ALLOCATION OF TRANSFUSION COMPATIBLE RED BLOOD CELL CONCENTRATES IN THE PRESENCE OF WARM-REACTIVE AUTO-ANTIBODIES - A RETROSPECTIVE COMPARISON OF TWO DIFFERENT STRATEGIES

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Background: Allocation of transfusion compatible red blood cell concentrates (RBCC) in patients carrying warm-reactive autoantibodies (WRA) is often hampered by interference of WRA with crossmatch procedure. Therefore, simultanously present alloreactive antibodies (ARA) may escape detection and may cause potentially life-threatening reactions upon transfusion. Various strategies to discover coexistent ARA or to overcome cross match difficulties are in use, e.g. autologous and homologous serum adsorption of WRA (ASA and HSA resp.), dilution strategies of patient's serum and modification of cross-match milieu. However, these serology based strategies are technically demanding and have limited antibody detection capacity. In addition, they have to be repeated frequently during transfusion episodes. In contrast, molecular genotyping (MGT) of receipient's red cell antigens to predict receipient's phenotype offers a new approach to assign phenotype identical RBCCs, which can be transfused irrespective of cross-match results. Retrospectively, we compared the performance of HSA versus MGT based strategies to allocate RBCC in patients with WRA.

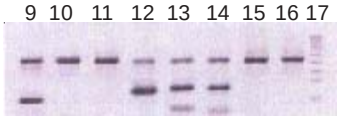
Methods: From 01.05.2003 until 30.06.2006 we worked up 67 patients with WRA. Until 10/2003, RBCCs were allocated exclusively by HSA. Starting in 11/2003, commercially available as well as in-house designed SSP- and RFLP-PCR assays for MGT (Figure 1 and 2) were applied progessively to allocate RBCC. Here, we present a retrospective comparison of the two strategies focusing on efficacy, co-existing ARA as detected by HSA, economic as well as outcome aspects.

Figure 1: MGT by SSP-PCR

A. Rh D Locus

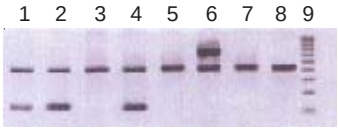
Lane 1 - 9: RhD exon scanning. 1: ex1+, 2: ex2+, 3: ex3+, 4: ex4+, 5: ex5+, 6: ex6+, 7: ex8+, 8: ex10+, 9: Marker, HGH: Human Growth Hormone (amplification control)

B. Rh CE/D Locus



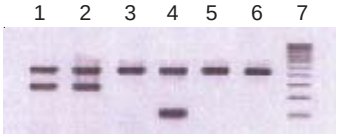
Lane 9 - 17: 9: Cw+, 10: c-, 11: E-, 12: e+, 13: DVII/DHMi+, 14: DVII/DAU+, 15: DNB697a-, 16: DNB697c-, 17: Marker

C. KKD - Systems



Lanes 1 - 9: 1: K1+, 2: K2+, 3: JKA-, 4: JKB+, 5: FYA-, 6: FYB+, 7: FYnull -, 8: FYX -, 9: Marker

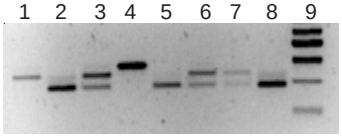
D. MNSs System



Lanes 1 - 7: 1: M+, 2: N+, 3: S-, 4: s+, 5: Vw-, 6: Mg-, 7: Marker

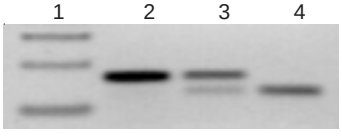
Figure 2: MGT by PCR-RFLP

A. DO Locus



Lanes 1 - 9: 1: DOAA, 2: DO BB, 3: DO AB, 4: undigested, 5: DO BB, 6: DO AB, 7: DO AB, 8: DO BB, 9: Marker
Endonuclease: *BseRI*

B. LU Locus



Lanes 1 - 4: 1: Marker, 2: LU AA, 3: LU AB, 4: LU BB
Endonuclease: *Aci I*

Results I: 30/67 (44,8%) patients requiring transfusions were managed by HSA as first line investigation and 37/67 (55,2%) patients were managed by MGT. Table 1 summarizes the clinical conditions of the patients requiring transfusions in the presence of WRA.

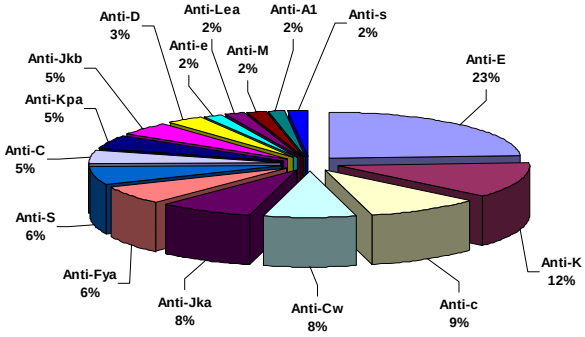
Table 1: Diseases of 67 patients with WRA requiring homologous RBCC transfusions

Clinical Condition	No of patients
CLL	15
Surgery	11
Idiopathic AIHA	9
Myelodysplastic Syndromes	6
Myeloproliferative Syndromes	5
Myeloma	5
CML	4
Lymphoma	4
Others	8

Results II: 27/67patients (40,3%) with WRA carried 63 clinically significant alloantibodies, which were detected by HSA (Figure 4). Anti-E was most often identified (15/63; 24%). Many patients carried multiple alloantibodies.

Figure 4: Specificities of 63 clinically significant ARA found in 27 patients with WRA

Anti-E	15
Anti-K	8
Anti-c	6
Anti-Cw	5
Anti-Jka	5
Anti-Fya	4
Anti-S	4
Anti-C	3
Anti-Kpa	3
Anti-Jkb	3
Anti-D	2
Anti-e	1
Anti-Lea	1
Anti-M	1
Anti-A1	1
Anti-s	1
Total	63



Laboratory workload, number of allocated RBCCs and posttransfusion outcome in the 67 patients with WRA are given in Table 2.

Table 2: Outcome of 67 patients with WRA needing homologous RBCCs. Comparison of two allocation strategies

Strategy	No Pat.	No Invest.	Rep. Invest.	Allo. RBCC	Time in h (total)	Pre ARA	Add ARA
HSA	30	38	8	196	8 (296)	13	3
MGT	37	37	0	762	6 (222)	45	0

Invest: investigation, RBCC: Red Blood Cell Concentrate, Allo.RBCC: number of allocated RBCCs, Time: average work-up time per investigation
Pre ARA: pre-existing allo-antibodies, Add ARA: additional allo-antibodies generated following transfusion

Conclusions

1. **MGT based strategies to allocate RBCCs for transfusion of patients with WRA are safe, efficient and economic.**
2. **Commercially available genotyping kits need to be completed by in house designed procedures to cover all the clinically relevant genotypes/phenotypes.**
3. **Transfusion of cross-match positive RBCCs that were allocated by MGT, requires appropriate patient's surveillance for transfusion related side effects. We recommend to search for newly formed ARA following transfusion of serologically incompatible RBCC.**

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