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Original Article

Role of therapeutic plasma exchange in reducing ABO titers in patients undergoing ABO-incompatible renal transplant

R.N. Makroo [a], S. Nayak [b,*], M. Chowdhry [c], S. Jasuja [d], G. Sagar [e], N.L. Rosamma [f], U.K. Thakur [g]

[a] Sr. Consultant and Director, Department of Transfusion Medicine and Immunohematology, Indraprastha Apollo Hospitals, New Delhi, India
[b] Registrar, Department of Transfusion Medicine and Immunohematology, Indraprastha Apollo Hospitals, New Delhi, India
[c] Consultant, Department of Transfusion Medicine and Immunohematology, Indraprastha Apollo Hospitals, New Delhi, India
[d] Sr. Consultant, Department of Nephrology, Indraprastha Apollo Hospitals, New Delhi, India
[e] Attending Consultant, Department of Nephrology, Indraprastha Apollo Hospitals, New Delhi, India
[f] Chief Technologist, Department of Transfusion Medicine and Immunohematology, Indraprastha Apollo Hospitals, New Delhi, India
[g] Sr. Technologist, Department of Transfusion Medicine and Immunohematology, Indraprastha Apollo Hospitals, New Delhi, India

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ABSTRACT

Background/aims: Our study presents an analysis of the trends of ABO antibody titers and the TPE (therapeutic plasma exchange) procedures required pre- and post-ABO-incompatible renal transplant.

Methods: Twenty-nine patients underwent ABO-incompatible renal transplant during the study period. The ABO antibody titers were done using the tube technique and titer reported was the dilution at which 1+ reaction was observed. The baseline titers of anti-A and anti-B antibodies were determined. The titer targeted was ≤8. Patients were subjected to 1 plasma volume exchange with 5% albumin and 2 units of AB group FFP (fresh frozen plasma) in each sitting. TPE procedures posttransplant were decided on the basis of rising antibody titer with/without graft dysfunction.

Results: The average number of TPE procedures required were 4–5 procedures/patient in the pretransplant and 2–3 procedures/patient in the posttransplant period. An average titer reduction of 1 serial dilution/procedure was noted for anti-A and 1.1 serial dilution/procedure for anti-B. Number of procedures required to reach the target titer was not significantly different for anti-A and anti-B ($p = 0.9$). The number of TPE procedures required pretransplant does not differ significantly with the baseline titers ($p = 0.062$). Outcome of the transplant did not differ significantly by reducing titers to <8 ($p = 0.326$). The difference

* *Corresponding author*. Tel.: +91 8586049759.
E-mail address: drswetanayak@gmail.com (S. Nayak).

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in the anti-A and anti-B titers at 14th day posttransplant was not found to be clinically significant ($p = 0.19$).

Conclusion: With an average of 4–5 TPE procedures pretransplant and 2–3 TPE procedures posttransplants, ABO-incompatible renal transplantations can be successfully accomplished.

1. Introduction

Renal transplant remains as the best treatment option for end-stage renal disease (ESRD) patients. This not only allows them a better quality of life but also eliminates or reduces the morbidities associated with dialysis. As per the study conducted by Agrawal et al.,[1] the prevalence of ESRD in India is nearly 785 per million populations. They found diabetes as the predominant cause of the disease. With growing burden of diabetes and the increasing proportion of elderly population, chronic kidney disease (CKD) has attended an epidemic status in the country.[1]

The first criterion that is taken into consideration for solid-organ transplants is ABO compatibility between donor and recipient, followed by HLA matching.[2] Availability of an ABO-compatible donor for ESRD patients is a challenge due to several reasons among which CKD in the family members and limited availability of cadaver organs for transplantation are a few.[1] The ABO antigens are expressed on the vascular endothelium, distal convoluted tubule, and collecting ducts in the kidney.[3] The naturally occurring antibodies against the ABO antigens that are absent on the recipients' red cell surface or the tissues are the mediators of antibody-mediated rejection (AMR). An AMR due to ABO antibodies, HLA antibodies, or any alloantibody against a blood group antigen that takes place within minutes to hours of transplant is considered a hyperacute rejection (HAR). This is the most significant obstacle for an ABO-incompatible renal transplant.

Renal transplants across ABO blood groups has been made possible by the implementation of antibody titer reduction techniques and by the introduction of drugs that can control, regulate, or destroy the antibody producing cells in the body. It is estimated that an additional 10–20% of living donor kidney transplantations can be performed through the implementation of such programs,[4,5] thereby, reducing morbidity and mortality in patients on the waiting list. A 30% increase in availability of organs for transplantation by performing ABO-incompatible transplants has been quoted.[6] Among the most significant developments in ABO-incompatible, solid-organ transplantation with immediate clinical applicability and impact are the application of plasma exchange and immunoadsorption protocols to reduce recipient isoagglutinin levels before and after transplantation.

Though few centers in our country are doing ABO-incompatible transplants, published literature from this region is limited. The trends in decline of the ABO antibody titers prior to the transplant and the role of therapeutic apheresis procedures therein have not been highlighted and there is paucity of data from the Indian subcontinent. We present an in-depth analysis of the ABO titers and the TPE procedures required to ensure better results in cases of ABO-incompatible renal transplantation.

2. Materials and methods

The data was compiled by the Department of Transfusion Medicine, Indraprastha Apollo Hospitals, New Delhi, prospectively from June 2012 to December 2015. The institutional ethical committee approval was taken. Thirty-nine patients underwent ABO-incompatible renal transplant during this period. Patients with donor-specific HLA antibodies, ABO antibodies with titers less than 8 at admission to the hospital, and those who underwent ABO titer reduction by application of antibody adsorption column were excluded. These criteria accounted to exclusion of 5 patients, and thus the remaining 34 patients were included for the study.

ABO antibody titers and therapeutic plasma exchange (TPE) for titer reduction were done at our department. All patients were evaluated for complement-dependent cytotoxicity (CDC) NIH anti-human globulin (AHG) augmented HLA crossmatch to detect donor-specific IgG antibodies to Class I and Class II. The blood group of the donors and the recipients were determined by the fully automated immunohematology analyzer Neo/Galileo (Immucor, INC Norcross, GA, USA). All the patients were screened for atypical antibodies against the red cells prior to the transplant and all of them were negative. All relevant clinical and laboratory data was recorded from the patients' case files and the patients were followed up until discharge from the hospital.

2.1. *Baseline antibody titer*

The ABO antibody titers were done using the tube technique. Known A and B blood group red cells, diluted to 2–5% suspension, were used for titration of corresponding antibodies. Serial dilutions of the patients' plasma were made. Two drops of the serially diluted plasma and 1 drop of the 2–5% cell suspension of A cells and B cells were mixed to get anti-A and anti-B titers, respectively. The tubes were incubated at 37 °C for 45 min and then washed 3 times to remove unbound antibodies. Two drops of AHG was added to each tube and reaction was read after centrifugation. The dilution of the plasma, at which 1+ reaction was observed, was the recorded titer. The titers of anti-A and anti-B antibodies were determined before the initiation of any immunosuppressive therapy. This was termed the 'baseline titer'. A titer of ≤8 was considered acceptable for the transplant. The titers