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Prevalence of Acridine Immunization to Subsaharians Africans Blood Donors

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Abstract: To conduct a study project on the inactivation of pathogens in whole blood using acridine derivatives in Africa, in order to prevent the transmission of pathogens, it is important to look for possible immunization to acridine in the blood donor population. It is therefore important to undertake an estimate of the prevalence in the sub-Saharan population in order to guide the design of the clinical study that will use the INTERCEPT Red Blood System procedure on whole blood for transfusion. to define the starting point in the evaluation of the immunological safety and transfusion safety of the product treated by this process. The objective of this study is to determine the prevalence of AAA among blood donors in sub-Saharan Africa. We conducted a multicenter prospective descriptive study of 902 blood donors collected in Côte d'Ivoire, Benin and Cameroon over the period from June 2015 to January 2017. Blood samples were collected from voluntary blood donors, of any sex, aged between 18 and 65, having given their consent for the study and having participated in the medical consultation for the donation of blood. The samples were analyzed according to the technique of the RAI gel card of the company BIORAD after centrifugation and incubation using test red cells treated with S-303 and glutathione. In the case of positive RAI results, to confirm the presence of anti-acridine, the donor plasma should be incubated with S-300. S-300 is a degradation product of S-303. The donor serum and S-300 are then incubated with the same red test cells. S-300 binds to the antibody and produces a negative result in the gel map in the presence of anti-acridin antibodies. Of the 903 samples tested both at the Abidjan laboratory in Côte D'Ivoire and at the Frankfurt laboratory, we found 1 positive sample and 8 reactive samples (positive for anti-erythrocyte antibodies). Positive donor plasma was incubated with S-300 which is the degradation product of S-303. The result is always positive, whereas according to the instructions of the reference laboratory of Frankfurt, it should be negative in case of presence of Locustacan. The results on AAA testing among 903 donors in three sub-Saharan countries show the absence of AAA in the sample of subjects included in the study according to the hypothesis emitted from this study. This opens the door to the prospect of conducting a clinical study on the inactivation of pathogens by acridine derivatives.

Keywords: Acridine, Immunization, Subsaharian, Blood Donors

1. Introduction

Inactivation of pathogens in the blood is a very important part of transfusion safety. For more than 20 years, this technique is used in the West and can significantly reduce the risk of transmission of infectious agent through the blood. To date, numerous inactivation technologies exist including Mirasol [1, 4] and Intercept [5, 8].

The intercept technology uses a molecule that is S-303 derived from acridine [7]. It is widely used for the inactivation of pathogens in plasma, platelets and red blood cell concentrates. Experimental laboratory studies on whole blood have been shown to be highly effective with no toxicity and no safety [8, 11]. In 2014, the CNTS Côte d'Ivoire was contacted by the Swiss Red Cross to conduct a study on the inactivation of pathogens in whole blood by the Red Blood System (CERUS) intercept process in order to develop a a project of international stature and to give the countries most in need of it an innovative technology. Since acridine is a molecule commonly used as a dye and preservative in food and laboratories [12, 14], it is likely to cause immune reactions in humans. This would result in the production of anti-acridin antibodies (AAA).

To conduct a study project on the inactivation of pathogens in whole blood using acridine derivatives to prevent the transmission of pathogens, it seems important to us to look for possible acridine immunization in the population of blood donors from sub-Saharan Africa.

The prevalence of these AAA has been studied in Germany in healthy donors and in patients who have never received inactivated products, as part of the Phase 3 clinical trial preparations which are now completed in Frankfurt. This prevalence was 1% [15]

To date no study in sub-Saharan Africa has been carried out to determine this prevalence and this work seems to us to be essential and a necessary preliminary basis before conducting a future clinical study in Sub-Saharan Africa.

It is therefore important to undertake an estimate of the prevalence in the sub-Saharan population in order to guide the design of the clinical study that will use the INTERCEPT Red Blood System procedure on whole blood for transfusion. to define the starting point in the evaluation of the immunological safety and transfusion safety of the product treated by this process.

The objective of this study is to determine the prevalence of AAA among blood donors in sub-Saharan Africa.

2. Methodology

We conducted a multicenter prospective descriptive study of 902 blood donors collected in Côte d'Ivoire, Benin and Cameroon.

The study lasted from June 2015 to January 2017. Blood samples were collected from voluntary blood donors of all sex, aged 18 to 65, who gave their consent for the study. study and participated in the medical consultation to donate blood.

Excluded were blood donors who failed to test for a positive viral marker, those whose additional tube samples could cause a blood volume surge and those who did not give informed consent to participate in the study.

Samples were taken on EDTA tube and after centrifugation for 5 minutes at 3400 rpm, they were frozen at -20°C (for samples from Cameroon and Benin) before shipment to Côte D'Ivoire and - 80°C for samples from the latter country. Samples from Benin and Cameroon were transported in carboglass in Abidjan.

The samples were analyzed according to the technique of the RAI gel card of the company BIORAD after centrifugation and incubation using test red cells treated with S-303 and glutathione.

In the case of positive RAI results, to confirm the presence of anti-acridine, the donor plasma should be incubated with S-300. S-300 is a degradation product of S-303.

The donor serum and S-300 are then incubated with the same red cells test. S-300 binds to the antibody and produces a negative result in the gel map in the presence of anti-acridine antibodies.

3. Results

Table 1. *Overall Results of AAA Screening in Three Countries.*

COUNTRIES	NUMBER OF SAMPLES	NEGATIF	REACTIVE (POSITIVE OR UNCERTAIN)
CAMEROUM	272	265	07
BENIN	297	296	01
COTE D'IVOIRE	334	333	01
TOTAL	903	894	9

08 samples yielded reactive (uncertainly qualified) results, 1 strongly positive sample (that from Côte d'Ivoire, and a total of 09 samples were retested at the Frankfort laboratory in Germany.

Table 2. *Results of antibody identification.*

INDENTIFICATION OF ANTIBODIES (n = 9)		COUNTRIES		
		COTE D'IVOIRE (n=1)	BENIN (n=1)	CAMEROUN (n=7)
PAN-AGGLUTINATION		0	0	2
ALLO-ANTIBODIES	Anti D	0	0	1
	Anti S		1	2

INDENTIFICATION OF ANTIBODIES (n = 9)		COUNTRIES		
		COTE D'IVOIRE (n=1)	BENIN (n=1)	CAMEROUN (n=7)
OTHERS ANTIBODIES	unknown specificity	0	0	1
	Probably antiglutathion	1	0	0

4. Comments

Of the 902 samples tested both at the Abidjan laboratory in Côte d'Ivoire and at the Frankfurt laboratory, we found 1 positive sample and 8 reactive samples (positive for anti-erythrocyte antibodies). The presence or absence of AAA results in preliminary and definitive results. The preliminary result is obtained at the end of the screening on 3 red cells group O tests. The final result sanctions the identification of the Ac (s) through a reference panel of 11 cells (DRK-BSD identification red cells). This screening panel allows the detection of antibodies corresponding to the antigens D, C, E, E, C, K, K, Kpa, Kpb, Fya, Fyb, Jka, Jkb, M, N, S, S, P1, Lea., Leb, Lub [16]. The positive blood sample was donor # 130 from Côte d'ivoire. The search for AAA by Gel Card technique is identical to the search for irregular agglutinin. These 2 tests follow the same principle. Of the 903 samples, 893 were clearly AAA negative, ie the serum did not contain anti-acridine antibodies. A previous screening study in Germany (unpublished) showed that a small proportion of patients (1%) receiving a blood transfusion had pre-existing antibodies to membrane-associated S-303 (acridine) adducts [15]. A neutralization test with progressive dilution of the acridine molecules was performed. Neutralization did not show a decrease in the reaction in the presence of acridine molecules. There is a reaction with the red cells treated but the reaction is not against acridine. Indeed, the plasma of the positive donor was incubated with S-300 which is the degradation product of S-303. The result is always positive, whereas according to the instructions of the reference laboratory of Frankfurt, it should be negative in case of presence of Locustacan. The hypothesis emitted is a reaction against Glutathione. It is probably an anti glutathione whose adduct in test red cells could justify the positivity of this sample. We launched an identification panel in erythrocyte systems on the positive sample of Côte d'Ivoire. No identification could be made because it does not correspond to any erythrocyte antibody. The donor's history of eating habits was quite subjective in view of the rather heterogeneous diet with both frozen and organic foods. This is a 23-year-old student from central Côte D'Ivoire whose diet is mainly based on starch and fat. However, we found the notion of intake of glutathione by ingestion of food compliments 3 weeks before inclusion in the stud.

5. Conclusion

Our study of blood donors in sub-Saharan Africa confirmed our initial hypothesis, which is based on the pre-existing prevalence of pre-existing AAA in the donor estimated at approximately 1 x 10e -2 in the donor populations of a European country, and that predicts an instantaneous prevalence of ≤ 1 x 10e -2 in the African donor population. Results on AAA testing among 902 donors in three sub-Saharan countries show the absence of AAA in the sample of subjects included in the study according to the hypothesis emitted from this study. This opens the door to the prospect of conducting a clinical study on the inactivation of pathogens by acridine derivatives.

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