Differential Effect of Antibody Removal on ABO Blood Group Type Chain Specific Antibodies Over Time

Andrew Bentall¹, Jeya Mylvaganam², Jean Pearcey², Bruce Motyka², Chris Cairo³, Todd Lowary³, Jillian Buriak⁴, Lori West² and Simon Ball¹

¹Department of Nephrology, University Hospital Birmingham, Birmingham, United Kingdom; ²Departments of Pediatrics, Surgery, and Immunology, University of Alberta, Alberta Transplant Institute, Edmonton, Canada; ³Alberta Glycomics Centre,, Univ of Alberta Dept of Chemistry, Edmonton, Canada and ⁴Dept of Chemistry, National Institute of Nanotechnology,, Edmonton, Canada.

BACKGROUND AND AIMS

Incompatible registry data find poorer outcomes in ABO incompatible kidney recipients((ABOi), but ABOi remains a potentially important treatment particularly for blood group O recipients. Outcomes are reported independently of the antibody titre, however there is significant variation in titre measurement.

The trisaccharide epitope defines A and B blood group antigens where antibody can bind to subtype chains (I-VI).

Only subtype II is expressed on cardiac vascular endothelium, which is also expressed on glomerular endothelium.

Following pediatric ABO-incompatible heart transplantation (ABOiHTx) there is evidence of humoral tolerance to subtype II but not other allograft blood group antigen subtypes.

This study reports subtype-specific antibody quantification in adult ABOi kidney transplant (ABOiKTx) recipients.

METHODS

From a previous published ABOi kidney transplant cohort, samples from pre-antibody removal, day of transplantation and at a late time point (6 or 12 months) were measured by a central haemagglutination (HA) assay and by a published microarray platform.

Antibody binding to ABH subtype antigens I-VI was quantified using a microarray platform in which the mean fluorescence intensity (MFI) of binding is proportionate to the concentration of antibody. The assay assessed IgM and IgG binding.

Plasma samples were obtained from 68 ABOiKTx recipients with blood group A donors – both O and B recipients

Patients received either plasma exchange or A-trisaccharide specific antibody removal (Glycosorb) columns for removal of anti-A antibodies.

Data were analysed by change in antibody measurement with treatment and over time with respect to specific blood group antigen subtype binding.

RESULTS

IgG anti-A subtype specific binding in O recipients of A-mismatched kidneys before and after plasma exchange or immunoadsorption

Pre-treatment to post EART less subtype III and IV reduction in IA than PEX. There was pan IgG removal in PEX, no Gal removal in IA

Anti-A subtype specific binding in O recipients of A-mismatched kidneys pre- and late-transplant (12 month)

Reduction anti-A antibodies at late timepoints, but not anti-Gal. Anti-subtype antibodies were higher in late IgG, but low in IgM isotypes. IgG binding to subtype II was similar to VI.

CONCLUSIONS

These data demonstrate that IA preferentially removes IgG to subtype II compared to IgG to subtypes III/IV (subtypes for which there is evidence of that these tetrasaccharides contribute to epitope generation). They also indicate that accommodation, as well as modulation of antibody production, may be more important in adult ABOiKTx than in paediatric ABOiHTx, in which there is evidence that tolerance is the most important phenotype.

Potential mechanisms for accommodation in this setting are currently under investigation.