Induction in Kidney Transplantation: Are There any Real-Life Advantages?

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Abstract

Background: Basiliximab is an interleukin-2 receptor antagonist used as induction therapy in kidney transplantation and is believed to reduce acute rejection episode (ARE). Our aims were to compare the impact of basiliximab induction therapy with no induction therapy on incidence of ARE, time requirement for serum creatinine (S.Cr) to normalize after transplantation, initial post-transplant hospital stay, infection in immediate post-transplant period, chronic allograft injury and graft survival at 1 and 3 years.

Methods: We retrospectively reviewed the medical records of patients who had undergone living related donor kidney transplantation in a tertiary care hospital of a developing country between July 2004 and June 2014. We selected patients who received calcineurin inhibitors, mycophenolate and prednisolone to classify as no induction therapy (n=50; group 1, receiving prednisolone, mycophenolate and cyclosporine as maintenance therapy) and induction therapy with basiliximab (n=61; group 2, receiving prednisolone, mycophenolate and tacrolimus as maintenance therapy).

Results: Among the 111 study subjects, only two had experienced ARE (one from each group, p=0.889). Patients who received basiliximab had a shorter mean hospital stay (11.4±3.3 versus 13.7±5.0 days, p=0.005) and shorter mean duration for normalization of S.Cr (4.7±2.3 versus 7.3±5.6 days, p=0.002) after transplantation. There was no significant difference in incidence of infection in immediate post-transplant period (p=0.134). One year graft survival rate was better in those who received basiliximab (98.2% versus 89.4%, p=0.010) but there was no significant difference at 3 years (79% versus 74%, p=0.549). Overall incidence of chronic allograft injury was less with basiliximab (11.5% versus 36%, p=0.002) induction.

Conclusions: Induction therapy with basiliximab was associated with shorter mean hospital stay, early renal function recovery, better 1 year graft survival and less overall incidence of chronic allograft injury. We have encountered minimum ARE to comment on benefit of basiliximab on ARE.

Key words: Basiliximab, induction therapy, kidney transplantation.

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Introduction

Chronic kidney disease (CKD) is a global public health problem. It is the 9th leading cause of death in the United States.¹ End stage renal disease (ESRD) patients need renal replacement therapy (RRT) for survival. Globally 1.4 million patients are receiving RRT and its frequency is growing by about 8% per year.² According to the UK Renal Registry 17th Annual Report, 56,940 adult patients were receiving RRT in the UK on 31st December 2013.³ Renal transplantation is the optimum form of RRT, it has an unequivocal superiority over dialysis considering life expectancy, quality of life and cost.⁴⁻⁷

First successful kidney transplantation was done in 1954 by Joseph Murray's team between identical twins.⁸ In the early era of transplantation, total body irradiation and 6-mercaptopurine were used for immuno-

suppression. Unacceptable rate of mortality, high rate of rejection and unsatisfying graft survival warranted the development of new immunosuppressive agents over decades. Introduction of cyclosporine in 1980s revolutionized the scenario followed by introduction of tacrolimus and different mono- or poly-clonal antibody induction agents over the next 3 decades.⁹ With the availability of antibody based induction agents, immunosuppressive protocols are now individualized on the basis of recipient characteristics (high or low immunological risk group (Figure 1).¹⁰ To minimize the side effects of steroid and to avoid the cyclosporine induced nephropathy, “steroid avoidance” and “calcineurin inhibitors (CNI) minimization” protocols are evolved. In our center, the first 50 cases received cyclosporine based immunosuppressive therapy [cyclosporine, mycophenolate mofetil (MMF) and steroid] and currently we are using basiliximab induction with triple immunosuppressive regimen (tacrolimus, MMF and steroid).

Basiliximab is an interleukin-2 receptor (IL-2R) antagonist used as induction therapy in kidney transplantation and is believed to reduce acute rejection episodes (ARE). Our aims were to compare the impact of basiliximab induction therapy with no

induction therapy on incidence of ARE, time requirement for serum creatinine (S.Cr) to normalize after transplantation, initial post-transplant hospital stay, infection in immediate post-transplant period, chronic allograft injury and graft survival at 1 and 3 years.

Methods

We retrospectively reviewed the medical records of patients who had undergone living related donor kidney transplantation in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh, between July 2004 and June 2014. We selected patients who received calcineurin inhibitors (cyclosporine or tacrolimus), MMF and prednisolone to classify as no induction therapy (n=50; Group 1, with oral prednisolone, MMF and cyclosporine as maintenance immunosuppression) and induction therapy with basiliximab (n=61; Group 2, with oral prednisolone, MMF and tacrolimus as maintenance immunosuppression). Collected records were then compared between group 1 and group 2 in respect of ARE, time required for normalization of serum creatinine (S.cr) level, infection and 1 and 3 year graft survival.

Induction agent

No induction < Basiliximab < Alemtuzumab < Anti-thymocyte globulin



Lower risk

Zero HLA mismatch
Live donor
Caucasian ethnicity
Low panel reactive antibody
Absence of donor specific antibody
Blood group compatibility
Immediate graft function
Short cold ischemia time
First transplant

Higher risk

Increased tt of HLA mismatche
Younger recipient and older donor age
African-American ethnicity
High panel reactive antibody
Presence of donor specific antibody
Blood group incompatibility
Delayed onset of graft function
Long cold ischemia time
Retransplant

Figure 1. Induction therapy choice based on risk assessment [Adopted from Hardinger et al. (2012), *Transplant International*]¹⁰

Results

Total number of patients were 111 with a male predominance (male:female=2.3:1) and mean age was 37.5 ± 10.6 years without any significant deference between the groups (Table-I). Patients who received basiliximab had a shorter mean hospital stay and shorter mean duration for normalization of S.Cr after transplantation (Table-II). There was no significant difference in incidence of infection in immediate post-transplant period ($p=0.134$). One year graft survival rate was better in those who received basiliximab but there was no significant difference at 3 years (Figure 2). Among the total of 111 study subjects only two had experienced ARE (one from each group, $p=0.889$). Overall incidence of chronic allograft injury was less with basiliximab (11.5% versus 36%, $p=0.002$) induction.

Table I. Demography of Group 1 and Group 2 patients

	Group 1*	Group 2**	p-value
Number of patients	50	61	
Male :Female	1.9:1	2.6:1	0.4839
Mean age (years)	36.8 ± 10.8	38.0 ± 10.4	0.5534

* Group 1: No induction; ** Group 2: Induction with Basiliximab

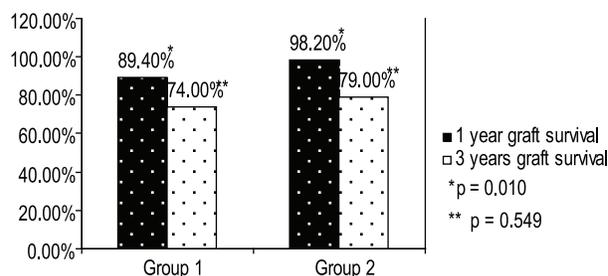


Figure 2. Comparison of graft survival between Group 1 and Group 2 patients

Table II. Comparison between Group 1 and Group 2 patients

	Group 1	Group 2	p value
Mean duration for normalization of S. Cr (days)	7.3 ± 5.6	4.7 ± 2.3	0.002
Mean S. Cr during discharge (mg/dl)	1.4 ± 0.91	1.3 ± 0.6	0.258
Incidence of infection in immediate post-transplant period	17	13	0.134
Mean post-transplant hospital stay (days)	13.7 ± 5.0	11.4 ± 3.3	0.005

Discussion

In current time, the world is divided into two regions, developed world and developing world, depending on economic and technological advancement between countries. About 80% of the world population resides in developing world who owns only about 25% of the total wealth and only 0.8 to 4% of fund is used in healthcare sector in comparison to 10 to 15% in developed countries.¹¹

Bangladesh is a developing country of South-Asia, with a population burden of 160 million (approx.). Nephrology is relatively a juvenile branch of medical science in our country. In most instances when a renal physician attends a CKD patient, he is already in stage 4 or 5 CKD or developed ESRD with other complications of the disease. First renal transplantation

was done in our country in 1982. Due to lack of facilities we could not perform few tests like donor specific antibody (DSA) or panel reactive antibody (PRA) but the other essential tests could be performed with high efficiency.

In our centre, BIRDEM General Hospital, first renal transplantation was performed in 2004. Initially we used the triple drug regime with steroid, cyclosporine and MMF. The optimum immunosuppressive therapy was not always possible to provide due to non-availability of all the usable drugs and high cost of them. Since December 2009, we have introduced tacrolimus (FK-506) instead of cyclosporine and the induction therapy with injection basiliximab in patients with 25% to 50% match in human leukocyte antigen typing. Though we have marked these patients as immunologically low risk

group, considering their history of blood transfusion and lack of sensitivity information regarding DSA or PRA, their actual immunological risk could not be defined.

We have found significantly better 1 year graft survival in our patients with basiliximab induction group with shorter time requirement for normalization of serum creatinine in post-transplant period and shorter post-transplant mean hospital stay. But there was no significant difference in graft survival at 3 years of transplantation. No comments could be made regarding acute rejection episode as the incidence was least in both groups.

Jurewicz WA et al. from UK reported that they have followed up 232 renal transplant recipients in the University Hospital of Wales, Cardiff for 6 years and found that tacrolimus-based immunosuppression was associated with superior short and long-term renal function than cyclosporine based immunosuppression.¹² Similar interpretation was made by Webster AC et al.¹³ in their report, where they reviewed 123 reports from 30 studies that involved 4102 kidney transplant recipients patients. Vardhan H et al. studied 296 kidney transplant recipients in India and found that acute rejection was significantly less in patients with basiliximab induction compared to those without induction as well as more favourable short and long term graft outcome in basiliximab induction group.¹⁴ On the other hand Koch M et al. reported that graft and patient survival was equivalent, 10 years after transplantation, with or without basiliximab induction therapy.¹⁵

In the studies, comparing the no induction group with basiliximab induction group of renal transplant recipients, the maintenance immunosuppressive protocol was cyclosporine based and the results reflected a less acute rejection episode with favourable short and long term graft survival effects.¹⁴ The same benefits have been achieved by using tacrolimus instead of cyclosporine.^{12, 13} As we are using basiliximab induction in conjunction with tacrolimus based maintenance immunosuppressive agents, it is not clear whether the favourable results are either due to basiliximab or tacrolimus.

It is important to ascertain whether the favourable outcomes like shorter mean hospital stay, early renal function recovery, better 1 year graft survival and less

overall incidence of chronic allograft injury, as we are observing in our transplant patients, is due to tacrolimus or basiliximab. In a developing country like ours, the extra economic burden of induction therapy must be justified. There is still scope of further study to clarify the role of tacrolimus and basiliximab individually regarding acute rejection, short and long term graft survival in our patient groups and also to justify the role of basiliximab induction therapy in our patients.

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