J Korean Med Sci 2003; 18: 669-72
ISSN 1011-8934

The Clinical Significance of Antibody Screening Test Including Di^{a+} Panel Cell in Asian-Mongoloid Populations

The Di^a antigen is well known as one of the antigens with low incidence among Caucasians; however, it has been discovered with a relatively higher incidence among Mongoloid populations. Thus, it has been speculated that the incidence of unexpected antibody against the Di^a antigen might be relatively higher among these populations. Hemolytic transfusion reactions (HTRs) and hemolytic disease of the newborns (HDNs) caused by anti-Di^a have been reported sporadically. However, there has been no prospective study on the incidence of anti-Di^a in Mongoloid populations particularly. The authors conducted a series of antibody screening tests on 11,219 Korean individuals for 25 months, by using three kinds of screening cells including Di^a cell. Anti-Di^a was detected in 8 patients, seven of whom had a history of transfusions or were multigravida. The incidence of anti-Di^a measured in this study was higher than expected, ranked third among unexpected antibodies identified during the period of the study, so it is strongly recommended that the Di^{a+} panel cell must be incorporated into antibody screening test for safer transfusion in Asian-Mongoloid populations.

Key Words : *Di^a Antigen; Blood Banks; Ethnic Groups; Anti-Di^a; Antibody Screening Test*

Tae Sung Park, Seung Hwan Oh, Jae Cheol Choi, Dae Dong Lee, Hyung Hoi Kim, Chulhun L. Chang, Eun Yup Lee, Han Chul Son

Department of Laboratory Medicine, Pusan National University College of Medicine, Busan, Korea

Received : 28 February 2003
Accepted : 30 May 2003

Address for correspondence
Hyung Hoi Kim, M.D.
Department of Laboratory Medicine, College of Medicine, Pusan National University, 1-10 Ami-dong, Seo-gu, Busan 602-739, Korea
Tel : +82.51-240-7418, Fax : +82.51-247-6560
E-mail : hhkim@pusan.ac.kr

*Supported by Research Grant from Pusan National University Hospital

INTRODUCTION

The Diego blood group represents the 10th red cell antigen system classified according to the International Society for Blood Transfusion (ISBT), which mainly consists of two independent pairs of antigens, called Di^a/Di^b and Wr^a/Wr^b. Each pair contains a low-incidence antigen and an antithetical high-incidence determinant, respectively (1, 2). As mentioned, the Di^a antigen is well known as one of the antigens with low incidence (0.01%) among Caucasians; however, it shows a relatively higher incidence among native American Indians and Asian-Mongoloid populations, which therefore demonstrates unique anthropologic significance (1-4). South American Indians have been shown to have an incidence of Di^a antigen as high as 36%, Chippewa Indians an incidence of 11%, Chinese an incidence of 5%, Japanese an incidence of 12%, and Koreans an incidence of 6.4-14.5% (3, 4). The cases of hemolytic transfusion reactions (HTRs) and hemolytic disease of the newborns (HDNs) related to anti-Di^a have been sporadically reported in the world, and these include severe cases (5-8). A few cases of anti-Di^a have been found in Korean patients who received repeated transfusions, and a case of HDN due to anti-Di^a was reported recently (3, 9). Therefore, for safer transfusion, it is extremely important that patients with anti-Di^a receive Di^a antigen-negative blood. Since a limited number of Caucasians carry the Di^a antigen, the Di^{a+} cell is hardly a part of antibody screening panels. Anti-Di^a have been found only sporadically even in the Asian-Mongoloid countries, because most Asian countries adopt identical panel cells used in Caucasians. In this study, the authors incorporated the Di^{a+} panel cell into antibody screening tests to estimate the incidence of anti-Di^a among Korean populations and also to evaluate its clinical significance.

MATERIALS AND METHODS

The authors examined the incidence of anti-Di^a in 11,219 patients who visited Pusan National University Hospital from March 2001 through March 2003 and received antibody screening test. The column agglutination method using LISS/Coombs card (DiaMed AG, Cressier, Morat, Switzerland) was used for the antibody screening test, with ID-DiaCell I+II (DiaMed AG) and ID-DiaCell Di^{a+} (DiaMed AG) as screening panel cells. The antibody identification test was conducted for those with positive results from the antibody screening test.

Antibody Screening Test

Fifty μL screening cells and 25 μL serum were added to LISS/Coombs card (DiaMed AG) and incubated at 37°C for 15 min. Using ID-Centrifuge (DiaMed AG), it was further centrifuged for 10 min. The results were interpreted as 5 phases : negative,

Table 1. Summary of clinical characteristics in eight patients with anti-Di^a

No. of patient	Sex/Age	Blood group	Di^a antigen phenotype	Diagnosis	Obstetrical history	Transfusion history
1	F/28	O+	NT	Tennis elbow	$G_2P_2A_0L_2$	Yes
2	F/29	B+	NT	Delivery, previous pelvic bone fracture	$G_4P_1A_2L_1$	Yes
3	F/35	AB+	-	Thyroid papillary cancer	$G_2P_2A_0L_2$	Yes
4	F/37	A+	-	Idiopathic thrombocytopenic purpura	$G_3P_1A_2L_1$	Yes
5	M/44	O+	-	Common bile duct stone	-	Yes
6	M/25	O+	-	Left acetabular fracture	-	Yes
7	M/53	O+	-	Tongue cancer	-	NI
8	F/44	A+	-	Acute monoblastic leukemia (M5a)	$G_5P_3A_2L_3$	Yes

NT, not tested; NI, no information; –, negative; G, gravida; P, parity; A, abortion; L, living birth.

1+, 2+, 3+, and 4+. If all of the red blood cells precipitated to the bottom of the column, the result would be negative, whereas if the red blood cells aggregated at the very top of the column the result would be 4+. The rest was interpreted according to the 1-4 grading system.

Antibody Identification Test

A method similar to the antibody screening test was used with Set ID-Diapanel (DiaMed AG) and with the identical interpretation system.

RESULTS

Of 11,219 patients who took the antibody screening test using LISS/Coombs card (DiaMed AG), positive results were found in 135 cases, with a 1.2% detection rate of unexpected antibody, and the distribution was as follows: the antibodies with highest detection rates were anti-E (36 cases), anti-Le^a (15 cases), anti-Di^a (8 cases), anti-M (6 cases), anti-E+anti-c (6 cases), anti-D (3 cases), and anti-e+anti-C (3 cases) with descending order. Anti-Di^a was detected in 3 men and 5 women, and in six of them the unexpected antibodies were further evaluated through Di^a antigenic phenotyping, enzyme phase, and additional tests using other panel cells (Table 1). All of the women with anti-Di^a was multi-gravida and transfusions, and two of three men also had a history of at least two episodes of transfusion of red cell concentrates. However, no transfusion history was documented in one of the male patients. In total, anti-Di^a was detected in 8 out of 11,219 patients, with its detection rate of 1/1,402 (0.07%). Anti-Di^a was not accompanied by other alloantibodies in each of the patients.

DISCUSSION

The clinically important unexpected antibodies causing HTRs or HDNs are usually formed as a result of exposure to red cell antigens from other persons through repeated transfusions or pregnancies (1-4). Based on recent studies of western countries, the clinically significant unexpected antibodies that occurred with the highest incidence after transfusion were anti-E and anti-Jk^a in common (10-13). In our country, the results of antibody screening test showed a large variation in terms of incidence and distribution of unexpected antibodies related to reported time and used methods (3, 14-16). The reports before 1990 using tube method showed the highest incidence of cold antibodies such as anti-Le^a and anti-P_1, which are less clinically significant (3, 14). Since the late 1990s in which column agglutination method was adopted, the higher incidence was found in anti-E or anti-E+anti-c depending on researchers, which is similar to the incidence measured in other countries (3, 15, 16). The identical pattern of the distribution was found in our study, which showed a higher incidence of unexpected antibodies against Rh blood group except anti-Di^a with a high detection rate.

The Diego blood group represents the 10th red cell antigen system classified according to the ISBT, which consists of a total of 21 antigens (1, 2). Among these, Di^b and Wr^b antigens belong to the high-incidence antigen groups without ethnic variation; however, other antigens including the Di^a antigen belong to the low-incidence antigen groups (1-3). The Di^a antigen is rarely found in Caucasians, and thus no active screening test is conducted for detection of anti-Di^a. The incidence of Di^a antigen is, however, relatively higher among the Mongoloid Asians and native American Indians from 3-4% up to 36%, which represents a unique anthropologic significance (1-4). Chae et al. have reported that Koreans have an 8.2% incidence of the Di^a antigen, similar to those Mogolian Asians (17). They also reported only one case of anti-Di^a in their series, with its detection rate of 1/1,846 (0.05%) (17). Although many Asian countries including Korea have been predicted to have a relatively higher incidence of anti-Di^a, the panel cells identical to those for Caucasians are used in the antibody screening test, and only a few sporadic cases have been reported on this issue (5-9). In this study, anti-Di^a alone, unaccompanied by any other alloantibodies, was identified in eight patients. Because of its limited availability of Di^{a+} panel cells, it has been difficult to entirely rule out the possibility of the unexpect-

ed antibodies present in any form of multiple alloantibodies consisting also of anti-Di[a]. However, it is important at this point to mention that no immediate hemolytic reaction had occurred during this research even if multiple alloantibodies, including anti-Di[a], were present. The reason for this is that adequate source of blood was issued upon cross-match between patient's serum and the given antigen negative blood by using indirect anti-globulin method, which was done among all of the patients with unexpected antibodies.

Type and screen is a policy in which the patient's blood sample is tested for ABO, RhD, and unexpected antibodies, then stored in the blood bank for future cross-match (1). If the result of antibody screening test is positive, the antibody must be identified and antigen-negative units for the clinically significant antibodies must be available for use if needed. However, if the antibody screen is negative, ABO- and Rh-compatible blood can be safely released after an immediate-spin or electronic cross-match (1, 3). Currently, a large number of medical institutions in Korea have adopted column agglutination method as antibody screening test instead of using traditional tube method. Along with this trend of application, the "type and screen" policy has also been implemented by an increasing number of hospitals. But the condition or obligation to this policy is that the panel cells used in screening must include all of the clinically significant antigens possessed by the specific group of people or race. The usual commercialized screening cells are produced on the basis of RBC antigen phenotypes of Caucasian. These blood cells generally include Rh, Kell, Duffy, Kidd, Lewis, P, MNSs, Lutheran, and Xg blood group antigens. Therefore, if clinically significant RBC antigens other than the above mentioned antigens are found within particular race, the cells having related antigens should be added to usual screening cells, bringing the even more safer "type and screen" possible. For example, the Miltenberger (Mi) classes represent a group of phenotypes of red cells that carry low frequency antigens associated with the MNSs blood group system (18). However, the Miltenberger class III phenotype (MiIII) has a relatively high incidence among people in South-East Asia: 9.7% in Thais, 7.3% in Taiwanese Chinese and 6.28% in Chinese blood donors in Hong Kong (19-21). Lin et al. reported that anti-Mi was the most common atypical alloantibody in both inpatients and pregnant women among Chinese patients in Hong Kong, being detected in 0.34% and 0.46% of them, which accounts for 31% and 48% of the total number of detected alloantibodies, respectively (19). For this reason, they recommended that MiIII cells should be included in screening panels when conducting type and screen on local Chinese population (19).

In our opinion, difference in the incidence of anti-Di[a] between reports is not caused by actual difference in the anti-Di[a] incidence, but because there is no addition of race-specific screening cells into antibody screening test. In conclusion, we strongly suggest that the Di[a+] panel cell should be incorporated into antibody screening tests conducted among Korean and Asian-Mongoloid populations for safer transfusion.

REFERENCES

1. Brecher ME. *Technical Manual. 14th ed. Bethesda, Maryland: American Association of Blood Banks, 2002; 315-92.*
2. Mollison PL, Engelfriet CP, Countreras M. *Transfusion in Clinical Medicine. 10th ed. Oxford: Blackwell Science, 1997; 201-2.*
3. Han KS, Park MH, Kim SI. *Transfusion Medicine. 2nd ed. Seoul: Korea Medical Publishing Co., 1999; 83-252.*
4. Harmening DM. *Modern blood banking and transfusion practices. 4th ed. Philadelphia: F. A. Davis Co., 1999; 200-12.*
5. Hinckley ME, Huestis DW. *Case report. An immediate hemolytic transfusion reaction apparently caused by anti-Di[a]. Rev Fr Transfus Immunohematol 1979; 22: 581-5.*
6. Alves de Lima LM, Berthier ME, Sad WE, DiNapoli J, Johnson CL, Marsh WL. *Characterization of an anti-Di[a] antibody causing hemolytic disease in a newborn infant. Transfusion 1982; 22: 246-7.*
7. Monestier M, Rigal D, Meyer F, Juron-Dupraz F, Baboin-Jaubert M, Marseglia GL. *Hemolytic disease of newborn infants caused by anti-Diego antibodies. Arch Fr Pediatr 1984; 41: 641-3.*
8. Kusnierz-Alejska G, Bochenek S. *Haemolytic disease of the newborn due to anti-Di[a] and incidence of the Di[a] antigen in Poland. Vox Sang 1992; 62: 124-6.*
9. Chung MA, Park EH, Lee CH, Oh CH, Namgung R, Kim HO, Park MS, Park KI, Lee C, Han DG. *A case of hemolytic disease in the newborn due to anti-Di[a] antibody. J Korean Soc Neonatol 2002; 8: 141-4.*
10. Pineda AA, Vamvakas EC, Gorden LD, Winters JL, Moore SB. *Trends in the incidence of delayed hemolytic and delayed serologic transfusion reactions. Transfusion 1999; 39: 1097-103.*
11. Heddle NM, Soutar RL, O'Hoski PL, Singer J, McBride JA, Ali MA, Kelton JG. *A prospective study to determine the frequency and clinical significance of alloimmunization post-transfusion. Br J Haematol 1995; 91: 1000-5.*
12. Pinkerton PH, Coovadia AS, Goldstein J. *Frequency of delayed hemolytic transfusion reactions following antibody screening and immediate-spin crossmatching. Transfusion 1992; 32: 814-7.*
13. Ness PM, Shirey RS, Thoman SK, Buck SA. *The differentiation of delayed serologic and delayed hemolytic transfusion reactions: incidence, long-term serologic findings, and clinical significance. Transfusion 1990; 30: 688-93.*
14. Han KS, Oh WI, Park MH, Kim EC, Kim SI. *Irregular blood group antibodies in Korean. Korean J Hematol 1989; 24: 145-53.*
15. Lee WH, Kim SY, Kim HO. *The incidence of unexpected antibodies in transfusion candidates. Korean J Blood Transfus 2000; 11: 99-103.*
16. Jung TK, Lee NY, Bae HG, Kwon EH, Park SH, Suh JS. *Unexpected antibody positivity with the use of the LISS/Coombs gel test. Korean J Clin Pathol 2001; 21: 422-5.*
17. Chae SL, Cho HI, Kim SI. *A study on the frequencies of U, Diego[a], and Kell blood group antigens and anti-Di[a] and anti-K in Koreans. Korean J Hematol 1988; 23: 183-8.*
18. Dahr W. *Miltenberger subsystem of the MNSs blood group system. Review and outlook. Vox Sang 1992; 62: 129-35.*

19. Lin CK, Mak KH, Cheng G, Lao TT, Tang MH, Yuen CM, Chan NK, Yang J. *Serologic characteristics and clinical significance of Miltenberger antibodies among Chinese patients in Hong Kong. Vox Sang 1998; 74: 59-60.*
20. Broadberry RE, Lin M. *The incidence and significance of anti-"Mi^a" in Taiwan. Transfusion 1994; 34: 349-52.*
21. Mak KH, Banks JA, Lubenko A, Chua KM, Torres de Jardine AL, Yan KF. *A survey of the incidence of Miltenberger antibodies among Hong Kong Chinese blood donors. Transfusion 1994; 34: 238-41.*