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Role of the Transfusion Medicine Department in Abo- Incompatible Renal Transplantation: A Case Study in a Government Tertiary Care Hospital

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Abstract: ***The Transfusion Medicine and Apheresis team play a crucial role in ABO-incompatible (ABO-I) renal transplantation by mitigating the immunological challenges associated with blood group incompatibility. This case study details the pre-transplant therapeutic plasma exchange (TPE), ABO antibody titration, intraoperative and postoperative management and blood component therapy. The study highlights how an established Transfusion Medicine Department facilitates complex procedures such as ABO-I renal transplantation in Government tertiary care hospitals. Additionally, it presents clinical findings from a specific case and reviews relevant literature on the topic.***

Keywords: ABO- incompatible renal transplantation, Therapeutic plasma Exchange, transfusion medicine, desensitization protocol, immunosuppressive therapy

Abbreviation: TPE-Therapeutic plasma exchange, ROTEM-Rotational thromboelastometry, IVIG-Intravenous immunoglobulin

1. Introduction

ABO- incompatible renal transplantation involves overcoming the recipient's immune response against donor ABO antigens. This requires the concerted efforts of a multidisciplinary team, with the Transfusion Medicine and Apheresis Team playing a key role in pre transplant desensitization and post-transplant immunological management

ABO-incompatible solid organ transplantation was previously not recommended, as ABO antigens are expressed on red blood cells and also in other tissues particularly in vascular endothelial cells leading to acute rejection of transplant. ABO-incompatible solid organ transplantation is routinely performed now with the development of various pretransplant desensitization and immunosuppressant modalities. [8]According to data from the Centre for Korean Network for Organ Sharing, from 2014 to 2019, there were a total of 6,129 registered kidney transplants (64.8% with living donors and 35.2% with deceased donors) and ABO-incompatible transplants totalled 17.4% of all transplants, and 15.0% of transplants were pre-emptive.

Pre transplant plasmapheresis and rituximab administration reduces the ABO antibody level to the specific threshold level. Post transplant ABO antibody level determines further modification of the treatment. The accurate measurement of ABO antibody levels plays a crucial role in establishing the treatment protocol. This study aims to highlight the pivotal role of the Transfusion Medicine Department in managing ABO-incompatible renal transplantation through desensitization protocols and therapeutic interventions, ensuring successful graft outcomes. The study is significant as it demonstrates how a well –equipped Transfusion Medicine Department in a Government tertiary care hospital can facilitate complex ABO-incompatible renal transplantation, thereby broadening accessibility to life-saving procedures.

2. Role of Transfusion Medicine Team

1) Pre-Transplant Plasma Exchange

The Apheresis team performs serial therapeutic plasma exchange sessions to remove and to reduce the anti ABO antibody titre and reducing the risk of acute renal rejection. In Therapeutic Plasma Exchange (TPE) automated cell separator extracts plasma from the blood, which is discarded and replaced with a designated replacement solution before reinfusing the remaining blood components in to patient. For ABO incompatible renal transplant, the replacement solution is decided by the Nephrologists depending upon patients clinical and laboratory parameters. Replacement Fluid may be Albumin, Fresh Frozen Plasma (FFP), or combination of Albumin and FFP, or Albumin FFP and Cryoprecipitate,

2) Removal of Anti Abo Antibodies

A favorable immune environment for the transplanted kidney is created by the Apheresis team by using the techniques either immune adsorption or centrifugal type therapeutic plasma exchange to remove anti ABO antibodies.

3) Monitoring Anti Abo Antibody Level

The treatment plan is scheduled as per the anti Antibody level. The apheresis team closely monitors the recipient's anti ABO antibody levels before and after plasma exchange and the Nephrologists adjust the treatment plan as needed.

4) Intraoperative Plasma Exchange

In selected cases, apheresis team may perform intraoperative plasma exchange to further reduce the anti ABO antibody levels.

5) Post Transplant Monitoring

Immunosuppressive treatment schedule is planned as per anti ABO antibody levels. The apheresis team closely monitors the post transplant anti ABO antibody levels.

6) Component Support;

As per the basic laboratory parameters and coagulation profile the appropriate component was issued by the Transfusion team.

7) Apheresis Device Selection

Depending upon patient's blood volume, antibody titer and renal function apheresis team selects the most suitable apheresis device for plasma exchange.

8) Plasma Exchange Protocol

Based on patient's specific needs and the transplant team's requirements a customized plasma exchange protocol is developed by the apheresis team.

9) Our Experience

A 31 years old male Patient with chronic kidney disease, Blood group O Rh positive with his wife as live kidney Donor, Blood group B Rh positive referred to our department for anti A/B antibody titer. Anti A/B antibody titer was done on 15.10.24 and found to be 512. We performed 9 cycles of TPE on alternate days. The antibody titer was done on the next day of plasma exchange and the same protocol is continued till the desired antibody titer of 8 was reached. The patient well tolerated the transplant and there is no post transplant increase in anti ABO antibody titer. Details of Therapeutic plasma exchange protocol and the antibody titer are given in Table1.

Table 1: Plasma Exchange Protocol

S. No	DATE –TPE CYCLE/VOLUME	Date of Titer	Anti Abo Titer Post Tpe
1	5.12.24- STANDARD VOLUME / FIRST CYCLE	6.12.24	256
2	7.12.24 - STANDARD VOLUME / SECOND CYCLE	10.12.24	128
3	9.12.24- STANDARD VOLUME / THIRD CYCLE	12.12.24	64
4	11.12.24- STANDARD VOLUME / FOURTH CYCLE	14.12.24	32
5	13.12.24- STANDARD VOLUME / FIFTH CYCLE	16.12.24	16
6	15.12.24- STANDARD VOLUME / SIX CYCLE	18.12.24	16
7	17.12.24- STANDARD VOLUME / SEVEN CYCLE	19.12.24	32
8	18.12.24- STANDARD VOLUME / EIGHTH CYCLE	20.12.24 transplantation done	8 pre transplant value
9	19.12.24- STANDARD VOLUME / NINETH CYCLE		

Table 2: Component Support

PERIOD	PRBC	FFP	CRYOPRECIPITATE	PLATELET
PRETRANSPLANT	NIL	NIL	1O	5
TPE	NIL	34	NIL	0
POST TRANSPLANT	2	6	6	4

ROTEM assay and coagulation profile was done on regular basis. Since fibrinogen level was found to be lower than normal we have transfused cryoprecipitate to the patient before and after transplantation and as the platelet level was in the range of 65000 to 77000, we transfused platelets before and after the transplantation. The details of component support based on laboratory values is given in Table2.

3. Discussion

ABO Antibodies;

ABO antibodies are naturally occurring IgM antibodies and differ from adaptive immune response. ABO antibodies belong to IgM class and IgG antibodies are found relatively frequently in type O, and the main subclass is IgG2. Each Institution monitors the Antibody levels according to their protocol.

[7] Two-fold dilution method is conventionally used to measure ABO antibodies titer. The reciprocal of endpoint titer obtained by serial dilution of the serum is taken as measurement of antibodies level. The endpoint that shows agglutination is interpreted as the antibody titer. The tube method and the column agglutination technique (CAT) are the two methods available for the titration of anti-A and anti-B antibodies .Our centre performed both tube and CAT method. We did a quality check by comparing now and then with the results obtained from designated laboratories. ABO titration method is illustrated in Figure 1.

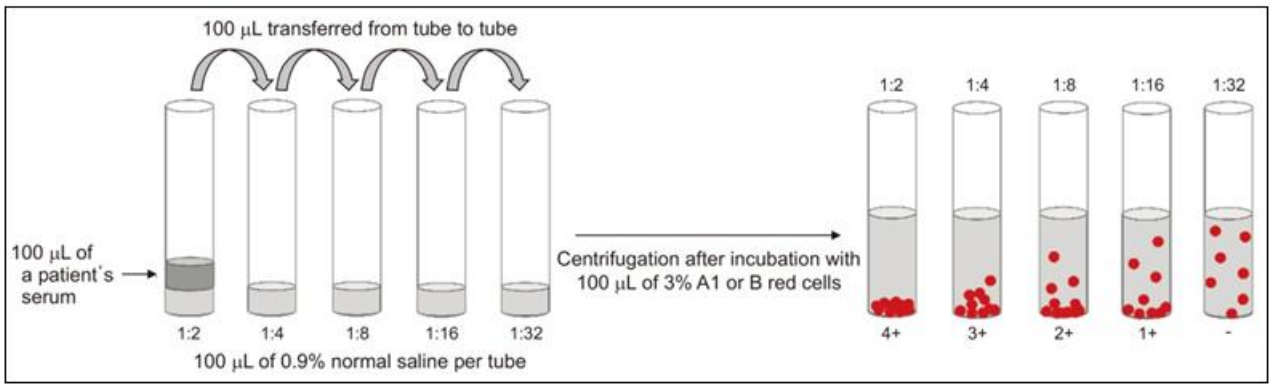

Figure 1

Chung Y, Ko D. **Laboratory support of ABO antibody monitoring for ABO-incompatible solid organ transplantation**. Clin Transplant Res 2022; 36:99-103. https://doi.org/10.4285/kjt.22.0011

ABO-Incompatible Kidney Transplant-Pretransplant Desensitization

[4]If the antibody levels are not brought down to the desired specific level ABO-incompatible kidney transplants are at risk of hyper acute and acute rejection. Pre transplant TPE has been proven to decrease anti-A and/or anti-B titers and facilitate graft survival. [2]The study'Removal of Anti-Thymocyte Globulin by Plasma Exchange in ABO-Incompatible and Positive Crossmatch Kidney Transplant Recipients by Patricia M. West-Thielke [a], Heather J. Ipema [b], Sally Campbell-Lee [c], Enrico Benedetti [a], Bruce Kaplan [a], James J. Thielke shows that plasma exchange removes a substantial amount of ATG in high-risk kidney transplant patients. Total ATG concentrations decreased a mean of 59.78 ± 13.91% after each plasma exchange session, and active ATG levels decreased a mean of 56.8 ± 17.08%. Mean daily concentrations reflect a lack of expected ATG accumulation.

Blood Component Support

The blood component therapy helped to correct the specific blood component deficiencies before, during and after Plasma exchange and Volume overload was thus avoided

[3]According to the study by Scornik JC, Schold JD, Bucci M, Meier-Kriesche HU." Effects of blood transfusions given after renal transplantation" HLA antibodies detected in post transplant period is likely to be by the graft rather than by any transfusions to the patient. The results suggest that post transplant transfusions do not have the sensitizing or down-regulatory effects.

[6] When albumin is used as replacement fluid in Plasma exchange significant reduction in fibrinogen and other coagulation proteins is observed after the procedure. [5]Platelet counts fell to a mean of 50% of pre-exchange levels and Plasma Fibrinogen concentration fell to a mean of 25% of initial levels during individual exchanges. The early detection and the replacement of exact dose of component are necessary.

Plasma Exchange Protocol

The Basics of Plasma Exchange Protocol is that the recipient's plasma is to reduce the levels of anti-A/B antibodies and the recipient is given IVIG and other immunosuppressant to avoid acute rejection of renal transplant. A more selective desensitization protocols like **Immunoadsorption (IA)**, that uses columns to remove anti-A or anti-B antibodies, Rituximob treatment for **B-cell depletion**, **Splenectomy** to improve the effectiveness of immunosuppressant are other procedures followed by few institutions. The graft and patient survival rates and control of antibody titers are possible through the combined effects of all measures. Plasma exchange is currently considered as a supportive therapy for ABO-incompatible kidney transplantation. [4]The study by Yoo S, Lee EY, Huh KH, Kim MS, Kim YS, Kim HO. "Role of plasma exchange in ABO-incompatible kidney transplantation" suggest to consider Plasma exchange be as a primary therapy for ABO-incompatible kidney transplantation. The Transfusion medicine team performed serial plasma exchanges till the antibody titer reduced to the desired specific level and the nephrology team took care of subsequent haemodialysis, and immunosuppressive therapy.

4. Conclusion

ABO incompatible renal transplantation requires a multidisciplinary approach, with the Transfusion Medicine Team playing a critical role in desensitization, plasma exchange, and post-transplant monitoring. This case study highlights the efficacy of well-coordinated Transfusion Medicine services in a government tertiary care hospital, demonstrating that such complex procedures can be successfully implemented with standardized protocols and vigilant patient monitoring.

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