Outcome of type and screen versus crossmatch in cardiovascular surgery patients: A comparative study

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Abstract:

BACKGROUND: The need for an anti-human globulin (AHG) cross-match (XM) when the antibody screen (ABS) is negative is debatable and a matter of policy.

AIM: (1) To compare the outcomes of type and screen (T and S) method versus the AHG-XM in terms of posttransfusion alloimmunization and hemolytic reactions. (2) Calculation of XM transfusion ratio in both groups.

MATERIALS AND METHODS: The study included 200 patients undergoing elective cardiovascular surgery. Group I patients (n = 100) were issued packed red blood cell units after ABO and RhD typing, an ABS followed by an immediate spin XM (T and S protocol), while Group II (n = 100) patients by an AHG-XM. In Group II patients, if incompatibility was found, then an ABS and identification were performed. A posttransfusion ABS and a direct antiglobulin test (DAT) was done on the 4th day. The XM, ABS (3-cell panel) and DAT were done using the gel technique (Bio-Rad, Switzerland). Thus, the outcomes of T and S method versus the AHG-XM in terms of posttransfusion alloimmunization and hemolytic reactions was measured. The XM transfusion ratio was also calculated in both groups.

RESULTS: In each of Groups I and II, 99 patients (99%) were transfused. There was no significant difference between the two groups based on previous transfusion (P = 0.621) or combined history of transfusion and pregnancy (P = 1). In Group I, all the patients were negative for ABS. In Group II, an AHG-XM was incompatible for 1 patient (1%) due to anti-c and anti-E alloantibodies and had a history of pregnancy as well as transfusion. In both the groups, none of the patients had any adverse transfusion reaction and the posttransfusion ABS and DAT were negative.

CONCLUSION: ABS is a better tool than AHG-XM in detecting alloantibodies in patients having the previous history of transfusion and/or pregnancy.

Keywords:
Antibody screen, cross-match, type and screen

Introduction

Pretransfusion compatibility testing comprises a series of policies and procedures, including laboratory tests, the goals of which are to provide blood for transfusion that will have the optimal clinical benefit without causing undue harm to the recipient. Current protocol in many centers across India, including ours, is ABO and RhD typing followed by the antihuman globulin (AHG) phase crossmatch (XM). However, if there is a history of multiple transfusions or pregnancy or a history of transfusion reaction, an antibody screening (ABS) of the recipient’s sample needs to be done.

In “type and screen” (T and S) method ABS is done on recipient’s sample to detect any irregular antibody, besides ABO and RhD typing. If the antibody screen is negative, blood units are issued after an immediate spin (IS) XM compatibility.

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of “T and S” are not only limited to saving cost and manpower by avoiding unnecessary XM till AHG phase, but it also avoids the need to reserve units for 72 h which is a routine practice after the XM, thus the inventory for rare blood group units can also be maintained at optimum level. It also permits early identification of clinically significant antibodies and antibodies which show “dosage” phenomenon, as there is “double dose” representation of such corresponding antigens in the screening and identifications of cell panels. Subsequently, the corresponding antigen-negative blood unit can be selected from the inventory and kept reserved for the patient. Disadvantages of “type and screen” method would be the chance of missing antibody against low-frequency antigens absent in the screening cell panel. It also misses antibody against antigens absent from the population from where the cell panel was prepared.

The present study was designed to compare the results of T and S method versus the conventional AHG XM using gel technique in patients undergoing cardiothoracic and vascular surgery. To detect any red cell sensitization by an alloantibody or red cell alloantibody formation a direct antiglobulin test (DAT) and antibody screen on posttransfusion sample collected 72 h after transfusion was also incorporated.

Materials and Methods

It was a prospective observational study conducted at our center in which a total of 200 patients undergoing cardiovascular surgery were included. The study was approved by the Institute Ethics Committee. At our institute, for cardiovascular surgery patients, the blood ordering schedule includes sending a blood requisition for four to five units of packed red blood cell (PRBC) units to our department. For pretransfusion testing, the blood requisitions of these patients were divided into two equal groups: Group I (n = 100) for “T and S” method and Group II (n = 100) for “AHG-XM” method. The method applied was random allocation as and when the blood requisitions were received. The patients’ demographic details such as age, gender, previous transfusion, and pregnancy history and diagnosis were recorded from the blood requisition form and the concerned clinician if details were missing. The patients were followed up posttransfusion and sample was collected on the 4th day (i.e., after 72 h) to perform a DAT and an antibody screen.

The blood grouping (ABO and RhD typing) and IS XM were performed using the standard tube technique. The AHG XM and DAT were performed using gel technique (LISS-Coombs AHG card, Bio-Rad, Switzerland). ABS and identification were also done using the commercial 3-cell panel (Diacell, Bio-Rad, Switzerland) and 11-cell panel (DiaPanel, Bio-Rad, Switzerland) with the gel technique (LISS-Coombs Card, BioRad, Switzerland).

Pretransfusion testing

Group I for “type and screen” method (n = 100)

For these requisitions, after ABO and RhD typing, ABS was done. If the ABS was positive, the antibody identification was performed, and the corresponding antigen-negative unit was issued after the AHG XM. While in case of a negative ABS, ABO, and RhD identical PRBC unit was selected and issued after an IS XM. If one unit was not compatible, another PRBC unit was selected from the inventory and checked for compatibility by an IS XM.

Group II for “anti-human globulin crossmatch” method (n = 100)

For these requisitions, after ABO and RhD typing, the AHG-XM was performed with an ABO and RhD identical PRBC unit. If it was not found to be compatible, the ABS and identification were performed and the corresponding antigen-negative PRBC unit was issued after it was found to be compatible on AHG XM.

In both the groups, the compatible units were kept ready for issue to the patient for the next 72 h after the XM as per the departmental protocol. Subsequently, these units were taken back into the inventory and a fresh sample was obtained from the patient for testing as per the Group I or Group II protocol. Furthermore, the pretransfusion sample and a tube segment of the compatible PRBC were retained.

Posttransfusion testing and assessment

In both Groups I and II, a posttransfusion sample of the patient after 72 h (i.e., on the 4th day) was obtained for performing an ABS and a DAT to look for any irregular antibodies and red cell sensitization with alloantibodies, respectively. Thus, the outcomes of T and S method versus the AHG XM in terms of posttransfusion alloimmunization and hemolytic reactions were measured. The XM transfusion ratio was also calculated in both groups.

Results

The mean age (± standard deviation) was 38.4 ± 24.7 years (Range: 5 months to 77 years) with a median of 44.5 years in Group I, while it was 29.3 ± 23.6 years (Range: 3 days to 77 years) with a median of 27.5 years in Group II. The age difference in the two groups was statistically significant (P = 0.015). Out of the total 200 patients, 124 were males (62%) and 76 were females (38%). The male-to-female ratio was 1.56 and 1.7 in Group I and Group II, respectively. With
respect to risk factors for alloimmunization including previous transfusion, pregnancy, and combined history of transfusion and pregnancy, both the groups were comparable [Table 1]. Table 2 depicts the distribution of patients according to diagnosis in Groups I and II.

In Group I, the antibody screen was negative for all the 100 patients during pretransfusion testing and thus were transfused PRBCs after an IS XM. While in Group II, incompatibility was observed during the AHG XM for 1 patient (1%) out of the four units which were being crossmatched for this patient. On antibody screen and identification, the alloantibodies identified were anti-c and anti-E. This patient was a 37-year-old female having a history of pregnancy (6 years back) as well as that of transfusion (10 years back) and she was posted for an atrial septal defect repair. Although four PRBCs which were c and E antigen-negative and compatible on AHG XM were kept ready for this patient, however, she did not require transfusion at all. The details regarding the number of PRBCs crossmatched and transfused are provided in Table 3.

In each of Groups I and II, 99 (99%) patients received transfusion and a total of 239 PRBC units were transfused. Overall, in Group I, 116 PRBC units were transfused out of the 348 units crossmatched, making the XM to transfusion (C: T) ratio as 3:1, while the C: T ratio was 3.1:1 in Group II, as 123 PRBC units were transfused out of the 386 units crossmatched.

After the transfusion of PRBCs, none of the patients in Group I as well Group II had any adverse reaction attributable to transfusion. Furthermore, the ABS and DAT were negative for all the patients in Groups I and II, where the posttransfusion sample taken after 72 h was tested.

Discussion

Many serological tests have been added to pretransfusion testing for providing safer blood products to the recipients. In 1984, the American Association of Blood Banks recommended that the AHG XM can be replaced by an IS XM if the antibody screen is negative

Table 1: Patient characteristics with respect to alloimmunization risk factors

| Characteristic                                      | Number of patients | P (Group I vs. Group II) |
|----------------------------------------------------|--------------------|--------------------------|
| History of previous transfusion                    | 3 (3)              | 0.621                    |
| History of pregnancy                               | 25* (64.1)         |                          |
| Combined history of transfusion and pregnancy      | 2 (2)              | >0.05                    |

*Out of 39 female patients

Table 2: Distribution of patients in Groups I and II according to diagnostic category

| Diagnosis                                      | Number of patients | Group I (n=100) | Group II (n=100) |
|------------------------------------------------|--------------------|-----------------|-----------------|
| Coronary artery disease                        | 35                 |                 |                 |
| Rheumatic heart disease                        | 17                 |                 |                 |
| Atrial septal defect                            | 6                  |                 |                 |
| Ventricular septal defect                       | 7                  |                 |                 |
| Tracheo-esophageal fistula                      | 7                  |                 |                 |
| Other congenital heart diseases                 | 10                 |                 |                 |
| Others - Aortic stenosis, Aortic regurgitation, | 18                 |                 |                 |
| Tricuspid valve repair, Mitral valve replacement, |                    |                 |                 |
| Aortic Dissection, pulmonary artery thrombus,   |                    |                 |                 |
| Pericardiectomy, Stemotomy, Aorto-pulmonary     |                    |                 |                 |
| repair, Hydatid cyst of lung, Double valve      |                    |                 |                 |
| replacement surgery, Double outlet right         |                    |                 |                 |
| ventricular surgery                             |                    |                 |                 |

*The number of patients was 100 in each group and so the percentage figure is same as number in each group

Table 3: Number of packed red blood cell units crossmatched and transfused in Group I and II patients

| Number of PRBCs | Group I | Group II | Total number of PRBCs | Group I | Group II | Total number of PRBCs |
|-----------------|---------|----------|-----------------------|---------|----------|-----------------------|
| 1 unit          | 5       | 0        | 5                     | 0       | 0        | 5                     |
| 2 units         | 4       | 0        | 8                     | 0       | 0        | 8                     |
| 3 units         | 9       | 15       | 27                    | 45      | 45       | 90                    |
| 4 units         | 82      | 84       | 328                   | 336     | 336      | 664                   |
| 5 units         | 0       | 01       | 0                     | 05      | 05       | 10                    |
| Total           | 100     | 100      | 348                   | 386     | 386      | 734                   |

PRBCs=Packed red blood cells
There are various studies showing the safety of “T and S” policy in western countries. A study by Boral and Henry (New York, 1976) showed that out of 12,848 samples, 96.1% of antibody was detected by T and S. The T and S was shown to be 99.9% effective as the corresponding antigen of undetected antibody were of low frequency. In a multicentric Canadian study (1992) which included 9128 patients, it was observed that although 8936 patients were antibody screen negative, 27 patients out of them had an AHG XM incompatible with detection of IgG antibody, but, none of them showed clinical or serological evidence of hemolysis. Heisto from Norway, in a study that analyzed 73,407 compatibility tests for 23,857 patients, concluded that when ABS was negative, additional AHG XM could only find a very weak anti-Le and two of the samples had a doubtful reaction.

There is limited evidence which can justify omitting the antibody screen while AHG XM is being performed. Alloimmunization will be higher (2.4%) in patients where the red cell phenotype varies a lot due to racial and ethnic differences between the donor and patient population as shown in a study in military veterans in New York (2008). In the Indian setting, as there is a comparatively lesser phenotypic difference between donor and patient population, the risk of alloimmunization could be lower. The alloimmunization prevalence in our study was 0.5% (1 out of 200), as none of the patients in Group I (n = 100) had a positive antibody screen and 99 out of the 100 patients in Group II had a negative antibody screen in the posttransfusion sample. Thus, the single patient in Group II was alloimmunized with anti-c and anti-E which was discovered only after an incompatible AHG XM. The safety of T and S policy needs to be further studied in the setting of our country because the screening panel in use are usually from Caucasian descent which lacks certain antigens like Mi III phenotype (Gp Mur), a subtype of Miltenberger system, is relatively common in Asian population including southeast coast of China and Taiwan. In such a scenario, alloantibody to such antigens could go undetected and this may be the limitation of T and S policy in our setting until we use the indigenous screening cell panels derived from our own population.

The cost factor is also one of the limiting factors in this regard as costs vary a lot in our country depending upon the type of healthcare setup. There have also been few studies in India to assess the safety of T and S policy. In a study by Chaudhary and Agarwal from Lucknow, the T and S procedure gave a safety of 91.6% only, but it helped in the detection of unexpected antibody in 0.75% of the patients. In another study by Pathak et al. from Delhi, not even a single case was found where antibody screen was negative but AHG XM was incompatible, out of the 45,373 patients who were included in the study. One more study by Agrawal (2014, New Delhi), where 354 patients were included for a comparative study, the AHG XM was incompatible only in one of the 4 cases with a positive ABS. However, in these studies, the patient characteristics were not taken into consideration, like the history of previous transfusion or pregnancy, and the posttransfusion outcome was not assessed as well, thus, the safety of T and S may not be generalized to different patient populations based on the findings in these studies.

In an intervention-based study by Alghamdi et al. in cardiac surgery patients, the C: T ratio dropped significantly from 2.36 to 1.56 after the implementation of a standard blood ordering protocol through the blood utilization committee. They implemented T and S instead of a XM when certain criteria were met like elective isolated valve, minimally invasive surgery, initial antibody screen negative, specific biochemical parameters (aspartate aminotransferase <50 U/L, creatinine <1.5 mg/dL), and hematocrit >30% (or hemoglobin >10 g/dL). We observed that the most frequent ordering from the CTVS department was of 4 PRBC units while most of the patients in both the groups were transfused only a single unit (86% and 78%, respectively). Many studies have suggested that a C: T ratio >2:1 is indicative of excessive crossmatching. In a retrospective study by Ural et al. in cardiac surgery patients the C: T ratio was found to be 3.17 (95% confidence interval, 2.61–4.03). Based on their study findings, to avoid unnecessary XM they implemented a specific blood ordering algorithm for a subset of patients undergoing coronary artery bypass graft with hemoglobin >10 g/dL, a negative antibody screen, and first-time sternotomy-only a T and S to be performed.

In each of our study groups, 99 out of 100 patients were transfused PRBCs and none of them had any adverse transfusion reaction. Posttransfusion DAT and ABS, on the 4th day, were also negative for all the patients in both groups. One case in Group II, where only AHG XM was done, had only one of the four units compatible in AHG. Had we crossmatched only single unit for this patient which was compatible, it could...
have led to transfusion of compatible PRBC, without the detection of alloantibodies (anti-c and anti-E) in the patient, which were clinically significant. Since the frequency of E and c antigens is approximately 20% and 58% respectively, in our population, the estimated combined frequency of antigen negativity would be 33.6%. Thus, there was an approximate one-third chance, which is quite high, of getting an AHG compatible PRBC unit for this patient which is negative for both the c and E antigens. Moreover, even if, either c or E or both the antigens are present on any PRBCs being selected for XM, where if only ‘single dose’ expression of these antigens is present, i.e., CcEe, Ccee or ccEe, the XM could still be compatible due to “dosage” phenomenon. Thus, ABS seems to be superior in such group of patients with a history of either transfusion or prior pregnancy where sensitization may occur and lead to alloimmunization with these clinically significant antibodies.

As evident from group I patients, none of the 99 transfused patients had DAT or ABS positivity, on 4th-day posttransfusion, which indicates that omitting the AHG XM was safe in terms of posttransfusion outcome. In Group II, the compatibility for AHG XM in all the 99 patients probably shows the absence of alloantibodies, as only one of them had a history of transfusion, although there was the history of pregnancy in around 24% of patients. However, a negative posttransfusion DAT and ABS indicate that there was no anamnestic response and they were not alloimmunized. Thus, an AHG XM without an antibody screen was safe in these patients. Policies could differ for different groups of patients depending on the clinical conditions and resource availability. We propose an algorithm [Figure 1] for pretransfusion testing of patients undergoing elective surgery based on the findings in our study.

Our study has certain limitations. First, our study group was restricted to patients undergoing cardiovascular surgery, and the protocol for AHG compatible units without antibody screen may not be suitable for all other group of patients since the underlying factors for alloimmunization may vary with the different patient population. Second, due to time factors and restricted hospital stay of patients, we could not have a longer follow-up of the transfused patients to look for any alloimmunization.

**Conclusion**

The AHG XM alone is enough as pretransfusion testing without an antibody screen in the case of patients with no history of transfusion and pregnancy to ensure optimal utilization of available resources. Antibody screen is a better tool than AHG XM in patients having the previous history of transfusion and pregnancy, as they are at a risk of alloimmunization.

![Algorithm for elective surgery patients](image-url)
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Conflicts of interest
There are no conflicts of interest.

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