Desensitization with the Use of an Antibody Removal–Free Protocol in ABO-Incompatible Kidney Transplant Recipients with a Low Anti-A/B Antibody Titer

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ABSTRACT

Background. Desensitization for ABO-incompatible (ABOi) kidney transplantation mainly comprises removal of antibodies with the use of apheresis and suppression of antibody (Ab) production with the use of rituximab. This study aimed to estimate the outcomes of ABOi kidney transplantation with the use of an Ab removal–free protocol to avoid complications associated with apheresis.

Methods. A total of 32 de novo consecutive adults who underwent ABOi living-donor kidney transplantation were retrospectively evaluated. Our protocol for ABOi recipients was stratified and fixed according to the anti-A/B Ab titer at baseline before desensitization. Desensitization was performed before transplantation with 0–4 sessions of plasmapheresis or double-filtration plasmapheresis and 1–2 administrations of rituximab at 100 mg/body. Graft outcomes, anti-A/B Ab titer, and plasma fibrinogen level were compared between the Ab removal ($n = 21$) and Ab removal–free ($n = 11$) groups.

Results. Between the Ab removal and Ab removal–free groups, the graft loss rate (4.8% vs 0.0%; $P = 1.0$), acute rejection rate (19.0% vs 0.0%; $P = .14$), and serum creatinine level (1.74 vs 1.40 mg/dL, $P = .53$) were similar. The anti-A/B Ab titer was maintained at a low level until postoperative month 12 in both groups. The plasma fibrinogen level on the operation day was significantly lower in the Ab removal group than in the Ab removal–free group (163.4 vs 250.2 mg/dL; $P < .001$).

Conclusions. Desensitization with the use of an antibody removal–free protocol for ABOi kidney transplant recipients with a low anti-A/B Ab titer can maintain excellent graft outcomes and avoid postoperative bleeding risk.

KIDNEY transplantation across the ABO blood group barrier was long considered to be an absolute contraindication [1]. ABO-incompatible (ABOi) kidney transplant recipients without preconditioning experience increased rates of early graft loss following antibody (Ab)–mediated rejection. Therefore, strategies have been developed and evaluated to overcome the ABO barrier in kidney transplantation [2–4]. Desensitization before transplantation has contributed to improvements in ABOi kidney transplantation outcomes [1]. Thus, ABOi kidney transplantation is now a routinely accepted treatment option with favorable outcomes similar to those after ABO-compatible kidney transplantation [5–8]. Presently, ABOi kidney transplantation accounts for ~30% of all living-donor kidney transplantations performed in Japan [9].

Recent desensitization approaches for ABOi kidney transplantation mainly involve both removal of Abs with the use of apheresis and suppression of Ab production with the use of rituximab [1]. Apheresis techniques for anti-A/B Ab removal, such as plasmapheresis (PP) and double-filtration

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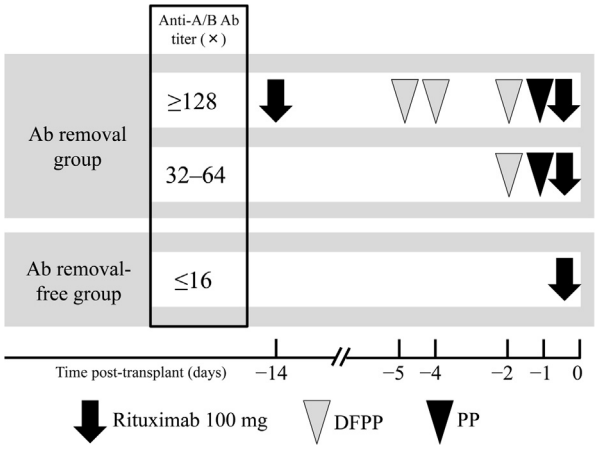

Fig 1. Stratified and fixed desensitization protocols according to the anti-A/B Ab titer. Abbreviations: Ab, antibody; DFPP, double-filtration plasmapheresis; PP, plasmapheresis.

plasmapheresis (DFPP), have several problems, including coagulation factor depletion, hypocalcemia, and anaphylaxis by fresh-frozen plasma [10]. Ab removal through apheresis for desensitization before transplantation has been routinely performed despite a low anti-A/B Ab titer. It is unclear whether Ab removal with the use of apheresis is necessary for not only ABOi kidney transplant recipients with a high anti-A/B Ab titer but also those with a low titer. Therefore, the present study aimed to evaluate the outcomes of ABOi kidney transplant recipients with a low anti-A/B Ab titer with the use of an Ab removal–free protocol to avoid complications associated with apheresis.

METHODS

Subjects and Study Design

A total of 33 de novo consecutive adult ABOi living-donor kidney transplant recipients underwent transplantation at Jichi Medical University Hospital from January 2013 to April 2017. One patient with anti-HLA Ab was excluded because desensitization was performed for the anti-HLA Ab regardless of the anti-A/B Ab titer. Therefore, we finally enrolled 32 ABOi kidney transplant recipients for this retrospective observational study. This study was conducted in accordance with the principles of the Declarations of Helsinki and Istanbul and was approved by the Institutional Review Board.

Desensitization Protocol and Patient Classification

Our protocol for ABOi recipients was stratified and fixed according to the anti-A/B Ab titer at baseline before desensitization (Fig 1). Desensitization was performed before transplantation with 0–4 sessions of PP or DFPP and 1–2 administrations of rituximab at a dose of 100 mg/body. In the case of an anti-A/B Ab titer ×128 or more, 4 sessions of PP or DFPP and 2 administrations of rituximab were performed. In the case of anti-A/B Ab titers of ×32 and ×64, 2 sessions of PP or DFPP and 1 administration of rituximab were performed. In the case of an anti-A/B Ab titer ×16 or less, 1 administration of rituximab alone without PP or DFPP was performed. Regarding the selection of apheresis, DFPP using albumin was performed, except on the previous day of the operation, and PP using fresh-frozen plasma was performed on the previous day of the operation for supplementation of coagulation factors. In the case of an anti-A/B Ab titer ×128 or more, rituximab was administered not only on pre-transplantation day 14 but also on the day before the operation, because its level in peripheral blood was depleted by PP or DFPP [3]. We classified patients who underwent desensitization with and without apheresis into Ab removal group and Ab removal–free group, respectively.

Immunosuppressive Therapy

All ABOi recipients received immunosuppressive therapy for induction with tacrolimus (0.1 mg/kg/d), mycophenolate mofetil (30 mg/kg/d), methylprednisolone (from 500 mg/d to a gradually decreased dose), and basiliximab (20 mg/d) at post-transplantation days 0 and 4. All ABOi recipients received the triple-drug combination of tacrolimus (trough level, C_0, 5.0 ng/mL), mycophenolate mofetil (1,000 mg/d), and methylprednisolone (4 mg/d) or everolimus (C_0, 3.0–5.0 ng/mL) for maintenance immunosuppressive therapy. Patients with deterioration of diabetes were considered for conversion of methylprednisolone to everolimus.

Table 1. Patient Characteristics

Characteristic	Ab Removal Group	Ab Removal–Free Group	*P* Value
n (%)	21 (65.6%)	11 (34.4%)	
Recipient sex, female, *n* (%)	6 (28.6%)	1 (9.1%)	.37
Recipient age at transplantation, y, mean ± SD	48.6 ± 13.2	47.2 ± 10.0	.76
Primary cause of ESRD, *n* (%)			
Diabetes	7 (31.8%)	5 (45.5%)	.47
Glomerulonephritis,	11 (52.4%)	3 (27.3%)	.27
Others	3 (13.6%)	3 (27.3%)	.38
Dialysis duration (d), median (range)	699 (0–3225)	615 (0–5525)	.97
Living-unrelated donor, *n* (%)	8 (38.1%)	7 (63.6%)	.27
Anti–donor-ABO blood group Ab, *n* (%)			.71
Anti-A Ab	12 (57.1%)	5 (45.5%)	
Anti-B Ab	9 (42.9%)	6 (54.5%)	
Anti-A/B Ab titer before desensitization, ×, median (range)			
IgM	32 (8–256)	8 (4–16)	<.001
IgG	64 (2–2048)	2 (2–4)	<.001

Abbreviations: Ab, antibody; ESRD, end-stage renal disease; Ig, immunoglobulin.