Section: Urology

Original Research Article

OVERCOMING ABO INCOMPATIBLITY IN RENAL TRANSPLANTATION: INSTITUTIONAL EXPERIENCE AND OUTCOME

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ABSTRACT

Background: Kidney transplantation is the preferred treatment for end-stage renal disease (ESRD); however, donor shortages limit access. ABO-incompatible (ABOi) transplantation, once considered high-risk, is now feasible with modern desensitisation and immunosuppressive strategies. This study aimed to evaluate institutional experience and outcomes of ABOi kidney transplantation. **Materials and Methods:** This Ambispective study included 19 adult patients with ESRD who underwent ABOi kidney transplantation at a tertiary centre. All patients received desensitisation protocols and induction with either basiliximab or anti-thymocyte globulin (ATG) based on immunological risk. Outcomes were assessed at three months and 1 year. Statistical analysis was performed using the chi-square test, with $p<0.05$ considered significant. **Result:** The mean age was 36.5 ± 9 years, with a male predominance (63.2%). Chronic glomerulonephritis (63.2%) was the most common cause of ESRD. Induction therapy included basiliximab in 57.9% and ATG in 42.1% of patients, and the most frequent donor–recipient blood group constellation was B+ to O+ (31.6%). Good graft function was achieved in 63.2% of patients, while 15.8% of patients expired. Graft loss occurred in 10.6% of patients (5.3% dialysis-dependent and 5.3% graft nephrectomy). Mortality and graft loss were higher in the ATG group (25% each). A majority of patients receiving Basiliximab induction had significantly better graft function compared to ATG (81.8 vs. 37.5%, p = 0.047). **Conclusion:** ABOi kidney transplantation is a safe and effective option for expanding the donor pool, offering favourable patient and graft survival. Basiliximab induction was associated with better short-term outcome, supporting its role as the preferred induction strategy in selected patients.

INTRODUCTION

Kidney transplantation is regarded as the most effective therapy for individuals with end-stage renal disease (ESRD), offering better survival rates and improved quality of life compared to dialysis.[1] The ongoing shortage of suitable donors worldwide has led to the implementation of plans to expand the donor pool, such as utilizing living donor kidney transplants across ABO blood group differences.[2] In the past, ABO-incompatible (ABOi) transplantation was avoided because of the high risk of hyperacute rejection caused by naturally occurring anti-A and anti-B antibodies.[3] Japan was the first to introduce ABOi kidney transplantation in the late 1980s and later refined desensitization protocols, leading to successful outcomes.[4]

ABOi transplantation is based on two important principles: removal of circulating anti-blood group antibodies and prevention of their rebound using strong induction and maintenance immunosuppression.[1] Early approaches included splenectomy with standard immunosuppressive drugs, but current methods involve plasmapheresis or double-filtration plasmapheresis, rituximab, and specific immunosuppressive combinations.[4] These developments have improved graft survival over the past two decades.[2] Studies suggest that patient survival after ABOi transplantation is comparable to that of ABO-compatible (ABOc) recipients.[5] A large U.S. study reported similar long-term survival in both groups, but noted a higher chance of graft loss

in the first 14 days for the patients in ABOi group.[6] Meta-analyses also confirmed good graft survival, 0.94 in the short term and 0.89 in the long term, with patient survival above 0.93.[1]

While most data come from adult populations, paediatric experience has also provided valuable understandings. Paediatric studies have shown that long-term graft function and survival of the patient in ABOi transplants is similar to that in ABOc transplants, even though acute rejection episodes are more frequent.[3] Comparable findings have been reported in adults with better immunosuppressive therapy and improved antibody removal techniques.[2] However, early graft loss and antibody-mediated rejection (AMR) remain major concerns, especially during the time soon after the surgery. Careful monitoring of antibody titres, tailored desensitization, and close perioperative management are used to reduce these risks.[7]

Short-term results suggest a higher chance of early acute rejection in ABOi transplants compared to ABO-identical procedures, but with proper preconditioning, long-term outcomes are similar.[8] These procedures are also more cost-effective than continued dialysis, although the initial cost is higher.[4] Reports show that while graft survival is comparable between groups, ABOi transplants are linked with higher rates of urological complications.[9] When carried out in experienced centres with modern desensitization methods, ABOi transplantation provides graft and patient outcomes, along with quality of life, similar to ABOc transplantation.[10]

In the past two decades, an improved understanding of rejection mechanisms and advanced methods for antibody removal have expanded the eligibility of living donor programs. In India, ABOi kidney transplantation is still developing, with approximately 200–250 procedures performed annually.[11] Despite this, only a few studies from India have reported on ABOi transplantation outcomes. Therefore, this study aimed to assess the institutional experience with ABO-incompatible renal transplantation. It also evaluated short-term (graft function and patient survival) and long-term (graft survival) outcomes following transplantation.

MATERIALS AND METHODS

This Ambispective study was conducted on 19 adult patients with ESRD who underwent ABOi renal transplantation at the Department of Urology, Government Kilpauk Medical College and Hospital, and Government Royapettah Hospital. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all patients before enrolment.

Inclusion criteria

The study included adult patients aged ≥ 18 years who had undergone desensitisation protocols as part of their management to overcome ABO incompatibility and had at least one year of regular follow-up after renal transplantation for the assessment of short- and long-term outcomes, including graft function, rejection rates, complications, and patient survival.

Exclusion criteria

Patients with ESRD, active infections, malignancies, or severe comorbidities that could affect survival were excluded. Patients with pre-existing severe or uncontrolled autoimmune disorders, such as systemic lupus erythematosus or rheumatoid arthritis, which could interfere with immunosuppressive therapy or graft survival, were also excluded.

Methods: Short-term outcomes were assessed at three months post-transplantation, and long-term outcomes were assessed at one year. All patients had undergone standardised desensitisation protocols to overcome ABO incompatibility and were monitored through regular outpatient follow-ups. Induction immunosuppression was administered with either anti-thymocyte globulin (ATG) or basiliximab (IL-2 receptor antagonist), based on the patient's immunological risk profile.

Graft function was evaluated using serum creatinine levels, estimated glomerular filtration rate (GFR), and urinalysis results. In cases of suspected acute rejection, kidney biopsies were performed to confirm the diagnosis and differentiate between antibody-mediated and cellular rejections. Post-transplant anti-ABO antibody titres were measured to detect any rebound. Corticosteroid dosing was monitored to ensure adequate immunosuppression while minimising side effects. Patients were also regularly tested for any infections after the transplant, including urinary tract infection, BK virus, and cytomegalovirus (CMV). Clinical and demographic data were collected from the patient records for analysis.

Statistical analysis: Data were presented as frequencies, means, standard deviations, and percentages. Comparisons between groups were performed using the chi-square test. Statistical significance was set at $p < 0.05$.

RESULTS

The mean age of the patients was 36.5 ± 9 years, with a male predominance (63.2%). The main cause of ESRD was chronic glomerulonephritis (63.2%), followed by IgA nephropathy (15.8%). Most recipients had compatible Human Leukocyte Antigen (HLA) matching (84.2%), and induction therapy was administered with either basiliximab (57.9%) or ATG (42.1%). The most frequent donor–recipient blood group constellation was B+ to O+ (31.6%) [Table 1].

The majority of patients (63.2%) demonstrated good graft function, whereas 10.5% had poor function. Mortality occurred in 15.8% of patients, and graft loss requiring dialysis dependency or graft

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nephrectomy was observed in 5.3% of patients [Table 2].

Table 1: Baseline characteristics of recipients and donors

Parameters	Category	Count (%)
Gender	Male	12 (63.2%)
	Female	7 (36.8%)
Primary cause of ESRD	Chronic glomerulonephritis	12 (63.2%)
	IgA nephropathy	3 (15.8%)
	Diabetic kidney disease	1 (5.3%)
	Malignant hypertension	1 (5.3%)
	Renal stone disease	1 (5.3%)
	Vesicoureteric reflux (VUR)	1 (5.3%)
HLA Matching	Compatible	16 (84.2%)
	Incompatible	3 (15.8%)
Induction type	Basiliximab	11 (57.9%)
	ATG	8 (42.1%)
Blood group constellation	B+ to O+	6 (31.6%)
	AB+ to B+	4 (21.1%)
	B+ to A+	3 (15.8%)
	AB+ to A+	2 (10.5%)
	A+ to O+	2 (10.5%)
	AB+ to O+	1 (5.3%)
	A+ to O−	1 (5.3%)

Table 2: Overall transplant outcomes

Outcome	Count (%)
Good function	12 (63.2%)
Poor function	2 (10.5%)
Expired	3 (15.8%)
Failure/dialysis dependent	1 (5.3%)
Graft nephrectomy	1 (5.3%)

Basiliximab was associated with a higher rate of good graft function compared to ATG (81.8 vs. 37.5). Mortality (25%), graft dysfunction (12.5%), and graft loss (12.5%) were more common in the ATG group. A significant difference was noted between both groups (p = 0.047) [Table 3].

Table 3: Comparison of outcomes between Basiliximab and ATG induction

Outcome	Basiliximab (n=11)	ATG (n=8)	P value
Good function	9 (81.8%)	3 (37.5%)	0.047
Poor function	1 (9.1%)	1 (12.5%)	
Expired	1 (9.1%)	2 (25%)	
Failure/dialysis dependent	0	1 (12.5%)	
Graft nephrectomy	0	1 (12.5%)	

DISCUSSION

ABOi kidney transplantation has emerged as a key to overcome the lack of suitable donors for patients with ESRD. However, concerns remain regarding early AMR, infection risks, and the choice for optimal induction therapy. This study aimed to evaluate our institutional experience with ABOi renal transplantation, focusing on graft function, survival outcomes, and the comparative efficacy of basiliximab and ATG as induction agents.

The average age of the patients was 36.5 ± 9 years, with a male predominance (63.2%). The leading cause of ESRD was chronic glomerulonephritis (63.2%), followed by IgA nephropathy (15.8%). Most recipients had compatible HLA matching (84.2%), and induction therapy was administered with either basiliximab (57.9%) or ATG (42.1%). Similarly, Gan et al. reported a median age of 41.5 years, with 57.7% of patients being male. The primary causes of ESRD were chronic glomerulonephritis and unknown causes, each accounting for 31% of the patients.[12] Shim et al. studied 4579 recipients and reported that 3655 received basiliximab (79.8%) and 924 received ATG (20.2%).[13] Thus, suggesting that ESRD is common among middle-aged males with chronic glomerulonephritis being a predominant cause, and basiliximab is the predominantly used induction therapy.

The majority of patients in our study (63.2%) demonstrated good graft function, whereas 10.5% had poor function. Mortality occurred in 15.8% of the patients, and graft loss requiring dialysis dependency or graft nephrectomy was observed in 5.3% of patients. Supporting our findings, Naciri Bennani et al. reported that all patients who underwent ABOi renal transplantation with high isoagglutinin titres had 100% graft survival. In their study, 37.5% of the patients experienced acute humoral rejection, and 25% developed chronic humoral rejection.[14] Zschiedrich et al. followed up ABOi renal transplant patients for 10 years and reported 99% patient survival and 94% graft survival. However, they also

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reported that surgical complications were more frequent in ABOi kidney transplant patients (33%) than in ABOc transplant patients (15%).[15] Further strengthening our findings, Oliveira et al. reported 100% graft survival during a follow-up period of approximately 47.6 months with no acute AMR.[16] Thus, indicating that the graft function and survival of the patients can be improved in ABOi kidney transplantation by the correct usage of immunosuppressive management. Additionally, basiliximab is linked with favorable short-term outcomes compared with ATG.

In our study, basiliximab was associated with a higher rate of good graft function than ATG (81.8 vs. 37.5%). Mortality (25%), graft dysfunction (12.5%), and graft loss (12.5%) were more common in the ATG group, and these associations were significant ($p = 0.047$). Similarly, Keown et al. noted that basiliximab is effective in reducing the incidence of acute rejection, with a 35% decrease in the relative risk of graft rejection.[17] Mei et al. compared basiliximab with ATG and found that the basiliximab group experienced less acute rejection cases (5.9% vs. 28.6%) and had better graft performance after transplantation. Additionally, patients receiving basiliximab had less infections and shorter hospital stays compared with those in the ATG group.[18] Patel et al. observed that adverse events were more frequent in the ATG group (71.4% vs. 48.3%).[19] For long-term outcomes, Wei et al. reported patient survival of 98% and graft survival of 97% in the basiliximab group, compared with 95% and 73% in the ATG group.[20] These findings suggest that ATG is linked with higher death rates and poorer long-term results than basiliximab.

Though we have analysed and compared the basiliximab with Rabbit ATG. Hafeez et al. reported that r-ATG induction therapy is associated with better outcomes than basiliximab in deceased donor kidney transplantation.[21] In a similar study, Kim et al. observed that, r-ATG when given in low-dose, provides comparable outcomes as the basiliximab in living donor kidney transplantation; however, more frequent BK virus and CMV infections were reported in the r-ATG group.[22] Thus, providing a better alternative to ATG and emphasising the need for future studies with different therapies.

Our findings indicate that ABOi kidney transplantation can achieve graft function and patient survival comparable to those of ABOc transplants when appropriate desensitisation and immunosuppressive strategies are employed. Basiliximab was associated with better short- and long-term graft outcomes than ATG.

Limitations: The study's limitations include a small sample size and being conducted at a single centre, which may reduce the generalisability of its results. A follow-up of at least 6 years is necessary to evaluate long-term graft survival and late complications.

CONCLUSION

ABOi kidney transplantation is associated with good graft and patient outcomes when appropriate desensitisation and immunosuppressive protocols are used. Basiliximab induction was associated with better outcomes than ATG, making it a safer and more effective option for lower-risk patients. Future studies should compare basiliximab, rATG, and newer biologics to create the optimal induction strategy.

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