Outcome of Different Induction Therapies in Living Donor Renal Transplant in Indian Population: A Single Center Experience

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Background

As of 2014, an estimated 9% of the global population aged 18+ years was affected by diabetes.[1] The World Health Organization (WHO) also estimated around 2.5% of deaths were attributed to diabetes in 2012 and more than 80% of those deaths occurred in low-middle income countries.[2] It is apparent that diabetes and its complications are becoming a global issue as an increasingly common, preventable, non-communicable disease.[3]

Along with cardiovascular disease, blindness, and neuropathy, end stage renal disease (ESRD) is one of the serious complications that can develop as a result of diabetes. In fact, diabetes is the leading cause of ESRD in both developed countries like the United States and developing countries like India.[4,5] India is a particularly interesting country to observe given their vast population base, rapid growing economy, genetic predisposition to diabetes and increased insulin resistance, and rising incidence of diabetes in the country. It is estimated that 100,000 patients develop ESRD each year in India with diabetes underlying as the main cause (44% of all ESRD cases).[5,6,7]

Once a patient develops ESRD, renal replacement therapy (RRT) is required to sustain life. RRT consists of one of three of three options: 1) hemodialysis (HD), 2) peritoneal dialysis (PD), or 3) a renal transplant (RT). Of the three options, renal transplant is considered to be the best in terms of quality of life and cost effectiveness, but only about 5% of all Indian patients with ESRD end up receiving a transplant.[4,8] A major difference in India is that most of the RT come from living donors rather than cadaveric donors like in the United States. Induction therapy with interleukin-2 receptor antagonist (IL2-RA) is recommended as a first line agent in living donor renal transplantation (LRT). However, comparative outcomes of induction therapy remains controversial in the Indian LRT population.

Our objectives were to 1) evaluate patient survival and allograft function in live donor renal transplants with a specific focus on the Indian patient population between 2010 and 2014, 2) access the impact of different induction therapies on the outcomes of Indian live donor renal transplant patients.

Methods

A single center (Medanta Medicity, Gurgaon, India) dataset was retrospectively studied for patients receiving LRT from 2010 to 2014 (N=901) to compare effectiveness of IL2-RA to other induction options (no-induction and rabbit anti-thymocyte globulin [r-ATG]). IL2-RA and no-induction were chosen for immunologically low risk patients. R-ATG was primarily given to the recipient with PRA>20% and HLA mismatch > 5 antigen out of 6.

Methods

Patient paper charts were analyzed for dates not present in the Medanta database which included follow-up dates with corresponding creatinine levels (at 3 months, 6 months,1 year, last follow up), date and type of rejection if applicable, graft loss and death. The data used for analysis was the patients most recent follow up at Medanta. The patient data was used to calculate rejection rate, graft failure, mortality, and hazard ratio (HR) for overall graft failure. The main outcomes were the risk of acute rejection at one-year and overall allograft failure (graft failure or death) post-transplantation through the end of follow-up.

Results

	No-induction	IL2-RA	r-ATG	P
N (%)	316 (35.1)	550 (61)	35 (3.9)	
DONOR				
Age	47.4±11.5	48.2±10.8	39.9±12.5	<0.001
Gender (male), %	30.7	24.7	33.3	0.13
Race (Indian), %	95.9	97.1	97.1	0.63
Relationship (family member), %	82.9	73.8	86.4	<0.001
DTPA measured GFR (ml/min)	94.7 ±10.6	94.7 ±10.5	98.7 ±11.3	0.81
RECIPIENT				
Age	38.2±12.6	41±13.2	37.1±9.3	0.01
Gender (male), %	82.6	81.8	65.7	0.05
Race (Indian), %	95.9	97.1	97.1	0.63
DM, %	17.7	27.8	20	<0.001
Pre-emptive transplant, %	14	19.9	12.5	<0.001
TRANSPLANT				
Maintenance immunosuppression (TAC/MPA/Pred), %	94.3	86.8	82.1	<0.001
Rejection rate, %	26.4	22.6	8.2	0.92
Graft failure, %	3.3	1	0	0.11
Mortality, %	2.2	2.3	4	0.85
Hazard Ratio (HR) for overall graft failure (95% CI)	1 (Reference)	0.76 (0.31-1.83)	1.24 (0.16-9.82)	

Table 1. Transplant characteristics of 3 induction categories

Donor, recipient, and transplant characteristics of three induction categories are shown in Table 1. Similar Kaplan Meier curves for overall graft survivals were observed among induction categories, shown in Figure 1. Rejection rate was higher in no-induction and IL2-RA groups (~25%) compared to r-ATG induction. On univariate Cox analysis, compared to no-induction therapy, overall allograft failure was similar among induction categories.

Results

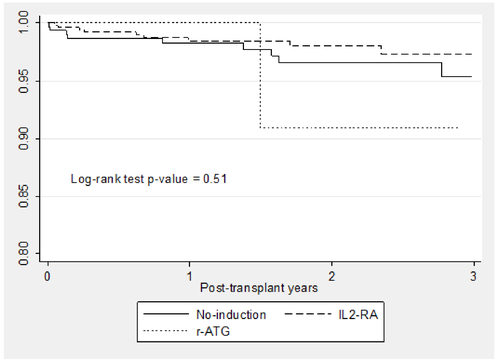

Figure 1. Kaplan Meier curves for overall graft survivals

Discussion

Compared to no-induction therapy, IL2-RA induction was not associated with better outcomes in Indian LRT recipients. r-ATG appears to be an acceptable and possibly the preferred induction alternative for IL2-RA in high rejection risk Indian patients as it offers lower rejection rates and probably better graft survival long term.

Among LRT patients in our study, we noted a distinct prevalence of females as donors (70.4%) with a large portion of recipients being males (76.7%). These results match those from a state funded live-donor renal transplant facility that noted 66.4% of donors were female while 83.2% of recipients were male.[9] This disproportionate amount of female donors could be attributed to the cultural obligations and undue burden placed on females in the Indian society. Awareness and changes in physician and public attitude are needed to protect women from unintended or premeditated bias.

In addition, we noticed the mean age of the recipients was 38.7 years old. In general, Indian patients are younger (mean age 42) than their United States counterparts (mean age 61) at the time of ESRD detection so these results do not come as a surprise.[8] The younger age indicates ESRD is creating a heavier burden on the Indian society since it is affecting people, often males who are the providers of their families, in the most productive years of their lives.[8] Not only are they younger at time of detection, but ⅔ of them seek a nephrologist only after they have reached the ESRD stage suggesting an inability to access renal services earlier when damages could be reversed.[8]

As the global prevalence of diabetes is estimated to increase, with the largest increases occurring in developing regions like India (151%), the gap between ESRD development and RRT accessibility is going to widen.[10] It is clear that diabetes prevention and education should be of early focus and RRT, particularly transplants, should be facilitated through a nationalized program.

Future

There is a limitation on drawing conclusions because around half of the patients in our study did not have follow up data within six months of our collection time. For those who did not have this information, we assumed no new events transpired since their last follow up. The process of following up at Medanta is difficult because there is no standard procedure, many patients are international, and patients often take their files in order to switch providers for their follow up care.

Our intent is to go back to Medanta to update and gather missing information on the patients who do not have follow up data within the last six months as this will allow us to increase the power of analysis. Additionally, we would like to expand our study by comparing induction therapies in LRT between Indian and United States cohorts. There is also a possibility to examine our dataset for infection rates, outcomes of ABO incompatible transplants, and a comparative cost analysis of transplantation.

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