

Hpa-I (human platelet antigen-I) antigens in the Ivorian population (West Africa)

Abstract

The knowledge of antigens of erythrocyte blood groups enabled better transfusion management with a reduction in transfusion accidents. In recent years, progress has been made in the discovery and characterization of platelet antigens and the search for antiplatelet antibodies which also improve the management of patients in neonatology, transfusion therapy and organ transplantation. Unfortunately in Africa, few studies on the distribution of the frequency of platelet antigens are available. Given limited resources, our work aims to have a distribution of the frequency of platelet antigens of the HPA-1 system in the population in the Ivory Coast. The phenotyping of the antigens of the HPA-1 system was carried out on each tube of citrated blood collected by the MAIPA method (Monoclonal Antibody-Specific Immobilization Platelet Antigen). 184 blood donors with a male predominance were included and the results obtained during our work report a predominance of HPA-1a antigens with 99.46% versus 0.54% for HPA-1b antigens. To the best of our knowledge, there are no data available in Ivory Coast. Therefore, this work will allow us to establish a distribution of the platelet antigen polymorphism of the HPA-1 system of the Ivorian population and to demonstrate the need to implement measures to control the prevalence of immunizations related to platelets.

Keywords: human platelet antigen, HPA-1 platelet system, donors, ivory coast, sub-Saharan Africa

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Introduction

Although platelet transfusion remains the standard therapy for the management of cases of extreme thrombocytopenia in neonatology, obstetrics, surgery, medicine and onco-hematology, providing an indication and prescribing platelet transfusion remain subtle. The administration of platelets is often associated with many problems including their availability, cost, infectious risk and immunogenicity. This immunogenicity is supported by allergenic systems that are defined by antigens lining the surface of the platelet membrane. Platelet blood group systems are of two types. The first type includes systems shared with other blood cells and possibly other tissues. These are the non-specific antigens of platelets. The second type of antigens is said to be specific to platelets. Twenty-nine human specific platelet antigens have been described to date.¹ HPA-1² is the first platelet system described. Clinically it is the most important because the most immunogenic. It is a biallelic system defined by the HPA-1a and HPA-1b antigens.²

The identification of the HPA-1 system ensures better compatibility between the platelet derivatives of the donor and those of the recipient and to reduce the antiplatelet alloimmunizations during pregnancy, transfusion or more rarely during bone marrow transplantation. When present, these alloimmunizations are responsible for alloimmune thrombocytopenia resulting from the immunization of a healthy subject against platelet alloantigen he does not possess.³ There are essentially three clinical situations caused by antiplatelet alloantibodies: Alloimmune neonatal thrombocytopenia, postransfusion purpura and refractory platelet transfusions.^{3,4} The frequency of HPA-1a antigen varies from 75 to 88.7% in North Africa, from 81% to

87% in Caucasian populations, and from 98.8% to 99.8% in Asian populations.⁵ In sub-Saharan African black Africa, particularly in Benin, Cameroon, and Congo, prevalence ranges from 98.7 to 99.2%.⁶ In Côte d'Ivoire, platelet systems, particularly the HPA-1 system, have not been studied. Since, poor data are available in our tropical area and especially in Côte d'Ivoire; our study will allow to determine the frequency of antigens of the HPA-1 platelet system for the implementation of programs to reduce platelet alloimmunization.

Materials and methods

Type of study and subjects

This is a prospective, cross-sectional observation study. It was carried out in the National Blood Transfusion Center in Abidjan, Ivory Coast, West Africa. Our study focused on 184 consecutive blood donors, Ivorians, voluntary and unpaid donors. A written consent was obtained prior to donation and HPA-1 testing and this research was approved by the National Ethics Committee. Blood samples were collected in the satellite bag, taken under vacuum at the bend of the elbow after aseptization of the venipuncture site during blood donation. Each tube of collected blood has been labeled with a bar code identifying the donation.

Screening for platelet antigens

We used the reagent of the laboratories Diamed "Platelet HPA-1a typing assay" which uses the MAIPA method (Monoclonal Antibody-Specific Immobilization Platelet Antigen). This immunocapture technique combines the specificity of monoclonal antibodies directed against glycoprotein's (GP IIb/IIIa) carrying the specific platelet Ags

HPA-1 and the immunoenzymatic sensitivity.

The results were obtained after reading with the spectrophotometer at 630nm:

- OD630≤0.3 Platelets are HPA-1b1b or platelets do not carry GP IIb/IIIa glycoprotein
- OD630≥0.5 Platelets are HPA-1a positive (HPA 1a1a or HPA 1a1b)
- OD630<0.5 the sample is retested

Statistical analysis

The barcode identification number, gender, ethnicity, blood group ABO RHD and the HPA-1 phenotype for each donor were recorded in an Excel database.

Results and discussion

Results

A total of 184 blood donors were enrolled and all meet eligibility criteria (blood donations criteria). The sex ratio was 6.66 in favor of men. Blood donors from 18 to 35years represented 85.87% of the blood donors. According to ethnic repartition, the Kwa was the most prevalent (61.95%). Table 1 97 blood donors representing 52.72% of the blood donors had blood group O, followed by A(22.82%), B(20.65%) and AB(3.80%). Concerning Rh blood group, 92.93% are Rh D positive while 7.08 are Rh D negative. Table 1 By the use of MAIPA assay, we determined HPA-1 antigens in all and we detected a single case of HPA 1b (HPA 1a neg) phenotype which corresponds to a prevalence of 5.4 per 1000. This patient with HPA-1b phenotype is a 22-year-old male subject, of Kwa ethnic group and O Rh D positive blood group (Table 1).

Discussion

Overall, epidemiological data such as distribution by age group, sex ratio and distribution according to the blood group are close to current data available on blood donors in the Ivory Coast (activity report). The frequency of the HPA-1a and HPA-1b phenotype observed in our population of 184 Ivorian donors is 99.46% and 0.54%, respectively. The phenotypic frequencies are superimposable to those found by Halle et al.⁶ in sub-Saharan African populations, particularly in Cameroon(99.1%), Benin(98.7%) and Congo(99.2%). It is also comparable to frequencies found in black Americans, and Asian populations where frequencies range from 98.8 to 99.8%.^{5,7} The results given concerning the frequency of platelet antigens of the system HPA 1 have some limits. Homozygous HPA-1b was inferred when there was lack of HPA-1a expression. For HPA-1b phenotypes, we have not considered the HPA-1b antigens included in the HPA-1ab heterozygous cases of our HPA-1a positive phenotypes. For the assessment of the risk of alloimmunization in the HPA 1 system in our population, it is necessary and better, to give allele frequencies (-1a and -1b) and genotype frequencies (-1aa, -1ab and -1bb) by performing molecular biology methods which is not available in our laboratory. On the other hand, the frequency obtained for HPA-1a in our work is higher than that found in the Caucasian and North African populations which vary from 81 to 87% and 75 to 88.7% respectively.

There are significant variations in the prevalence of platelet antigens, particularly in the HPA-1 system between different peoples and ethnic groups.⁸ These variations may be the cause of platelet all

immunization when a new platelet antigen is delivered during a blood transfusion. The risk of all immunization exists but could be less important in black and Asian populations, compared to Caucasian and North African populations where the risk of all immunization varies from 17% to 36%. Antiplatelet alloimmunization during pregnancy, for example, results from maternal immunization against a fetal platelet antigen inherited from the father whose mother is lacking. The most frequently involved systems are HPA-1 and HPA-5, however, many other systems are involved. In the Caucasian population, the incidence of Fetal/Neonatal alloimmune thrombocytopenia (FNAIT) due to HPA-1a antigen is 1/1000 to 1500 live births.^{3,9} The consequences of this immunization are not negligible. The major risks of fetal thrombocytopenia are intracranial hemorrhages found in about 20% of cases, 10% of which are the cause of death or severe neurological sequel of the child. As for alloimmune neonatal thrombocytopenia, its clinical diagnosis will be discussed in the presence of a term newborn said "healthy" with skin hemorrhagic signs such as petechiae and purpuras, and more rarely we will note visceral hemorrhage and, in some cases, intracranial hemorrhage.

Table 1 HPA-1 phenotype and demographic characteristic of enrolled patients

Items	Number	%
Blood donation number	184	100
Age range (Years)		
18-25	66	35.87
26-35	92	50
36-45	20	10.87
Sup 45	6	3.26
Age moyen	28.9	
Sex		
Féminin	24	13.05
Masculin	160	86.95
Ethnic groups		
Mande	11	5.98
Krou	38	20.65
Gur	21	11.41
Kwa	114	61.95
ABO/D blood group		
A	42	22.82
B	38	20.65
AB	7	3.8
O	97	52.73
Rh D positive	171	92.93
Rh D negative	13	7.07
HPA phenotype		
Ag HPA 1a	183	99.46
Ag HPA 1b	1	0.54

These thrombocytopenias are considered as the platelet equivalent of neonatal hemolytic disease, but some aspects differ from it, such as fetal involvement in 50% of cases from the first pregnancy.^{3,10} Antiplatelet alloimmunization may also result from platelet transfusion. The posttransfusion accident is posttransfusion purpura, which is a severe but rare transfusion complication with a life-threatening risk due to deep thrombocytopenia in patients.¹¹ In France, the actual incidence is unknown but more than 250 cases have been reported with a marked decrease since leukocyte depletion of blood products.

Some platelet transfusions are ineffective. It is transfusion inefficacy or of “refractory state”. This state constitutes a brake on therapeutic advances to which the clinician often has to face. We distinguish non-immunological causes most often related to a quantitative insufficiency of platelets but mainly immunological causes due to an ABO incompatibility, the presence of anti-HLA antibodies or anti-HPA antibodies. The percentage of refractory patients varies from 10 to 70% according to the studies, depending on factors specific to patients and leukocyte-depleted or non-leukocyte depleted infused concentrates.¹² To the best of our knowledge, there are no data available in the Ivory Coast, on the other hand in Nigeria, authors report a high prevalence of anti-HPA antibodies, particularly anti-HPA 5 that would be more strongly involved in the onset of neonatal thrombocytopenia.¹³ These studies suggest the systematic recognition of neonatal thrombocytopenia's in all newborns by platelet counts during the first few days of life in order to detect them in time for better management. All unexplained severe neonatal thrombocytopenia's (<50.109/L) or moderate (<100.109/L) as well as all accidents of intracranial hematoma in utero or neonatal should lead to the search for maternal-fetal antiplatelet alloimmunization. A family study (in the sisters of the parturient) of the platelet phenotype will be carried out in order to detect women at risk.¹⁴

The distribution of blood groups ABO and Rh D in our sampling¹⁵ is not different from that we observed in the Ivorian population. There is no relationship between blood groups ABO and Rh D and the presence of platelet antigens HPA-1. On the other hand, the generation of anti-HPA-1 antibodies is independent of blood groups ABO. On the other hand, M Ahlen et al shows that the risk of neonatal thrombocytopenia due to anti-HPA-1 antibodies (Anti- HPA-1a) is correlated with the maternal blood group ABO.¹⁶ There would be genetic foundations that would influence the immune response to the origin of severe neonatal thrombocytopenia in the newborn from a mother with anti-HPA-1a antibodies.

Conclusion

Knowledge of platelet systems allows for a better therapeutic approach to refractory states to transfusions of platelet concentrates and ant platelet alloimmunization. Our results allow us to establish a first definition of the polymorphism of the antigens of the HPA 1 system of the Ivorian population and suggest the exploration of the HPA-1 system and the other allergenic platelet systems in molecular biology. On the other hand, we advocate performing systematically platelet counts in newborns and the screening of ant platelet alloantibody for any possible cause of immunization. In the context of platelet transfusion, the presence of a refractory state or posttransfusion purpura in a polytransfused patient should raise suspicions about the existence of specific antiplatelet antibodies and prescribe their research. For this it is necessary to have a register of typical donors and a technical platform allowing the research of antigens and platelet antibodies.

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Conflict of interest

The author declares no conflict of interest.

References

1. Immuno Polymorphism database: All HPA alloantigen/protein data.
2. Metcalfe P1, Watkins NA, Ouwehand WH, et al. Nomenclature of human platelet antigens. *Vox Sang.* 2003;85(3):240–245.
3. Cécile Kaplan. Alloimmunisations antiplaquettaires et diagnostic biologique. *RFL.* 2012;439:49–54.
4. Sentot Santoso. Human platelet alloantigens. *Transfus Apher Sci.* 2003;28(3):227–236.
5. Jedidi I, Romdhane H, Chakroun T. Fréquences géniques des systèmes HPA-1 et HPA-2 et risque potentiel d'allo-immunisation dans une population tunisienne. *IBS.* 2013;28:115–119.
6. Halle L, Bigot A, Mullen-Imandy G, et al. HPA polymorphism in sub-Saharan African populations: Beninese, Cameroonians, Congolese, and Pygmies. *Tissue Antigens.* 2005;65(3):295–298.
7. Rozman P. Platelet antigens. The role of human platelet alloantigens (HPA) in blood transfusion and transplantation. *Transpl Immunol.* 2002;10(2-3):165–181.
8. Mangerona CM, Garcia FB, Moraes-Souza H. Frequency of human platelet antigens (HPA)-1, -2, -5 and -15 in Brazilian blood donors and establishment of a panel of HPA-typed donors. *Transfusion Medicine.* 2015;25:189–194.
9. Peterson JA, McFarland JG, Curtis BR, et al. Neonatal alloimmune thrombocytopenia: pathogenesis, diagnosis and management. *Br J Haematol.* 2013;161(1):3–14.
10. Husebekk A, Mette K Killie, Jens Kjeldsen-Kragh, et al. Is it time to implement HPA-1 screening in pregnancy? *Curr Opin Hematol.* 2009;16(6):497–502.
11. Cecile Kaplan. Le purpura post-transfusionne. *Hematologie.* 2006;12(1):61–65.
12. Virginie Moalic, Claude Ferec. Etat réfractaire aux transfusions de plaquettes chez les patients adultes: revue de la littérature. *Médecine thérapeutique.* 2005;11(3):182–189.
13. Zaccheaus Awortu Jeremiah, Anne Ifeanyi Atiegoba, Osaro Mgbere. Alloantibodies to human platelet glycoprotein antigens (HPA) and HLA class I in a cross section of Nigerian antenatal women. *Human Antibodies.* 2011;20:71–75.
14. Vauthier-Brouzes D, Lefebvre G, Saada P, et al. Allo-immunisation plaquettaire materno-fœtale découverte devant une hémorragie intracérébrale fœtale in utero: proposition de prise en charge pour la grossesse suivante. *Journal de Gynécologie Obstétrique et Biologie de la Reproduction.* 2000;29:73–76.
15. Dembele B, Inwoley KA, Kouamé KO. Les fréquences phénotypiques et génotypiques des systèmes ABO et Rhésus (D) dans la population ivoirienne. *Cah Santé publique.* 2009;8(1):41–49.
16. Maria Therese Ahlen, Anne Husebekk, Mette Kjær Killie, et al. The development of severe neonatal alloimmun thrombocytopenia due to anti-HPA-1a antibodies is correlated to maternal ABO genotypes. *Clin Dev Immunol.* 2012;156867:5.