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ARS Medica Tomitana - 2020; 1(26): pag. 10- 13
doi: 10.2478/arsm-2020-0003

INFLUENCE OF BLOOD PRODUCTS ADMINISTRATION IN HIV ADULT PATIENTS ON INFLAMMATORY MARKERS

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ABSTRACT

One of the most common manifestations in HIV infected patients are hematological. Few studies on these manifestations have been conducted in Romania and worldwide. Anemia and infections occur frequently among people living with HIV and reflect the immune suppression of the host. Besides, the etiology of anemia in HIV infection often remains unclear. Therefore, C Reactive Protein (CRP) and fibrinogen can be used as markers of the degree of immune suppression. It is noteworthy that anti-anemic therapies may accelerate the progression of HIV disease. Primary infection or reactivation of known or unknown pathogens is still a major concern associated with blood transfusions and possibly lead to a reduced prognosis. Existing data suggest that severe anemia is one of the main factors. Chronic inflammation and increased hemostasis in HIV-infected persons are thought to be a consequence of viral replication or persistence and it is associated with poor prognostic in HIV-infected patients. Whether low levels of viremia predispose to increased inflammation is unclear. We investigated the relationship between anemia, inflammatory markers, and blood transfusions. The present study is an effort to evaluate correlation as well as the association between inflammatory markers and blood products administration in HIV/AIDS patients.

Keywords: HIV, blood products, C reactive protein, Fibrinogen levels

Introduction

Even though information on the use of blood and blood products is available, HIV patient management and the role of transfusion in these patients are less represented (1). This article aims to provide an analysis of the inflammatory markers abnormalities and clinical situations encountered in the HIV setting.

There is a popular misconception that an HIV-infected patient doesn't warrant transfusion as the prognosis is poor anyway. Anecdotal reports of dying patients following transfusion led to the unjustifiable practice of withholding blood transfusion from HIV-positive patients. At the start of the HIV pandemic, patients presented with advanced disease and generally had little prospect of effective management . Today, with highly effective ART and prophylaxis, HIV is a chronic manageable disease with an excellent outcome. Transfusion best practice and a rational approach to the management of anemia apply, independent of HIV status (1).

Fibrinogen may contribute to the development of vascular dysregulation by increasing viscosity, facilitating platelet aggregation, modulating endothelial function, and promoting smooth muscle proliferation and migration. The association between elevated fibrinogen levels and atherosclerosis may also

be mediated by inflammation as fibrinogen is an acute phase reactant (2). A large meta-analysis of 31 prospective studies of fibrinogen levels and subsequent vascular morbidity and mortality reported that a 100 mg/dL increase in fibrinogen levels was associated with a hazard ratio of 2.42 (95%CI 2.24–2.60) for coronary heart disease (3).

Material and methods

The research is a retrospective study. We gathered information from 678 hospitalizations in the Adult HIV Department, from Constanta Clinical Infectious Diseases Hospital, between 2015 and 2017.

We used two inflammatory biomarkers (C reactive protein and Fibrinogen levels) for evaluating the clinical status of HIV patients before and after blood products administration, along with demographics.

Different medical equipment was used to determine inflammatory and immune markers. All the blood samples were collected under standard precautions at Constanta Clinical Infectious Diseases Hospital

For evaluating CRP levels, blood was collected in a test tube without anticoagulant and performed on Conelab Prime 30i analyzer, using turbidimetry method.

Fibrinogen tests were performed on the automatic coagulation Thrombalyzer Compact X analyzer using an optic method. The samples were immediately brought to the Immunology lab for processing.

For every admitted patient it was performed a CBC count also, before and after blood products administration, the hemoglobin value being the most important criteria of blood administration. For CBC we used BC-5300 Auto Hematology Analyzer.

The blood products used for these patients were as follows: whole blood, packed red blood cells, platelets, freshly frozen plasma, depending on CB count.

Results

The patients within the study were divided into two groups. The first group is the one with patients that didn't receive blood products and the second group contains patients that received different types of blood products. The second group contains 45 hospitalizations, representing 6.6% of the total study group.

Most of the patients presented multiple comorbidities, more than half of the patients with blood products transfusion, and more than three-quarters of the patients from the non-transfusion group presenting four or more secondary diagnoses. Their distribution can be observed in Figure 1

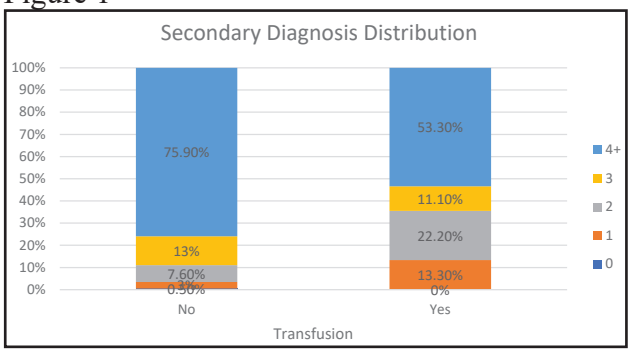

Figure 1 Secondary diagnosis distribution

The average age of the patients was 32.9 years, with a median of 28 years and a standard deviation of 10.87 years. In the case of patients without transfusion, their average age was 32.75 (SD 10.78 years), while for the patients that received blood products, their average age was 35.11 (SD 12.0 years) (Table 1)

Table 1 Descriptive statistics for age

	Transfusion		
	No	Yes	Total
N	633	45	678
Mean	32.75	35.11	32.90
Std. Deviation	10.78	12.00	10.87
Median	28	28	28
Minimum	18.0	20.0	18.0
Maximum	73.0	67.0	73.0

We observe a slightly lower age for the patients that didn't need and receive transfusions, and this can be correlated with a higher value of the hemoglobin.

Overall, gender distribution indicates a higher percentage of women (54.1%). When analyzing the data, we observed that in the case of patients that received blood products transfusion, the percentage of males is significantly higher compared to patients from the non-transfusion

Table 3 Descriptive statistics for hemoglobin values

Gender	Transfusion	N	Mean	Std. Deviation	Median	Minimum	Maximum
Female	No	349	12.09	1.9560	12.400	3.0	20.0
	Yes	18	10.34	2.0457	10.850	7.1	13.3
	Total	367	12.01	1.9938	12.400	3.0	20.0
Male	No	284	13.91	2.0916	14.300	5.5	18.0
	Yes	27	10.82	2.1752	10.800	6.6	15.3
	Total	311	13.64	2.2698	14.100	5.5	18.0
Total	No	633	12.91	2.2101	13.000	3.0	20.0
	Yes	45	10.63	2.1138	10.800	6.6	15.3
	Total	678	12.76	2.2745	12.850	3.0	20.0

group (60% vs 44.9%) (Table 2). The difference is statistically significant (p=0.049).

Table 2 Gender distribution

		Transfusion		Total
		No	Yes	
Gender	Female	55.1%	40.0%	54.1%
	Male	44.9%	60.0%	45.9%
Total		100.0%	100.0%	100.0%

Hemoglobin values

The mean hemoglobin value, at admission, for all patients was 12.73 g/dl (sd 2.27 g/dl), being significantly lower for patients that received blood products transfusions (p=0.002) (Table 3).

There was a weak, positive, statistically significant correlation between hemoglobin values and CD4 counts (r=0,076, p=0,049).

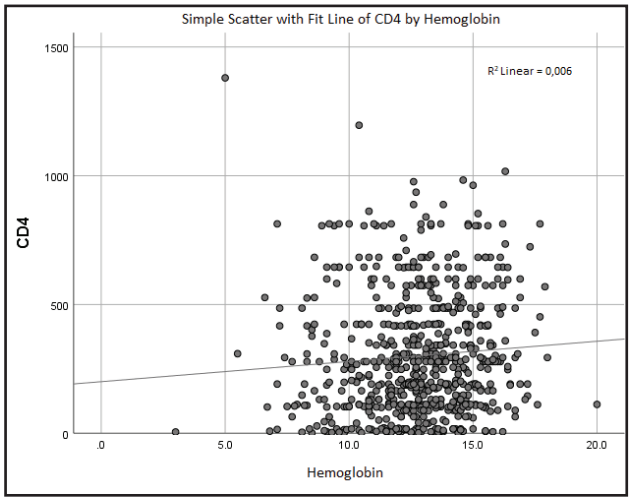

Figure 2 Hemoglobin values - CD4 relationship

Transfusion should not be the first line of intervention in iron deficiency; oral iron is generally effective in managing stable patients. The transfusion is reserved for patients with decompensated anemia (e.g. patients with signs of hypoxia, angina, cerebrovascular compromise, heart failure). Transfusion with red cell concentrate ('packed cells') can ameliorate symptoms in these patients. Each unit of packed red cells contains (replaces) approximately 250 mg of iron. (1)

C Reactive Protein

The acute-phase protein C-reactive protein (CRP) is a sensitive marker of inflammation and tissue damage. We measured CRP in 665 HIV-1 antibody-positive patients admitted to the hospital for investigation.

C Reactive Protein (CRP) values were lower in the no transfusion group (22.39 mg/dl3 , SD 37.16 mg/dl3) compared to the transfusion group (36.506 mg/dl3, SD 42.07 mg/dl3).

Table 4 - C Reactive Protein

		Unadjusted		Adjusted	
	N	M	SD	M	SE
Non-transfusion	631	22.395	37.161	22.926	0.89
Transfusion	34	36.506	42.07	26.656	3.84

An ANCOVA test was run to determine the effect of blood products transfusion on post-intervention CRP concentration, after controlling for pre-intervention. After adjusting for pre-intervention CRP, there was not a statistically significant difference in post-intervention CRP, F=0.894, p=0.345, partial η2=0.001.

In the international literature, the relationship between CRP concentration and HIV is still under debate. Lower levels of CRP have been associated with longer survival in HIV-infected patients. For a patients with HIV infection, the level of CRP is considered to be relatively low, which indicates that HIV infection is not a highly inflammatory disease (4). CRP appears useful for diagnosis and monitoring of intercurrent infection in HIV-1 antibody-positive

patients.

In HIV-1 antibody-positive patients, without intercurrent infection, CRP values higher than in the general population might reflect a sustained acute-phase response as a consequence of HIV infection. (5)

Fibrinogen

Fibrinogen values were lower in the no transfusion group (Table 5).

Table 5 Fibrinogen

		Unadjusted		Adjusted	
	N	M	SD	M	SE
Non-transfusion	630	273.15	113.65	273.46	1.69
Transfusion	35	281.03	106.94	275.4	7.18

We assessed the effect of blood products transfusion on post-intervention fibrinogen values, after controlling for pre-intervention values. There was no statistically significant difference in post-intervention fibrinogen $F=0.07$, $p=0.791$, $\eta 2<0.005$.

Conclusions:

Quantitative CRP might be considered a a reliable marker of disease progression and a cheaper alternative for routine disease monitoring and predicting HIV – related outcomes, especially in a resource-poor setting, but in association with blood products administration, its prognostic value decreases substantially.

Receipt of a blood transfusion was not independently associated with higher mortality risk. Thus, we found no evidence to support concerns regarding the potential adverse impact of the administration of blood transfusions to HIV-infected adults

Among the subjects mostly belonged to lower socioeconomic status followed by medium and high socioeconomic status, this may contribute to a higher education status and more awareness among medium and high socioeconomic class patients.

Other coinfections and lifestyle factors might independently contribute to a persistent inflammatory state in HIV infected individuals despite transfusions or medication.

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