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A Feasibility Study on the Provision of Extended Matched Red Cells for Transfusion Support in Chronic Haematological Diseases

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INTRODUCTION

Myelodysplasia (MDS), Chronic Myelomonocytic Leukaemia (CMML), Myelofibrosis (MF) and Aplastic Anaemia (AA) are haematological disorders that result in bone marrow failure; therefore, a patient will become transfusion dependent to improve their quality of life. The risk of antibody production is thought to be raised with an increased exposure to different donor red blood cells (RBC).

Antibody production is a burden to society and causes provision of donor RBCs for transfusions to become challenging. This can be detrimental to the patient as they are at a greater risk of having a transfusion reaction and becoming non-transfusable.

AIM

The aim of this project is to see if antibody production can be reduced in a group of patients who are transfusion dependent, by providing phenotype matched donor RBC units for transfusion.

- **PART A** – Perform a red cell phenotype and genotype on 20 newly diagnosed patients with MDS, CMML, MF and AA prior to any RBC transfusion where possible and determine if it is feasible to provide extensively matched donor RBC units to this group of patients; therefore, improving patient care and potentially reducing the rate of alloimmunisation;
- Propose an addition to the Oxford University Hospital (OUH) transfusion guidelines to supply extensively matched donor RBC units to this group of patients;
- **PART B** – Determine the incidence of alloimmunisation in 200 previously diagnosed patients with MDS, CMML, MF and AA and assess whether extensively matched donor RBC transfusions would have prevented the alloimmunisation.

METHODS & RESULTS

PART A

24 patients were identified as having newly diagnosed MDS, CMML, MF or AA and with no transfusions in the last three months – see figures i and ii.

A Direct Antiglobulin Test (DAT) was performed on all 24 patients to ensure that there were no antibodies bound to red cell surface antigens. All those found to be negative (21 patients) were then serologically phenotyped in house consisting of the Rh, Kell, Duffy, Kidd, MNS blood group systems using either; the Indirect Antiglobulin Test (IAT) method or a direct agglutination technique according to departmental SOP's and manufacturer's product inserts.

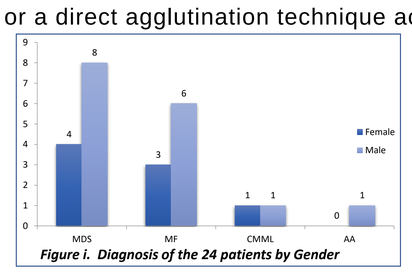

Figure i. Diagnosis of the 24 patients by Gender

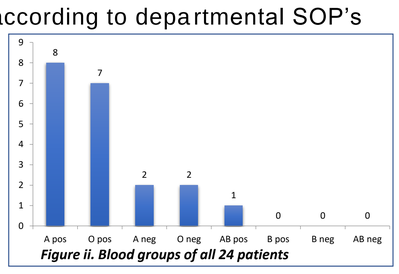

Figure ii. Blood groups of all 24 patients

Any patients found to have a positive DAT (3 patients) could not be serologically phenotyped in house, due to interference with the IAT method employed for some of the serological tests.

A molecular RBC genotype was performed by NHSBT for all patients.

20 patients had both their phenotype and genotype carried out; 8 patients were found to have discrepancies between the two; with discrepancies seen in 14 alleles in total. The most common blood group systems where discrepancies were seen were the Kell, Rh, Duffy and Kidd – see table i

Blood Group System	Allele discrepancy found in:	Event occurrence		Total event occurrence per blood group system	
		n	%	n	%
Rh	E	1	7.1	3	21.3
	C	2	14.2		
Kell	K	3	21.3	4	21.3
Kidd	Jk^a	1	7.1	3	21.3
	Jk^b	2	14.2		
Duffy	Fy^a	2	14.2	3	21.3
	Fy^b	1	7.1		
MNS	N	1	7.1	2	14.2
	S	1	7.1		
Total:		14			

Table i. The different types of discrepancies that were found between the phenotypes and genotypes
***n** = number of event occurrence*
% = percentage of discrepancies of that blood group system out of all 14 discrepancies

It was then investigated if three fully phenotypically matched donor RBC units could be provided from routine stock, three times monthly, for three months as a measure of feasibility.

Providing fully phenotype matched donor RBC units for every transfusion from routine stock was only possible for 5 patients. 7 of the patients could not even be provided with any phenotype matched donor RBCs. Donor RBC units would need to be ordered from the NHSBT which would cause significant delay in transfusion. However, donor RBC units matched for Rh/Kell only could be provided for all 20 patients from routine stock.

PART B

200 patients with MDS, CMML, MF and AA were retrospectively identified who had been transfused with non-phenotype matched blood and it was determined how many of them had become alloimmunised – see figure iii

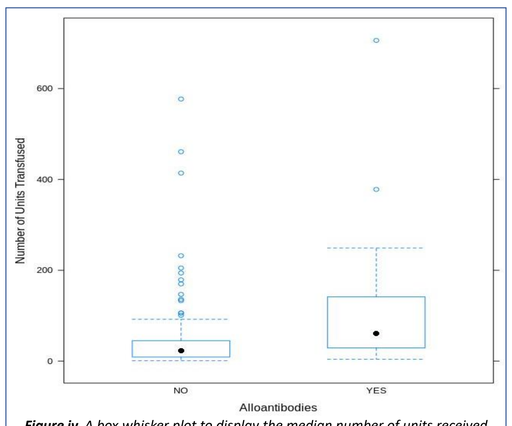

***Figure iv.** A box whisker plot to display the median number of units received between the two groups – non-alloimmunised (NO Alloantibodies) and alloimmunised (YES Alloantibodies). The black dot represents the median number of units (23 and 61 respectively), the blue box represents the middle 50% (the inter-quartile range) with the horizontal blue dash lines representing the upper and lower extremes. The blue outlined dots represent outliers*

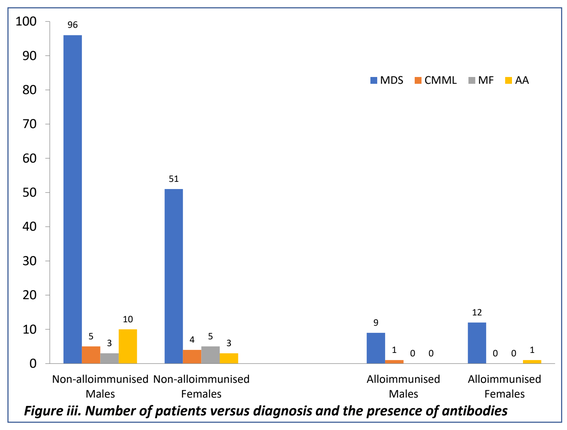

Figure iii. Number of patients versus diagnosis and the presence of antibodies

Transfusion history was looked at to see whether there was any difference in the number of units transfused to the 177 non-alloimmunised patients versus the 23 alloimmunised patients – 23 and 61 respectively. This was deemed to be significant with a p value of 0.0001 – see figure iv.

The rate of alloimmunisation due to transfusion was determined to be 12% (23/200 patients). 43% of those patients developed just a single antibody, 57% developed multiple antibodies.

7 patients developed antibodies to only Rh or K antigens (Rh/K). 5 patients developed antibodies to Rh/K antigen plus a non Rh/K antigen. 11 patients developed antibodies only to non Rh/K antigen. Anti-E was the most common allo-antibody, followed by anti-Kpa and K – see table ii.

Subgroup:	Rh				Kell		Kidd	Duffy	MNS		Other			
Specific Antibody:	E	D	C	C^w	K	Kp^a	Jk^a	Fy^a	M	S	Auto	Chido	Le^a	Bg^a
Antibody Occurrence:	10	2	1	2	3	4	2	1	1	1	7	2	1	1

Table ii. The antibodies represented in the alloimmunised patients and their occurrence

CONCLUSIONS

Of the 200 patients in part B, 23 became alloimmunised (12%). The non-alloimmunised group received a median of 23 units, versus 61 units in the alloimmunised group (p=0.0001). 7 of the patients developed antibodies to Rh/K only and 5 patients to Rh/K plus an additional antibody. Anti-E was the most common antibody.

Rh/K matching of donor RBCs, majority of which would always be available in routine stock, would have prevented 30% of alloimmunisation in this transfusion dependent group of patients. If fully phenotype matched RBC were to be given, 43% of alloimmunisation could be prevented but delays in provision could have been significant. Performing a serological phenotype and providing Rh/K matched donor RBC units was determined to be the most cost-effective option. We are currently discussing next steps with Clinical Haematology colleagues with a view to implementing Rh/K matching in the next few months.

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