

Anaesthetic implications and transfusion practices in ABO incompatible living donor liver transplantation: Case series

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ABSTRACT

ABO incompatible liver transplants (ABOi LT) are considered as a life-saving option when compatible donor grafts are unavailable. Fourteen adults (right lobe graft) and three children (left lateral segment/lobe) who underwent ABOi LT from living donors between 2011 and 2020 period were analysed for transfusions and desensitisation protocols. All recipients received packed red blood cells (PRBC) of their own group. AB plasma that does not contain any antibody was transfused in eight patients and donor group plasma in others. None of the patients developed transfusion related complications. Plasmapheresis and rituximab/bortezomab desensitisation was practised in 11 patients, only rituximab in four, only plasmapheresis in one, and no treatment in a 1 year child. Rejection was manifest in three patients while nine patients developed infections and sepsis. A working knowledge of the blood and product transfusions in ABOi LT is crucial for the anaesthesiologist. Perioperative management and impact of desensitisation protocol are discussed.

Key words: ABO incompatibility, liver transplantation, living donors

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INTRODUCTION

With growing awareness of the feasibility of living donor liver transplantation, options for survival in end-stage liver disease (ESLD) patients has progressed. Non-availability of group matched altruistic living donors results in challenges in some patients. Introduction of successful desensitisation protocols offers ABO incompatible liver transplants (ABOi LT) as an option when group matched donors are unavailable.^[1-3] There is little published literature on the anaesthetic management of patients undergoing ABOi LT.

Seventeen patients who underwent ABO iLT between 2011 and 2017 were included. The arrangement of blood products was as per the protocol [Appendix 1].^[4] Packed red cells belonging to Group O and plasma of Group AB have no antigens. Platelets are mildly

antigenic by virtue of the plasma in which they are transfused. Major incompatibility refers to the presence of recipient antibody against the donor red blood cells while in minor incompatibility donor antibodies are directed against recipient red cells which can lead to haemolysis and passenger lymphocyte syndrome which is usually self-limiting. Bidirectional incompatibility refers to the presence of both types of incompatibilities [Appendix 2].^[4,5]

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CASE DESCRIPTION

Case 1-3

Case 1 was a 1-year-old with biliary atresia post Kasai who did not receive desensitisation but who developed vascular complications post-surgery. Case 2 was a 5 year old with acute liver failure (ALF) of indeterminate aetiology and underwent one cycle of rituximab, while case 3 was a 12 year ALF who received rituximab and two cycles of plasmapheresis [Table 1]. Case 2 received a lateral segment graft and case three left lobe graft, both patients developed sepsis relating to desensitisation postoperatively. Transfusion details are shown in Table 2.

Cases 4-6

Three adult patients with ALF, case four was rat poison induced and cases five and six, acute viral hepatitis underwent ABOi LT. All received rituximab or bortezomab, case four received two cycles of plasmapheresis and case six one cycle. Cell-mediated rejection (ACR) was seen in case four and antibody-mediated rejection (AMR) in case five. All patients received blood matched to recipient blood group and AB plasma. Platelets and cryoprecipitate transfusions were in accordance to the donor group [Table 2].

Cases 7-17

Eleven adult patients underwent ABO iLT for chronic liver disease and received right lobe grafts from living

donors. Cases 10 and 16 received only rituximab while case 13 only plasmapheresis while the other patients received a combination of both. Case 10 developed ACR while cases 7, 8, and 12 developed sepsis from overwhelming immunosuppression. Transfusions are shown in Table 2. Packed red blood cell (PRBC) transfusions varied between 4 and 18 and were recipient blood group. Plasma was AB + in five patients, and donor blood group matched in the rest. Platelet and cryoprecipitate transfusions were according to the donor group [Table 2]. Two patients developed major bleeding complication in the first 6 weeks following transplant.

All patients who underwent transplant were induced by a standard anaesthetic technique with lorazepam (0.05 mg/kg), propofol (2-2.5 mg/kg), fentanyl (2 µg/kg) and cis-atracurium (0.15 mg/kg) or suxamethonium 1.5 mg/kg. Prostaglandin E 1 (PGE1/Alprostadil) was infused at a rate of 0.25 µg/kg/h after reperfusion and continued for 96 h postoperatively. Patients were extubated 12–16 h after surgery. The pattern of immunosuppression was similar to that in compatible transplants and consisted of tacrolimus, mycophenolate, and steroids. Tacrolimus dosing was titrated to maintain a trough level of 5–10 ng/ml. Mycophenolate was maintained at between 1,000 and 1,500 mg/day. Steroids were given at 500, 250, 125, and 75 mg on days 1–4, and maintained at 20 mg/day

Table 1: Details of ABO iLT and desensitisation protocols

No.	Age (years)	Gender	Aetiology	MELD/PELD	Wt. kg	Graft	GW/RW	Isoagglutinin titre (IgG: IgM)	R: NOC	P: NOC	Complication
Paediatric											
1	1	F	CLD	24	8	LLS	3.7	0: 8	-	-	Graft failure
2	5	F	ALF	36	12	LLS	2.0	16:64	1	-	Sepsis,
3	12	F	ALF	40	31	LL	0.75	NA	1	2	Sepsis
Adult ALF											
4	23	M	ALF	35	75	RL+MHV	0.90	64:64	1	2	ACR, AMR,
5	48	M	ALF	40	79	RL+MHV	0.81	4:32	1	-	AMR, HAT,
6	24	M	ALF	36	55	RL+MHV	1.1	2: 32	B**	1	
Adult CLD											
7	56	M	CLD	34	78	RL+MHV	0.73	64:64	2	3	Sepsis,
8	55	M	CLD	31	54	RL+MHV	1.1	64:128	2	1	Sepsis,
9	44	M	CLD	28	50	RL+MHV	0.7	1:64	1	1	
10	40	F	CLD	18	71	RL+MHV	0.84	4:32	1	-	ACR
11	37	M	CLD	26	68	RL+MHV	0.96	16:256	1	1	
12	52	M	CLD	28	72	RL+MHV	0.86	2:8	1	1	Sepsis
13	47	M	CLD	19	51	RL+MHV	1.5	32:64	-	1	
14	50	M	CLD	28	82	RL+MHV	0.76	64:128	1	1	
15	50	M	CLD	21	74	RL+MHV	0.72	512: 512	1	2	
16	59	M	CLD	18	53	RL+MHV	0.95	16: 64	1	-	Intracerebral bleed
17	50	M	CLD	28	57	RL+MHV	0.96	32: 8	1	2	Gastrointestinal bleed

CLD: Chronic liver disease; ALF: Acute liver failure; LLS: Left lateral segment ;LL: Left lobe ;RL+MHV: Right lobe+middle hepatic vein; GW: RW: Graft weight/ recipient weight ratio; R NOC: Rituximab, number of cycles; PNOc: Plasmapheresis, number of cycles; B **: Bortezomab; ACR: Cell mediated rejection; AMR: Antibody mediated rejection

Table 2: Blood product use in ABO incompatible transplants

	Donor group	Recipient Group	PRBC		FFP		Group	SDP Nos	Cryoprecipitate
			Group	Nos	Group	Nos			
Pediatric									
1.*	B+	O+	O+	0.5	B+	1	B	1	6
2.*	A+	O+	O+	1	A+	4	A+	2.5	
3.*	B+	O+	O+	4	AB+	4	AB	3.5	
Adult ALF									
4*	AB+	B+	B+	4	AB+	4	AB+	1	20
5*	A-	O+	O+	3	AB+	10	A+	2	10
6*	AB+	A+	A+	7	AB+	15	AB	2, 2 R	10
Adult CLD									
7 *	B+	O+	O+	18	AB+	16	B +	10 R, 2	37
8 *	B+	O+	O+	6	AB+	8	AB+	5 R	20
9 #	A+	B+	B+	5	AB+	5	AB+	1,14 R	5
10*	AB+	B+	B+	4	AB+	5	AB+		10
11*	B-	O+	O+	4	AB+	11	B +		5
12 [†]	A2+	B+	B+	11	A+	7	AB+		
13*	A+	O+	O+	12	A+	11	A	2	5
14 [†]	B+	A+	A+	4	B+	9	B	8 R	
15*	A2+	O+	O+	7	A+	3	A+	1, 4 R	14
16*	B+	O+	O+	5	B+	3	B	0.5	
17*	A-	O+	O+	16	A+	14	A+		10

*Major incompatibility. [†]Bidirectional Incompatibility. R: Random donor platelets, CLD: Chronic liver disease, ALF: Acute liver failure

and tapered at 3 months. Protocols were modified based upon rejection or presence of side effects.

DISCUSSION

We looked at the transfusion practices amongst ABOiLT with a view to formulate clearer guidelines during transfusions. We did not follow-up beyond the stay in the intensive care unit (ICU) as our primary concerns were related to the anaesthesia, transfusions, and immediate intensive care although a longer follow-up would have provided more insights on management. Among the 17 patients in our group, major ABO incompatibility was seen in 14 patients, bidirectional incompatibility in three patients [Appendix 2].

The transfusion protocol was as per recommended guidelines.^[6,7] While AB plasma is the first choice as it contains no antibodies, donor group plasma is acceptable in the background of non-availability. The recommendations for platelets and cryoprecipitate are to be of the donor group to minimise reactions following transfusion. Rhesus (Rh) compatibility should be adhered to during transfusion. In an event that Rh + blood is transfused to a Rh - patient, then Rh immunoglobulins should be administered particularly for a female in the reproductive age group. Packed red blood cells (PRBC) should be Rh-compatible with the recipient's blood group and platelet concentrate, fresh frozen plasma, and

cryoprecipitate should be Rh-compatible with that of the donor.^[6]

The consequences of ABO incompatibility are graft rejection and haemolytic complications. Rejection has been described as hyperacute, acute, and chronic and is because of the recipient antibody against the donor antigens. A high incidence of infections in the initial part of the programme appeared to decrease with less aggressive desensitisation protocols in the later part of the programme.^[8]

The basis of administering PGE1 is to improve the hepatic arterial blood flow, accelerate recovery of mitochondrial function and stabilise the membrane micro viscosity.^[3,9] Prostaglandin E₁ also decreases the cell mediated cytotoxicity against the hepatocytes and enhances the level of DNA synthesis in cell by stimulating the cyclic adenosine monophosphate production and increasing the ATP level in hepatic tissue.^[10] All our patients included had infusions of Prostaglandin E₁ administered intravenously at 0.25 µg/kg/h that we believed could enhance graft blood flow.

Rituximab acts by a reduction of precursor cells responsible for clonal expansion during AMR.^[11] Our current strategy involves administration of a single dose of rituximab 375 mg/m² body surface area or less, 1-4 weeks prior to the ABOiLT.

The blood group A2+ among donors is unique in that it is associated with lower antigen expressivity than the A1 group. Skogsberg^[12] presented 10 patients belonging to group O who received grafts from A2+ deceased donors managed without plasmapheresis, immune absorption or splenectomies preoperatively with an 80% graft survival. Kluger *et al.*^[13] have shown that A2 grafts could survive well even in the presence of a high anti-A or anti-B antibody titres. In our experiences with two such donors, the first recipient underwent both plasmapheresis and rituximab and succumbed to sepsis perhaps from overaggressive desensitisation which may not have been needed with an A2+ graft. The second did receive both plasmapheresis and single dose of rituximab and made an uneventful recovery. With the current knowledge, desensitisation can perhaps be minimised with A2+ donors to avoid side effects of excessive desensitisation.

Children less than 2 years are believed to have decreased immune responses and comparable results with compatible liver transplants are reported.^[14] This has been attributed to the decreased immune responses in children, reducing the rejection. Only one child less than 2 years underwent ABOi LT in our group but succumbed to graft failure following technical issues with vascular anastomosis. Haemolytic complications from passenger lymphocyte syndrome^[4] and increased incidence of biliary strictures are associations of ABO iLT.^[15]

The desensitisation protocol may carry a risk of excessive immunosuppression that makes the recipient predisposed to infections. Meticulous asepsis in the care of the patient postoperatively is indicated. The use of postoperative steroids as immunosuppression can enhance this vulnerability. Postoperative management involves care of patients with special attention to immunosuppression and graft function and vigilance for infection and biliary tract dysfunctions as they are more prone to complications.

CONCLUSIONS

ABOi LT has evolved as viable treatment strategy in ESLD patients with unavailability of group matched living donors. Meticulous attention to group matched products, attention to asepsis and anticipation of specific problems relating to desensitisation and biliary problems is essential for the anaesthesiologist or intensivist in providing the best supportive care and enhancing outcomes.

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Conflicts of interest

There are no conflicts of interest.

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APPENDICES

Appendix 1: Protocol for Blood and product transfusion in Major and Bidirectional Incompatibility.^[5,7,12]

Recipient group	Antibody in the recipient	Donor group	PRBC	FFP		Platelets		Cryoprecipitate
				1 st	2 nd	1 st	2 nd	
O	Anti A anti B	A	O	AB	A	A	AB, B, O	A, AB
O	Anti A anti B	B	O	AB	B	B	AB, A, O	B, AB
O	Anti A anti B	AB	O	AB	A	AB	A, B, O	AB
A	Anti B	AB	A/O	AB	A	AB	A, B, O	AB
B	Anti A	AB	B/O	AB	B	AB	A, B, O	AB
B	Anti A	A	B/O	AB	A	AB	B, A, O	AB
A	Anti B	B	A/O	AB	B	AB	B, A, O	AB

PRBC: Packed red blood cells, FFP: Fresh frozen plasma

Appendix 2: Definition of major and minor ABO Incompatibility

Recipient Blood Group	Donor Blood Group
Major ABO incompatible	
O	A
O	B
O	AB
A	AB
B	AB
Minor ABO incompatible	
A	O
B	O
AB	O
AB	A
AB	B
Bidirectional Incompatible	
A	B
B	A