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Prevalence of G6PD Deficiency in HIV Positive Child Group on Antiretroviral Treatment in Cocody University Hospital

Kouakou C, Dainguy M E, Grobi A, Mansou A, , Djoman A, Djivohessoun A, Kouadio E. Angan G, Yapi C, Oka G, Acquah P, Zobo N and Folquet A M.

Department of Pediatric CHU Cocody, Medical School, University Felix Houphouët Boigny, Abidjan, Côte d'Ivoire.

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ABSTRACT

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common erythrocyte enzymopathy in the world. Its frequency and its involvement in the occurrence of anemia in a group of HIV-positive children was studied. A cross-sectional descriptive and analytical study was conducted from 1st to 30th October 2015 at the Pediatric Department of the Cocody Teaching Hospital including all HIV-positive children undergoing antiretroviral treatment. Hemoglobin (g / dl), G6PD activity, antiretroviral regimen, and grade of anemic toxicity were collected. The severity of anemia was assessed according to the grade classification of hemoglobin in AIDS. Of 171 HIV-positive patients 1,17.5% had G6PD deficiency (30/171). The mean duration of antiretroviral (ARV) was 52.75 months and their regimen contained Zidovudine[R] in 75.43% of cases. More than ¾ (82%) of our patients had anemia. Grades I and II of anemic toxicity were predominant in 37% in both cases. There was a statistical relationship between G6PD deficiency and grade of anemic toxicity (p = 0.0000). This toxicity was more pronounced when exposed to ZIDOVUDINE[R] (p = 0.0000). This study confirms that the prevalence of G6PD deficiency remains high (17.5%) and thus allows us to advocate for the introduction of the G6PD assay in the initial assessment of HIV.

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) is the first enzyme of pentoses way which generates the NADPH. Glutathion-reductase allows the peroxides elimination generated in the red blood cell by oxygen linked to haemoglobin. If this enzyme is lacking, the oxidising agents can denature the haemoglobin and lipids of cell membrane, supporting the cell lysis [1]. This enzymopathy is characterized by its frequency and potential gravity. It is the most frequent enzymatic erythrocyte deficit in the world, reaching approximately 400 million individuals. This affection is more frequent in black Africa's and America's people. One also meets it in the countries of the Mediterranean circumference and in Asia [2]. The gravity of the deficit is due to the risk of acute intra vascular hemolysis at the birth, during some drugs and food absorption or during infections, with possible clinical consequences as an acute renal failure by tubular necrosis and shock state. At the new-born baby, because of the functional immaturity of the liver, there exists some risk of nuclear jaundice. The deficit in G6PD can also induce a chronic haemolytic anaemia. In some Southeast Asia countries, the frequency justified the neonate screening. The Ivory Coast, located in sub-Saharan Africa, has high incidence [3], but no systematic screening reflecting the real incidence exist and anaemia frequent is high in childhood [4]. Our study proposes to determine the frequency of this deficit in G6PD and its repercussion in term of morbidity, particularly in occurrence of anaemia in a group of HIV positive children.

Method

It was a cross-sectional study with descriptive and analytical aiming which proceeded from 1st to October 30th, 2015 (1 month) in Pediatric department of Cocody University Hospital. Were included, all the HIV positive children with the VIH1 on antiretroviral treatment follow-ups cohort and whose parents gave their consent of participation. Once the enlightened assent obtained, the blood sample was carried out in a tube containing an anticoagulant for the determination of Numeration Formulates Blood and of the activity of the G6PD. The rate of haemoglobin before the lysis of the red blood cell was determined; then in a tube, the red blood corpuscles were washed 3 times with a NaCl 0,9% solution. The globular base was preserved and added to 0.5 ml of the solution of lysis to the washed globular base. The mixture was preserved at the refrigerator at a temperature ranging between 2 and 4°C during 15 minutes to one hour. Then the lysate was passed to the centrifugal machine with 3000 turns by minute during 5 minutes. The supernatant was preserved. We determined the spectrophotometric activities to 340 Nm by using the reagent Enzopak Glucose-6-phosphate dehydrogenase laboratory RECKON DIAGNOSES. Tests were carried out in accordance with the instructions provided by the manufacturer of reagents. The proportioning of the G6PD activity was carried out by quantitative spectrophotometer. There was deficit in G6PD for values lower than 4.6 UI /g Hb. Anaemia was defined for values of lower haemoglobin for the age according to the recommendations of the ANAES and the severity of anaemia was appreciated according to classification in rank of the rate of haemoglobin of the AIDS [5].

Tele:
E-mail address: doccyprien@yahoo.fr

The data were collected using a card of investigation. We were interested in the following parameters: the age, the sex, concept of parents consanguinity, the geographic origin, the rate of haemoglobin (g/dl), the proportioning of the G6PD activity, the type of HIV, the clinical HIV stage, the antiretroviral therapeutic mode, the cotrimoxazole treatment, exposure time to antiretroviral treatment and the feeble rank of toxicity. The data were seized on Excel 2010. They were analyzed by the software Epi Info2000. The comparisons were made according to the statistical chi square (X^2) test and Student test. The selected threshold of significance was 5% ($p<0,05$) and the confidence interval at 95%.

Results

During our study period 171 HIV positive patients ranging from 1 to 25 years old were included. The sex ratio was 1.13. The older children of more than 24 months were most numerous. The median age of HIV screening was 06 years (69.16 months). The Ivorian children were accounted of 89%. The concept of consanguinity was found in 1.2% of the cases. The pathological history were marked by pneumonia with Community germ (21%) (36/171), skin diseases (17.5%) (30/171), tuberculosis and variants (15.8%) (27/171) and malnutrition (7.6%) (13/171). The average duration of setting under antiretroviral (ARV) was 52.75 months (04 years). Our patients were mainly with the stages B and C respectively in 41.5% (71 cases) and 37.4% (64 cases). 52.6% (90 cases) presented a severe immune deficiency at the time of the enlistment. They all were under prophylactic treatment containing Cotrimoxazole. The therapeutic mode was an association of antiretroviral containing Zidovudine in 75.43% of the cases. More ¾ (81.9%) of our patients presented an anaemia. The anaemia rank of toxicity I and II prevailed in 72.14% of the cases. The characteristics of the children are presented in table 1.

Table 1.Child Characteristics

	Number (n=171)	%
Age (month)		
< 12	1	0.6
12 – 23	6	3.5
> 24	164	95.6
Sex		
Male	91	53
Female	80	47
Geographic origin		
Ivoiry Coast	153	89
Other countries	18	11
Consanguinity		
Yes	2	1.2
No	169	98.8
Antiretroviral therapy		
ARV with AZT	129	75.4
ARV without AZT	42	24.5
Anemia		
Yes	140	82
No	31	18
Type of anemia (n=140)		
normochromic normocytic Anemia	88	62.8
hypochromic microcytic Anemia	16	11.4
Macrocytic Anemia	36	25.7
Anemia rank of toxicity (n=140)		
Rank I	101	72.1
Rank II	25	17.8
Rank III	14	10
Blood transfusion (n=140)		
Yes	22	15.7
No	118	84.2

Characteristics of patients with G6PD deficiency

Table 2. Characteristics of patients with G6PD deficiency.

		Number G6PD + (n=30) %		Number G6PD - (n=141) %		p	OR
Sex							
Male		11	37	80	57	0,04	0, 04 [0,19-0,99]
Female		19	63	61	43		
Antiretroviral therapy							
ARV with AZT		26	87	103	73	----------	
ARV without AZT		41	3	38	27		
Anemia							
Yes		27	90	113	80	0,20	
No		3	10	28	20		
Anemia rank of toxicity (n=27)							
Rank I	Yes	10	37	91	81	0,000	0,14 [0,05-0,35]
	No	17	63	22	19		
Rank II	Yes	10	37	15	13	0,003	3,84 [1,4-9,9]
	No	17	63	98	87		
Rank III	Yes	7	26	7	6	0,002	5,3 [1,6-16,7]
	No	20	74	106	94		
Blood transfusion							
Yes		5	19	15	13	0 ,35	
No		25	81	126	87		

Table 3. Anemia gravity on patients with G6PD deficiency and exposed to AZT.

		Number G6PD+ (n=26) %		Number G6PD - (n=103) %		P	OR
Anemia							
Yes		25	96	95	92	0,49	
No		1	4	8	8		
Anemia rank of toxicity							
Rank I	Yes	8	32	79	83	0,0000	0,09 [0,0350,25]
	No	17	68	16	17		
Rank II	Yes	10	40	13	14	0,002	4,2 [1,5-11,3]
	No	15	60	82	86		
Rank III	Yes	7	28	3	3	0,0000	11,9 [2,8-50,5]
	No	18	72	92	97		
Blood transfusion							
Yes		4	15	14	14	0,05	
No		22	85	89	86		

Children had a G6PD deficiency in 17.5% of cases (30/171). They came from the Ivory Coast in 93.3% of cases. The sex ratio was 0.58. The concept of consanguinity has not been found. The pathological antecedents were marked by community-acquired pneumonia (20%) (6/30), dermatoses (16.7%) (5/30), tuberculosis in all forms (13.3%) (4/30) and malnutrition (20%) (6/30). Our patients were predominantly in stages B and C respectively in 14 (46.6%) and 13 (43.3%). They were all infected with HIV 1 and were on prophylactic therapy with Cotrimoxazole®.The average duration of ARV was 52.75 months (04 years); Almost all children with a disability (86.66%) were exposed to AZT and 90% (27/30) of them were anemic with predominantly normochromic normocytic anemia (74%) (20/27).Grades I and II of anemic toxicity were predominant in 37% of cases respectively. The characteristics of children with G6PD deficiency are shown in Table 2 and Table 3 presents the exposure to Zidovudine^R and the severity of anemia. There was a statistical relationship between G6PD deficiency and grade of anemic toxicity ($p = 0.0000$).

This toxicity was more pronounced when exposed to ZIDOVUDINE^{R} ($p = 0.0000$).

Discussion

This study enabled us to carry out the screening of the G6PD and to determine the prevalence of anaemia in HIV children infected. The prevalence of the deficit in G6PD was de17.5 %. This rate is comparable with previous studies in Abidjan (22%) [6], with Cocody Hospital University (18.3%) [7]. In other studies in Mali [8] in Niger [9] and in Nigeria [10], the prevalence was respectively of 19%, 11.80% and 37.3%. High rates were also observed in certain Western areas because of immigration of the people. For this purpose Nockl and al. in the United States of America found a prevalence of 11.1% in new-born babies tested [11]. Kouakou et al. found a prevalence of 12% in a study made at the hospital Louis Mourier in France [12]. These various results confirm the report of the WHO according to which the deficit in G6PD is very frequent in Sub-Saharan Africa [3]. This hospital prevalence (in our department), must be regarded as a possible cause of anaemia in the children and specially those infected by HIV. Indeed, anaemia is the hematologic complication most frequent during the HIV infection [13],[14]. It can be associated or not with others cytopenia. An analysis of the factors associated with the incidence with anaemia at 328 6 7 infected by the HIV, in the United States, in 1998, showed that this one was associated not only with the immunizing deficit, but also with neutropenia, the thrombopenia, bacterial septicaemias, the use of the drugs like the Zidovudine, it to Ganciclovir, the Fluconazole and with the lack of disease prevention by the trimethoprime-sulfametoxazole [14]. The frequency of anaemia among our patients is estimated at 82%. This very high frequency was reported by several authors [15],[16]. It would raise mainly of a medullary insufficiency of production [17],[18] due to a medullar destruction, the inhibition of some cytokin like TNFα, TGFβ and lymphocytes CD8 very increased during the viral infection, a deficit of production of growth factors like IL3 and the IL6 [19],[20] or even a primitive attack of the hematopoietic stem cells [21]. One would explain that these anaemia's do not correct spontaneously and join readily a greater mortality in this population than in the pilot population, because of frequent decompensation in the absence of intervention. In the event in G6PD deficiency we have two different mechanisms which contribute to a reduction in the rate of haemoglobin. On the one hand haemolytic anaemia in the event of oxidative stress, and on the other hand the medullary toxicity of the VIH and Zidovudine. Indeed anaemia was more frequent in the overdrawn children than in the no overdrawn children but the difference observed was not significant.

Conclusion

This study carried out on HIV children confirms the results of the former studies showing a high prevalence of the deficit in G6PD of 17,5%. We make a plea for introducing the proportioning of G6PD activity in the initial assessment and the switch of Zidovudine by the another less toxic molecule for best taken in charge of the HIV child infected**.**

Conflicts of interest

The authors state that they have no competing interests.

Authorship

The authors have read and approved the final manuscript**.**

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