



Transfusion support in hematopoietic stem cell transplantation

Dong Wook Jekarl¹, Jae Kwon Kim¹, Jay Ho Han¹, Howon Lee¹, Jaeeun Yoo², Jihyang Lim³, Yonggoo Kim¹

Departments of Laboratory Medicine, ¹Seoul St. Mary's Hospital, College of Medicine, Seoul, ²Incheon St. Mary's Hospital, College of Medicine, Incheon, ³Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

p-ISSN 2287-979X / e-ISSN 2288-0011
<https://doi.org/10.5045/br.2023.2023004>
Blood Res 2023;58:S1-S7.

Received on January 3, 2023
Revised on January 16, 2023
Accepted on January 20, 2023

*This study was supported by a grant from National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (2021R1F1A1046464).

Correspondence to

Yonggoo Kim, M.D., Ph.D.
Departments of Laboratory Medicine,
Seoul St. Mary's Hospital, College of
Medicine, The Catholic University of
Korea, 222 Banpo-daero, Banpo-dong,
Seocho-gu, Seoul 06591, Korea
E-mail: yonggoo@catholic.ac.kr

© 2023 Korean Society of Hematology

Abstract

Transfusion support for hematopoietic stem cell transplantation (HSCT) is an essential part of supportive care, and compatible blood should be transfused into recipients. As leukocyte antigen (HLA) matching is considered first and as the blood group does not impede HSCT, major, minor, bidirectional, and RhD incompatibilities occur that might hinder transfusion and cause adverse events. Leukocyte reduction in blood products is frequently used, and irradiation should be performed for blood products, except for plasma. To mitigate incompatibility and adverse events, local transfusion guidelines, hospital transfusion committees, and patient management should be considered.

Key Words Transfusion, Hematopoietic stem cell transplantation, ABO blood group, RhD blood group

INTRODUCTION

Transfusion support is one of the major supportive care procedures performed for hematologic malignancies and patients with benign hematologic diseases. Hematopoietic stem cell transplantation (HSCT) is a curative therapy for these patients and requires human leukocyte antigen (HLA) matching, which is a major barrier to donor selection. Rigorous matching is associated with favorable outcomes [1]. ABO and Rh matching statuses are not considered before HSCT, but crossing the ABO and Rh barrier has caused complications after HSCT and difficulties in selecting optimal transfusion products [2]. In this review, we discuss the various aspects of transfusion support before, during, and after HSCT.

ABO BLOOD GROUP ANTIGENS

ABO antigens are multiple sugar chains or oligosaccharides

that are attached to the surface of red blood cells (RBCs) or N-glycans or O-glycans. ABO antigens are assembled by attaching sugars to an enzyme that can add sugar to a preexisting sugar molecule (Fig. 1A). The A and B blood antigens are formed by the sequential attachment of sugars (Fig. 1B) [3]. In the final step, the ABO gene located on chromosome 9q34 encodes a glycosyltransferase that adds A- or B-specific sugars at the end of the H antigen [4-6]. These antigens are located in the RBCs, platelets, and endothelium of vascularized organs.

These ABO blood group antigens are not a prerequisite for T cell sensitization for the production of antibodies and are poor inducers of T cell-specific response [7-10]. ABO antibodies are mostly IgM or IgG, which are formed by extrafollicular B-1 cells, whereas anti-peptide antibodies are formed by follicular B-2 cells [11-13].

The ABO blood group is important in solid organ transplantation and can cause hyperacute rejection via preexisting isoagglutinin (anti-A and/or anti-B). The importance of ABO blood group matching status is less critical in HSCT than

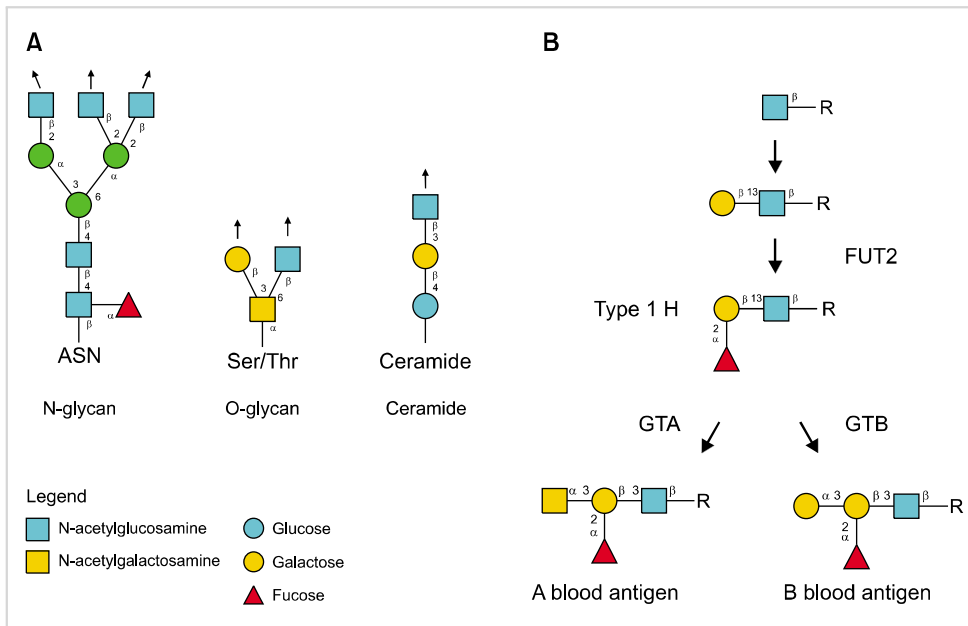


Fig. 1. The attachment site of ABO blood group antigen and ABO blood group antigen formation. These figures are modified based on previous studies [1]. Reproduced from The Korean Society for Laboratory Medicine, Laboratory Medicine 6th edition, page 1063, Figure 92-1 with permission from The Korean Society for Laboratory Medicine.

Table 1. Donor and recipient relationship associated with RhD.

Donor antigen	Recipient antigen		
	D negative with anti-D	D negative without anti-D	D positive
D negative with anti-D	Identical	Identical	Minor incompatibility
D negative without anti-D	Identical	Identical	Minor mismatch
D positive	Major incompatibility	Major mismatch	Identical

This table was modified based on previous studies [14-16].

in organ transplantation, such as the kidney or liver [8, 9]. However, ABO-incompatible HSCT can cause some transfusion-related issues.

RhD COMPATIBILITY

RhD incompatibility should also be considered. If RhD antigens differ between donors and recipients, the HSCT would be a RhD blood group antigen mismatch. The presence of anti-RhD antigens in donors or recipients before HSCT is incompatible with the RhD blood group antigen (Table 1) [14-16]. A minor RhD mismatch can be defined as a negative donor with a RhD-positive recipient. A major RhD mismatch can be defined as RhD-positive donors with RhD-negative recipients. Several studies showed that alloimmunization of RhD or anti-D production occurred in 9% of minor RhD mismatch HSCT, whereas 1% occurred in major RhD mismatch HSCT RhD blood group mismatch [17, 18].

RhD-negative blood is recommended for transfusion unless both the donor and recipient have RhD blood antigens. Because RhD-negative blood is rare in some regions, an alternative strategy may be considered. For RhD-positive

recipients and RhD-negative donors, RhD-positive blood can be transfused until RhD antigens are weakened. For RhD-negative recipients and RhD-positive donors, RhD-negative blood should be selected until the RhD antigen appears to some degree, and then RhD-positive blood should be selected. In the case of platelets, anti-RhD should be administered before RhD-incompatible transfusion [17, 18].

HUMAN LEUKOCYTE ANTIGEN (HLA)

HLA molecules are located on the short arm of chromosome 6 (6p21.3) with diverse polymorphic features. Class I HLA molecules (HLA-A, -B, and -C) are expressed in platelets and all nucleated cells, except neurons, corneal epithelial cells, trophoblasts, and germinal cells [19-21]. Only trace amounts are expressed in RBCs, designated as the Bg^a (HLA-B7), Bg^b [HLA-B17 (B57, B58)], and Bg^c [HLA-A28 (A68, A69)] blood groups [3, 4]. Class II HLA molecules (HLA-DR, HLA-DQ, and HLA-DP) are expressed in lymphocytes, monocytes, macrophages, dendritic cells, the intestinal epithelium, and early hematopoietic stem cells. Under certain conditions, endothelial cells or resting T cells can be induced to express HLA [3, 4].

These molecules are closely located and inherited en bloc, with one haplotype from the paternal and the other from the maternal side. This inheritable pattern results in a 25% chance of matching siblings. This close location also results in linkage disequilibrium, indicating that certain pairs of HLA molecules are more frequently found [20, 21-23].

Because HLA molecules are immunogenic factors, the HLA locus should be matched to overcome the histocompatibility barrier. As HLA matching status is the main criterion for donor selection and HLA genes are inherited independently from the ABO gene, 40–50% of HSCT procedures are performed across the ABO blood group [24-26].

The estimation of the effect of HLA mismatch is complicated by the diversity of HLA alleles and the occurrence of a mismatch from different loci with different allele combinations. These variables were simplified and yielded averaged results for many variables. A speculated hazard ratio of HLA-A, HLA-B, HLA-C, and HLA-DRB1 mismatching compared to perfect matching resulted in overall mortality as follows: 1.17 to 2.20; 1.16 to 1.90; 1.13 to 2.12 and 0.97 to 1.81, respectively [23-26].

HSCT

HSCT is a curative treatment for certain hematologic diseases. The type of HSCT can be classified as autologous, related, or unrelated allogeneic, HLA-matched, or mismatched allogeneic depending on the donors [26-28]. Autologous HSCT procedures were performed for plasma cell myeloma (50%) and lymphoma (40%), and allogeneic HSCT is performed for malignant diseases, including acute myeloid leukemia (40%), acute lymphoid leukemia (15%), and others (35%) [19]. HSCT using stem cell sources can be classified as bone marrow, peripheral blood stem cells, and cord blood. For patients lacking suitable donors, a haploidentical donor from a first-degree related donor can be used for HSCT [25, 29].

The advantages and disadvantages of peripheral blood HSCT include rapid engraftment compared to bone marrow transplantation and the incidence of chronic graft versus host disease (GVHD) has increased compared to bone marrow transplantation, respectively. For cord blood transplantation, rapid collection and administration of grafts are possible with lower infections and GVHD and less stringent HLA matching criteria, whereas engraftment has been delayed, and graft rejection and relapse have increased [30].

GENERAL CONSIDERATIONS FOR TRANSFUSION SUPPORT IN HSCT

Transfusion support is a critical supportive method for the patient before (Phase I), during (Phase II), and after (Phase III) HSCT [3, 10]. The general principle of transfusion is to transfuse cells or plasma that exactly matches the donor and recipient. However, these circumstances are usually un-

met for patients undergoing HSCT. Therefore, additional principles are required to ensure a safe transfusion. If exact matching is unavailable, transfusion should be performed on the recipient using a product expressing fewer antigens and antibodies. For example, packed red blood cells (PRC) with blood group O can be transfused into recipients with an AB blood group. As antibodies are an important factor for transfusion with abundant plasma components, platelets, fresh frozen plasma, or cryoprecipitate with blood group AB can be transfused to a recipient. Determination of ABO and Rh typing is important for transfusion. Cell typing and serum typing results should be considered when determining blood groups [3-6].

PATIENT BLOOD MANAGEMENT (PBM)

A restrictive RBC transfusion threshold of 7 g/dL hemoglobin is recommended for hemodynamically stable adults. The recommended transfusion threshold is 8 g/dL for patients with underlying diseases such as cardiovascular disease, evidence of end-organ damage, acute brain injury, anemia-related symptoms, or unexplained hypotension [9, 31]. Platelets should be transfused for nonbleeding, non-febrile adult patients with a platelet count $\leq 10 \times 10^9/L$. Active bleeding and febrile adult patients might be transfused at platelet count $\leq 20 \times 10^9/L$ or higher depending on the patient status. For patients scheduled for invasive procedures, a platelet count threshold of $\leq 50 \times 10^9/L$ is recommended, and for patients scheduled for procedures involving closed anatomical spaces, a platelet count threshold of $\leq 100 \times 10^9/L$ is recommended [29-31]. Implementation of the PBM program substantially decreased the transfusion of PRC and PLT products. Warner *et al.* [29] reported that, before PBM implementation, 80.7% (284/352) patients received PRC, whereas 63.2% (225/356) received PRC after implementation ($P < 0.001$). Among PLT products, 73.4% received PLT, whereas 48.8% received PLT after implementation ($P < 0.001$) [9, 29]. For patients scheduled for induction chemotherapy or HSCT, Leahy *et al.* [32] reported that PRC and PLT quantities decreased from 111 units to 72 units and from 121 units to 78 units, respectively, from 2010 to 2015. PBM of fresh frozen plasma or cryoprecipitate is beyond the scope of this review [33-37]. It has been reported that peritransplantation RBC transfusion is associated with increased acute GVHD and higher mortality, which might be triggered by minor blood antigens in RBC and platelets or inflammation after transfusion [38]. Transfusion should be carefully planned during HSCT to maximize transfusion effects and minimize adverse events.

Patients with hematologic diseases or undergoing HSCT require transfusion products that are incomparable to those of other patients with chronic disease, and ABO or RhD barriers hinder the selection of the blood group [9, 29]. The institutional transfusion officer or PBM team could intervene in the selection of optimal blood products before, during, and after HSCT. In addition, PBM programs for HSCT could reduce transfused blood products without adverse clin-

ical outcomes [29].

BLOOD PRODUCT AND IRRADIATION

Packed RBC, leukocyte-reduced RBC, packed platelet, single donor-derived platelet, fresh frozen plasma, cryoprecipitate, and granulocytes are some of the most commonly transfused products. Most of the products are irradiated with gamma rays or X-ray irradiators (25–50 Gy) to prevent GVHD and leukoreduction (leukocyte $<1 \times 10^6/\text{unit}$), except for granulocyte products [39, 40]. The British Society of Hematology recommends that irradiated components should be continued until all the following criteria are met [41]:

1. >6 months have elapsed since the transplant date;
2. The lymphocyte count is $>1.0 \times 10^9/\text{L}$;
3. The patient is free of active chronic GVHD;
4. The patient is off all immunosuppression.

As patients might have GVHD, administration of immunosuppressants, different HSCT conditions, underlying diseases, and previous treatments, usually, lifetime use of irradiated blood administered as immunological reconstitution status is difficult to confirm [42].

MAJOR INCOMPATIBILITY

ABO incompatibility could be classified as major, minor, or bidirectional incompatibility (Table 2). Major incompatibility can be defined as the recipient having pre-formed antibodies or isoagglutinin against the donor RBCs or graft. This occurs in recipients with O blood type with donors with non-O blood type and recipients with A or B blood group with donors with AB blood group [2, 43].

The clinical complications of major incompatibility include hemolysis, delayed RBC engraftment, pure red cell

aplasia (PRCA), and delayed granulocyte or platelet engraftment. To prevent hemolytic anemia (HA) complications, erythrocytes can be depleted using bone marrow-derived grafts. Isoagglutinins can be removed from recipients if the titer is greater than or equal to 1:128 via plasmapheresis or extracorporeal immunoadsorption. The prevention or treatment of sinusoidal obstruction syndrome or veno-occlusive syndrome can be performed using ursodeoxycholic acid or defibrotide, respectively [44, 45].

HA associated with HSCT could be associated with an underlying disease, infection, drug-induced HA, and passive transfer of ABO antibodies. After HSCT, acute HA due to isoagglutinin, thrombotic microangiopathy, and autoimmune HA should be excluded [44–47]. PRCA is a complication associated with major or bidirectional incompatibility after HSCT and is characterized by anemia, reticulocytopenia, and the absence of erythroid progenitors. Other causes of RBC depletion, such as infection, hemolysis, relapse, and drug effects, should be excluded [44, 45]. Reduced-intensity conditioning, cyclosporine administration for GVHD prophylaxis, high initial isoagglutinin levels, sibling donor as stem cell sources are the known risk factors [46, 47]. Treatment of PRCA includes plasmapheresis, transfusion support, high-dose erythropoietin, donor lymphocyte infusion, anti-thymocyte globulin, rituximab, and steroids [47, 48]. In addition, an increase in transfusion amount was noted for major and bidirectional incompatibilities compared to minor incompatibilities [47, 49].

MINOR INCOMPATIBILITY

Minor incompatibility can be defined as a donor with antibodies or isoagglutinin against the recipient RBCs. This occurs in recipients with A, B, or AB blood groups and donors with O blood group or recipients with AB and donors

Table 2. Transfusion strategy for peritransplantation.

ABO incompatibility	Recipient	Donor	Phase I	Phase II				Phase III
			All product	RBC	PLT 1st	PLT 2nd	Plasma	All product
Major	O	A	Recipient	O	A	AB, B, O	A	Donor
	O	B	Recipient	O	B	AB, A, O	B	Donor
	O	AB	Recipient	O	AB	A, B, O	AB	Donor
	A	AB	Recipient	A	AB	A, B, O	AB	Donor
	B	AB	Recipient	B	AB	B, A, O	AB	Donor
Minor	A	O	Recipient	O	A	AB, B, O	A	Donor
	B	O	Recipient	O	B	AB, A, O	B	Donor
	AB	O	Recipient	O	AB	A, B, O	AB	Donor
	AB	A	Recipient	A	AB	A, B, O	AB	Donor
	AB	B	Recipient	B	AB	B, A, O	AB	Donor
Bidirectional	A	B	Recipient	O	AB	B, A, O	AB	Donor
	B	A	Recipient	O	AB	A, B, O	AB	Donor

This table was modified based on previous studies [1–3].

with A or B blood groups. Clinical complications of minor incompatibility include acute HA or passenger lymphocyte syndrome (PLS), which causes delayed hemolysis [3-6].

PLS is an unpredictable complication usually occurring at 1-3 weeks after HSCT and is caused by hemolysis of recipient RBCs produced by donor lymphocytes. GVHD prophylaxis by sole cyclosporine or reduced-intensity conditioning is common in PLS in patients with the A blood group receiving stem cells from the O blood group. When antibodies are produced against the ABO blood group, hemoglobin and haptoglobin levels decrease, whereas laboratory parameters associated with intravascular hemolysis increase. Elevated lactate dehydrogenase, aspartate aminotransferase, indirect bilirubin, and urine hemoglobin levels have been reported [2, 43].

Alloimmunization against minor red blood cell antigens can occur and persist for several years [3, 5]. These antibodies are known to be either produced by the donor or recipient immune system against residual RBCs. The incidence of alloantibody formation against minor ABO antibodies is from 2.1% to 3.7% [44, 45].

Prevention of clinical features for minor incompatible cases includes alleviating PLS by a selection of a graft from peripheral blood stem cells, administration of calcineurin inhibitors, or exchange of donor RBCs before HSCT. Treatment strategies applied to autoimmune HA, such as intravenous immunoglobulin therapy or rituximab administration, can be considered [45]. Late engraftment of leukocytes has been noted for minor incompatibility compared to major and bidirectional incompatibility [46, 47].

BIDIRECTIONAL INCOMPATIBILITY

Bidirectional incompatibility can be defined as a recipient having A or B blood groups and a donor having B or A groups, respectively. Transfusion of RBCs can be performed using the O blood group, and for platelets and plasma transfusion, the AB blood group can be selected. Bidirectional incompatibility can have features of both major and minor incompatibilities [46-49].

CORD BLOOD HSCT AND ADDITIONAL TRANSPLANTATION

The advantages of cord blood include lower immunogenicity and lower incidence, severity of chronic GVHD, whereas disadvantages include delayed engraftment, low cell dose, and increased infection risk [50]. HLA-matched, double CD34 cell dose was used for sufficient cell dose, which often results in two different ABO blood groups transplanted. Therefore, transfusion support is requested in some rare clinical situations. Cord blood HSCT in adults often requires two donors, and incompatible ABO blood groups are common in cord blood transplantation. Additionally, a patient undergoing a second HSCT with an incompatible ABO blood group

from the first donor could be performed, in which RBCs of the O blood group and platelets or plasma of the AB blood group are usually selected [50, 51].

GRANULOCYTE TRANSFUSION

Granulocytes are white blood cells involved in the innate immune system. They perform phagocytosis, produce reactive oxygen species, release cytokines and chemokines, and are related to neutrophil extracellular traps [52-54]. Granulocyte transfusion (GT) can be administered to patients undergoing chemotherapy or HSCT for infection control. GT can cause logistic problems and difficulties in recruiting designated donors. The indications for GT are as follows [55, 56]:

1. Proven or probable bacterial or fungal infection with fever for 24-48 hours with persistent morbidity;
2. No response to antimicrobials, defined as failure to reach neutrophil recovery ($<1.0 \times 10^9/L$);
3. Absolute neutropenia ($<0.5 \times 10^9/L$);
4. Expected recovery of bone marrow function.

As decreased granulocytes can provoke or sustain the microbial infection, GT can be a therapeutic option as a bridging therapy until the recovery of white blood cells [53-58]. However, there are various obstacles to GT. Recruiting designated donors at the time of GT requirements is difficult. Mobilization of granulocytes using G-CSF or dexamethasone could raise ethical problems and donor safety issues, and at least three days are required for the donor pre-transfusion test, mobilization, and collection of granulocytes using apheresis. The banned use of hydroxyethyl starch because of renal toxicity during the apheresis process could hinder the granulocyte dose from reaching a therapeutic level. Pooled granulocytes from approximately 10 units of whole blood can provoke alloimmunization by HLA molecules on leukocytes [55-57]. Additionally, the efficacy of GT differed by patient group, depending on organ function at the time of GT.

GT effectiveness was evaluated by risk factors composed of the area under the curve of leukocytes, secondary AML, prothrombin time, blood urea nitrogen, bilirubin, alanine aminotransferase, phosphorus, and lactate dehydrogenase [55]. There were four risk groups: lower, intermediate, high, and very high risk. The probability of 30-day survival and mean survival days for lower, intermediate, high, and very high was as follows: 87.6% (99/113), 27.5 d; 55.9% (33/59), 23.6 d; 21.1% (4/19), 13.9 d; 0% (0/19), 3.3 d, respectively [55]. Although this was not a prospective randomized controlled trial, administration of GT in the lower- or intermediate-risk group was statistically significant compared to the higher-risk group [55-57]. As GT is not a feasible treatment modality, the cost and benefit should be weighed before starting its administration. Adverse effects, including fever, alloimmunization, and pulmonary reactions, should be considered. Further studies, along with risk stratification of patients, could provide an impact on GT undergoing HSCT [58-60].

LEUKOCYTE REDUCTION

Red blood cell products contain about 2×10^9 leukocytes, or 2×10^6 leukocytes are present in platelet products [61]. Prestorage leukoreduced products could be administered, or a leukocyte reduction filter could be applied during transfusion. Leukocyte reduction through centrifugation or filtration reduces more than 99.9% of leukocytes, which results in a leukocyte count of less than 10×10^6 /unit. Transfusion-transmitted infections, such as HTLV-1, HTLV-2, CMV, herpesvirus, Epstein-Barr virus, and *Trypanosoma cruzi* could be prevented or reduced. Febrile non-hemolytic transfusion reactions and alloimmunization to leukocyte antigens including HLA could be mitigated [61]. The disadvantages of leukocyte reduction are extra cost and time, a 2% loss of RBCs, and a 10% loss of platelets. However, the benefit is higher than the disadvantages; therefore, leukocyte-reduced products are highly recommended for patients before, during, and after HSCT [61-64].

CONCLUSIONS

Transfusion support for HSCT is an essential part of supportive care and should be performed considering the patient and donor ABO blood group results. Local transfusion guidelines, hospital transfusion committees, and patient management should be considered for transfusions.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

- Adkins BD, Booth GS, Vasu S. Transfusion support for stem cell transplant recipients. *Semin Hematol* 2020;57:51-6.
- Cohn CS. Transfusion support issues in hematopoietic stem cell transplantation. *Cancer Control* 2015;22:52-9.
- Korean Society for Laboratory Medicine. Laboratory medicine. 6th ed. Seoul, Korea: Panmuneducation, 2021:1065-86.
- Fung M, Eder AF, Spitalnik SL, Westhoff CM. Technical manual. 19th ed. Bethesda, MD: AABB Press, 2017:683-91.
- Han K, Park K, Song E. Transfusion medicine. 4th ed. Seoul, Korea: Korea Medical Book Publishing Company, 2014:179-97.
- Reid ME, Lomas-Francis C, Olsson M. The blood group antigen factsbook. 3rd ed. New York, NY: Academic Press, 2012:27-52.
- Jekarl DW, Yoo J, Lee S, Yu H, Kim M, Kim Y. Blood group antigen and phenotype prevalence in the Korean population compared to other ethnic populations and its association with RBC alloantibody frequency. *Transfus Med* 2019;29:415-22.
- Koo TY, Yang J. Current progress in ABO-incompatible kidney transplantation. *Kidney Res Clin Pract* 2015;34:170-9.
- Kim H, Ko DH. Transfusion in ABO-incompatible solid organ transplantation. *Korean J Blood Transfus* 2020;31:70-2.
- Kwon SW, Ahn A, Chung Y. Biological meaning of the histo-blood group antigens composed of sugar chains. *Korean J Blood Transfus* 2015;26:103-22.
- Lim YA, Cho HS, Choi YS, et al. Report on external proficiency testing for the ABO and D blood group typing tests in blood centers (2015). *Korean J Blood Transfus* 2016;27:68-78.
- Cho D, Lee SY, Ryang DW. ABO subgroup studies in Korea. *ISBT Sci Ser* 2015;10:332-5.
- Yoo J, Yu H, Choi H, et al. Evaluation of the automated immunohematology analyzer DAYMATE M. *Lab Med Online* 2017;7:163-9.
- Kim T, Park Y, Shin L, Jung YS, Youn M, Kim Y. The experience of RHD genotyping in D-negative blood donors. *Korean J Blood Transfus* 2021;32:91-101.
- Chung YN, Kim TY, Yu H, Bae JC, Cho D. Molecular basis of serological weak D phenotypes and RhD typing discrepancies identified in the Korean population. *Blood Transfus* 2021;19:327-34.
- Chan JY, Tokessy M, Saidenberg E, Giulivi A, Tay J, Allan DS. Rh D alloimmunization in allogeneic HSCT. *Bone Marrow Transplant* 2013;48:459-60.
- Cid J, Lozano M, Klein HG, Flegel WA. Matching for the D antigen in haematopoietic progenitor cell transplantation: definition and clinical outcomes. *Blood Transfus* 2014;12:301-6.
- Kim D, Kim KH, Seo YH, Park PW, Ahn JY, Seo JY. Transfusion in RhD mismatch hematopoietic stem cell transplantation. *Korean J Blood Transfus* 2020;31:159-64.
- Robinson J, Barker DJ, Georgiou X, Cooper MA, Flicek P, Marsh SGE. IPD-IMGT/HLA database. *Nucleic Acids Res* 2020;48:D948-55.
- Fürst D, Neuchel C, Tsamadou C, Schrezenmeier H, Mytilineos J. HLA matching in unrelated stem cell transplantation up to date. *Transfus Med Hemother* 2019;46:326-36.
- Jekarl DW, Lee GD, Yoo JB, et al. HLA-A, -B, -C-DRB1 allele and haplotype frequencies of the Korean population and performance characteristics of HLA typing by next-generation sequencing. *HLA* 2021;97:188-97.
- Copelan EA. Hematopoietic stem-cell transplantation. *N Engl J Med* 2006;354:1813-26.
- Passweg JR, Baldomero H, Bader P, et al. Hematopoietic stem cell transplantation in Europe 2014: more than 40000 transplants annually. *Bone Marrow Transplant* 2016;51:789-92.
- Worel N. ABO-mismatched allogeneic hematopoietic stem cell transplantation. *Transfus Med Hemother* 2016;43:3-12.
- Morishima Y, Kashiwase K, Matsuo K, et al. Biological significance of HLA locus matching in unrelated donor bone marrow transplantation. *Blood* 2015;125:1189-97.
- Ayuk F, Beelen DW, Bornhäuser M, et al. Relative impact of HLA matching and non-HLA donor characteristics on outcomes of allogeneic stem cell transplantation for acute myeloid leukemia and myelodysplastic syndrome. *Biol Blood Marrow Transplant* 2018;24:2558-67.
- Yuan S, Yang D, Nakamura R, Zhuang L, Al Malki MM, Wang S. RBC and platelet transfusion support in the first 30 and 100 days after haploidentical hematopoietic stem cell transplantation.

- Transfusion 2019;59:3371-85.
28. Zhang X, Xiao Y, Ran Q, et al. Clinical observation factors in the efficacy of blood component transfusion in patients following hematopoietic stem cell transplantation. *PLoS One* 2012;7:e36912.
 29. Warner MA, Jambhekar NS, Saadeh S, et al. Implementation of a patient blood management program in hematopoietic stem cell transplantation. *Transfusion* 2019;59:2840-8.
 30. Milkins C, Berryman J, Cantwell C, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfus Med* 2013;23:3-35.
 31. The Korean Society of Blood Transfusion. Transfusion guideline. 5th ed. Seoul, Korea: The National Institute of Organ Tissue and Blood Management, 2022.
 32. Leahy MF, Trentino KM, May C, Swain SG, Chuah H, Farmer SL. Blood use in patients receiving intensive chemotherapy for acute leukemia or hematopoietic stem cell transplantation: the impact of a health system-wide patient blood management program. *Transfusion* 2017;57:2189-96.
 33. Mueller MM, Van Remoortel H, Meybohm P, et al. Patient blood management. Recommendations from the 2018 Frankfurt Consensus Conference. *JAMA* 2019;321:983-97.
 34. Carson JL, Guyatt G, Heddle NM, et al. Clinical practice guidelines from the AABB: red blood cell transfusion thresholds and storage. *JAMA* 2016;316:2025-35.
 35. Storch EK, Custer BS, Jacobs MR, Menitove JE, Mintz PD. Review of current transfusion therapy and blood banking practices. *Blood Rev* 2019;38:100593.
 36. Seo Y, Kim MJ, Kim S, Kim HO. Audit of appropriateness of fresh frozen plasma transfusion. *Korean J Blood Transfus* 2012;23:136-44.
 37. Lim YA, Kim KH, Jung YZ, Choi SR, Song CE, Kim JN. Satisfaction survey of the regional networks for blood transfusion management project. *Korean J Blood Transfus* 2020;31:34-42.
 38. Hosoba S, Waller EK, Shenvi N, et al. Peritransplantation red blood cell transfusion is associated with increased risk of graft-versus-host disease after allogeneic hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant* 2018;24:973-82.
 39. Janatpour K, Denning L, Nelson K, Betlach B, Mackenzie M, Holland P. Comparison of X-ray vs. gamma irradiation of CPDA-1 red cells. *Vox Sang* 2005;89:215-9.
 40. Meli A, Balanant MA, New HV, et al. A comparison of the effect of X and gamma irradiation on red cell storage quality. *Vox Sang* 2022;117:39-48.
 41. Hosseini E, Kianinoddeh F, Ghasemzadeh M. Irradiation of platelets in transfusion medicine: risk and benefit judgments. *Platelets* 2022;33:666-78.
 42. Foukanelli T, Kerr P, Bolton-Maggs PHB, et al. Guidelines on the use of irradiated blood components. *Br J Haematol* 2020;191:704-24.
 43. Carreras E, Dufour C, Mohty M, Kroger N. The EBMT hand book. Hematopoietic stem cell transplantation and cellular therapies. Switzerland: Springer Open, 2019.
 44. Holbro A, Passweg JR. Management of hemolytic anemia following allogeneic stem cell transplantation. *Hematology Am Soc Hematol Educ Program* 2015;2015:378-84.
 45. Moosavi MM, Duncan A, Stowell SR, Roback JD, Sullivan HC. Passenger lymphocyte syndrome; a review of the diagnosis, treatment, and proposed detection protocol. *Transfus Med Rev* 2020;34:178-87.
 46. Marco-Ayala J, Gómez-Seguí I, Sanz G, Solves P. Pure red cell aplasia after major or bidirectional ABO incompatible hematopoietic stem cell transplantation: to treat or not to treat, that is the question. *Bone Marrow Transplant* 2021;56:769-78.
 47. Woo KS, Kim JE, Kim KE, et al. Effect of ABO-incompatibility on allogeneic hematopoietic stem cell transplantation. A single institute study. *Korean J Blood Transfus* 2009;20:235-41.
 48. Migdady Y, Pang Y, Kalsi SS, Childs R, Arai S. Post-hematopoietic stem cell transplantation immune-mediated anemia: a literature review and novel therapeutics. *Blood Adv* 2022;6:2707-21.
 49. Ataca Atilla P, Akkus E, Atilla E, et al. Effects of ABO incompatibility in allogeneic hematopoietic stem cell transplantation. *Transfus Clin Biol* 2020;27:115-21.
 50. Ballen KK, Gluckman E, Broxmeyer HE. Umbilical cord blood transplantation: the first 25 years and beyond. *Blood* 2013;122:491-8.
 51. Shin S, Roh EY, Yoon JH. Current status for cord blood transplantation and public cord blood bank in Korea. *Korean J Blood Transfus* 2013;24:103-10.
 52. Lee M, Lee SY, Bae YS. Emerging roles of neutrophils in immune homeostasis. *BMB Rep* 2022;55:473-80.
 53. Bae GH, Kim YS, Park JY, et al. Unique characteristics of lung-resident neutrophils are maintained by PGE2/PKA/Tgm2-mediated signaling. *Blood* 2022;140:889-99.
 54. Vorobjeva NV, Chernyak BV. NETosis: molecular mechanisms, role in physiology and pathology. *Biochemistry (Mosc)* 2020;85:1178-90.
 55. Yoo J, Cho HS, Yoon JH, et al. Risk stratification by 30-day prognostic factors of clinical outcomes after granulocyte transfusion in acute myeloid leukemia: a single center retrospective study. *PLoS One* 2022;17:e0273827.
 56. Estcourt LJ, Stanworth S, Doree C, et al. Granulocyte transfusions for preventing infections in people with neutropenia or neutrophil dysfunction. *Cochrane Database Syst Rev* 2015;2015:CD005341.
 57. Price TH, Boeckh M, Harrison RW, et al. Efficacy of transfusion with granulocyte from G-CSF/dexamethasone-treated donors in neutropenic patients with infection. *Blood* 2015;126:2153-61.
 58. Tanhehco YC. Granulocyte transfusion therapy. *Ann Blood* 2022;7:5-11.
 59. Lee JM, Choi SJ, Kim HS, et al. Analysis of hematologic parameters of donors, patients, and granulocyte concentrates to predict successful granulocyte transfusion. *Blood Res* 2019;54:52-6.
 60. Valentini CG, Farina F, Pagano L, Teofili L. Granulocyte transfusions: a critical reappraisal. *Biol Blood Marrow Transplant* 2017;23:2034-41.
 61. Shapiro MJ. To filter blood or universal leukoreduction: what is the answer? *Crit Care* 2004;8(Suppl 2):S27-30.
 62. Cho GE, Kim JH, Suh IB. Reduction of influenza A (H1N1) virus through a leukoreduction filter. *Korean J Blood Transfus* 2010;21:65-73.
 63. Youk HJ, Chung Y, Kim H, Ko DH. Is leukoreduction needed for plasma products? *Korean J Blood Transfus* 2022;33:182-94.
 64. Shin GS, Kim SH, Kim B, et al. Proposal of evaluation method for leukoreduction blood filter and evaluation of domestic filter. *Korean J Blood Transfus* 2017;28:256-63.