Seroprevalance of Hepatitis B, Hepatitis C and Human Immune Deficiency Virus and immunity status in patients with sickle cell disease

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ABSTRACT

Aim: The aim of the study was to investigate the prevalence of transfusion related infections and the immunity status in patients with sickle cell anemia (SCA) receiving multiple blood transfusions.

Material and Method: Ninety three patients with SCA were screened for hepatitis B surface antigen (HBsAg), hepatitis C virus antibodies (anti-HCV) and human immunodeficiency virus antibodies (anti-HIV) in the Hematology Clinic from 2004 to 2011. The immunity status of the patients in terms of influenza virus, pneumococ, haemaphilus influenzae type b and hepatitis B were assessed using medical history data.

Results: The patients had a history of blood transfusion and/or erythrocyte exchange. Of the 93 patients**, two** were HBsAg positive (2.1%), six were anti-HCV positive (6.4%), and none was anti-HIV positive. While HBsAb was positive in seven patients (7.5%) without vaccination, 40 patients (43%) were vaccinated for hepatitis B (HBV). HBsAb titers were >10 mIU/ml in 47 patients (50.5%). Twenty patients (21.5%) had pneumococ vaccination and 21 patients (22.5%) had influenza virus vaccination but none of them had vaccination for *Haemaphilus influenza type 1* (Hib). Vaccination rates were significantly higher in females ($p<0.05$).

Conclusion: Although sickle cell disease is associated with frequent and often severe infections, vaccination rates are not high enough. Data banks should be established and vaccination follow-ups should be achieved.

Key words: Sickle cell anemia, hepatitis B, hepatitis C, HIV, immunization, Turkey

Asma S, Gereklioglu Ç, Erdogan F, Unsal A, Solmaz S, Boga C, Ozdogu H. Seroprevalance of Hepatitis B, Hepatitis C and Human Immune Deficiency Virus and immunity status in patients with sickle cell disease. TJFMPC 2013;7(1):13-17.

Introduction

Sickle cell disease is the most frequent hemoglobinopathy in the world. It affects mostly African descent, but is also present in whites in Greece, Turkey, Italy and India. The responsible gene is autosomal co-dominant and only individuals homozygous for the gene are symptomatic. The condition is characterized by hemolytic crises and cardio-pulmonary, digestive, neurological, ocular and osteoarticular manifestations (1,2). Patients have a life-long, often severe anemia resulting primarily from extra vascular hemolysis. Sudden exacerbation of the anemia often results from splenic sequestration, aplastic, hyper hemolytic, and megaloblastic crises (2).

Blood transfusions can be performed in case of vasooclusive and/or hemolytic crisis (3). Transfusion-dependent patients are more prone to acquire various transfusion-transmitted infections such as hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) (4). Patients

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Received: January 2nd,2013
Accepted: March 11th, 2013

with sickle cell disease should be vaccinated for hepatitis B, pneumococcal infections, influenza, and Hemophilus influenza type b (5,6). Vaccinated patients should maintain an immunity threshold titer of antibodies for hepatitis B surface antigen >10 IU/l for hepatitis B immunization programs to be cost effective and clinically beneficial.

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Blood transfusions can be performed in case of vasooclusive and/or hemolytic crisis (3). Transfusion-dependent patients are more prone to acquire various transfusion-transmitted infections such as hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) (4).Patients with sickle cell disease should be vaccinated for hepatitis B, pneumococcal infections, influenza, and Hemophilus influenza type b (5,6). Vaccinated patients should maintain an immunity threshold titer of antibodies for hepatitis B surface antigen >10 IU/l for hepatitis B immunization programs to be cost effective and clinically beneficial.

The aim of the study was to investigate the prevalence of transfusion related infections and the immunity status in patients with sickle cell anemia (SCA) receiving multiple blood transfusions.

Patient selection and data collection

The medical files of 93 patients admitted to the Baskent University Hematology Outpatient Clinic between April 2004 and March 2011 were reviewed retrospectively. Of 93 patients, 33 **(**5,5**.%)** were male and the mean age was 31.3±9.7 years (range=16-58 years) (Table 1).

Table 1: Age and hemoglobin values of the patients

	Gender			
	Female (60)	Male (33)	Total (93)	p
Age (year, mean±SD)	32,0±10,1	29,9± 8,9	31,3±9,7	0,312
Hb (gr/dl, mean±SD)	8,49±1,44	9,10±1,50	8,70±1,48	0,058

Hb: hemoglobin, SD: Standard deviation

Detection of HBV, HCV and HIV Infections

HBsAg, anti-HBsAg, anti-HCV and anti-HIV tests in blood donors were assayed by Chemiluminescent microparticle immunoassay (CMIA) method, using Architect® (*Abbott, Diagnostic Division, Finishlin Business Park, Slingo, Ireland*) with a range of <0.05 IU/ml for non-reactive and ≥0.05 IU/ml as reactive for HBsAg, Microparticle Enzyme Immunoassay (MEIA) with Axsym® with a cutoff point <10.0 mIU/ml for nonreactive and ≥10.0 mIU/ml for reactive (*Abbott, Max-Planch-Ring 2, 65205 Wiesbaden, Germany*) for anti-HBs. Anti-HCV and anti-HIV were detected with CMIA method using Abbott kit Architect®, and with a threshold of <1.00 s/co as nonreactive and ≥1.00 s/co for reactive (*Abbott, Max-Planch-Ring 2, 65205 Wiesbaden, Germany, Abbott Diagnostic Division)*.

Table 2: Seroprevalence for HBV, HCV and HIV among SCA patients

	Gender				Total		p
	Female		Male				
	%	n	%	n	%	n	
HBsAg (+)	3,5	2	0	0	2,2	2	0,405
Anti-HCV(+)	8,8	5	3,1	1	6,7	6	0,293
Anti-HIV(+)	0	0	0	0	0	0	

Statistical Analysis

Statistical Package for Social Sciences (SPSS, version 11.5) software was used for data analyses. Statistical analysis was performed using Student t test, Pearson chi square test and Fisher's Exact test. P values <0.05 were considered statistically significant.

Results

All patients had a history of blood transfusion and/or erythrocyte exchange. The prevalence of HBV was 2.2% and HCV was 6.7%. None of the patients was positive for HIV. HBsAb was positive in 7.5% of patients without vaccination, 43% of patients were vaccinated for HBV. HBsAb titers were >10 IU/ml in 47 patients (50.5%). While 20 patients (21.5%) and 21 patients (22.5%) were vaccinated for pneumococ and influenza, respectively, none of them were vaccinated for *Haemaphilus influenzae.* Vaccination rates were significantly higher in females (p<0.05). HCV infection was more prevalent than HBV infection (Tables 2 and 3).

Table 3: Immunization status of the SCA patients

	%	n
Post-hepatitis immunity	7,5	7
Vaccination against HBV	43	40
HBsAb	50,5	47
Vaccination against Hib	0,0	0
Vaccination against Influenzae	22.5	21
Vaccination against pneumococ	21,5	20

Discussion

Homozygous SCA is prevalent among the people living in the Mediterranean region of Turkey. It has been reported that hemoglobin S is seen 3.9% of Turkish population (7). The main clinical features of SCA are caused by chronic hemolysis, microvascular ischemia, and organ damage. The most common complication is vasoocclusive crisis (8,9). Most patients with SCA receive transfusions at some point in their life to reduce the incidence of complications (2,8). Patients with SCA are prone to acquire various transfusion-transmitted infections (2).

Patients with sickle cell disease are included in the group for whom hepatitis B immunization is routinely prescribed. Antibody to hepatitis B surface antigen was measured in paired sera of thirty patients with sickle cell disease compared with a control group of healthy medical staff, five years post vaccination. There was no significant difference between patients with sickle cell disease and normal controls in the levels of antibody maintained or numbers that required booster vaccination (5).

In a study performed by Ocak et alin 1996, of 399 patients, three were HBsAg positive (0.75%), 18 were anti-HCV positive (4.5%), and none was anti-HIV positive (4). Researchers studied the prevalence of anti HIV-1 and 2, anti-HTLV-I, anti-Hepatitis B and C viruses (HBV and HCV) antibodies, anti-HBV vaccinal coverage, transfused patients and alloimmunizations frequencies among adult sickle cell patients attending the sickle cell center (SCC) of Guadeloupe. Among the studied samples (n=331) no transfusional HIV contamination was observed. All patients with positive HTLV-I (3.3%, n=11)and anti-HCV (2.7%, n=9) serology had transfusion history. Five patients (1.5%) had active hepatitis B. Vaccination for HBV was efficient in 247 patients (74.4%) and 57 had post-hepatitis B antibodies (10).

In our study, among the patients with HBsAb titers >10 IU/ml, seven had post hepatitis antibodies and 40 (43%) had vaccination.

The result of the study performed by Fosala et al in Nigeria showed that HBV infection was slightly but insignificantly higher than HCV infection among SCA patients. In addition, the results showed that the mean number of transfusion was higher in patients who were seropositive for both HbsAg (5.0±6.6) and anti-HCV (4.6±6.7) when compared to patients who were negative for both viruses (2.7± 3.0 and 2.9±3.2) for HBsAg and anti-HCV, respectively (11). The HCV antibody positivity is directly related to the number of transfusions given, and the prevalence rate in patients with transfusion is more than 10% (2).

In a study from Congo, 186 sickle cell patients (95 males and 91 females) aged 0-21 years were regularly followed over a three year period. The hepatitis B surface antigen was

detected in 15 patients (10%) and HIV serology was positive in 17 patients (11.3%) (12).

In the study of Richard et alfrom United States, hepatitis B core antibodies were positive in 14% of patients (12 out of 86) and hepatitis C viral antibody titers were positive in 16.5% (15 out of 91). There was a relationship between positive serology and transfusion for hepatitis C virus (HCV), but not for hepatitis B virus (HBV) (13).

In our study, the prevalence of HBV and HCV were found to be 2.2% and 6.7%, respectively. As 40 patients were vaccinated for HBV and seven had post-hepatitis B antibodies, the prevalence of HBV infection was lower than expected.

Bacterial infection is frequent in patients with sickle cell disease. Pneumococcal bacteremia is particularly severe in young children. The risk persists in adults, especially for nosocomial infections (14). Seventy percent of septicaemias and meningitis among under-fives with sickle cell disease is caused by Str. Pneumoniae (15). Conjugated pneumococcal vaccines are effective in protecting infants and should therefore be used in sickle cell patients (14,16). Immunization of patients with sickle cell disease and patients with splenectomy results in a significant increase in antibody amounts which persist for long periods of time (17). Among 33 adults, only four patients (12%) had complete coverage, with up-to-date coverage against pneumococcus 21%, Hib 18% and MenC 15%. Current (ie, within the last year) immunization against viral influenza was found in only 12% of adults and 8% of children (6). The pneumococ immunization rates in our study are 21.5% (20) and there is similarity with other studies. Influenza vaccination rate is 22.5%. None of them was vaccinated for *Haemaphilus B.*

In conclusion, although sickle cell disease is associated with frequent and often severe infections, vaccination rates are not high enough. The low vaccination rates may be related to inadequate medical records and the lack of periodic examinations of the patients with sickle cell disease. Data banks should be established and vaccination follow-ups should be achieved.

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