Impact of antiretroviral therapy on anaemia and inflammation in HIV-infected people

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Background: in HIV patients several mechanisms are responsible of chronic anemia and this is not always resolved by combination antiretroviral therapy (cART). This study aims to characterize iron homeostasis and inflammation before and after cART in a group of HIV-patients with mild anemia.

Materials/methods: retrospective cohort study among HIV patients in the University Department of Infectious and Tropical Diseases of the University of Brescia with i) hemoglobin (Hb) between 9.5 and 13 gr/dl, ii) CD4+ cell> 200/mm3 before cART (T0) and HIV RNA<37 copies/ml 12 months after cART (T1). Exclusion criteria were: acute HIV-infection, severe diseases, congenital disorders of Hb synthesis. Iron homeostasis and inflammation markers tested were serum C reactive protein, iron and transferrin, percentage of transferrin saturation, serum ferritin, Hb, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-18, IL-22, interferon-γ, tumor necrosis factor-α, tumor necrosis factor-b, macrophage inflammatory protein-1-α, macrophage inflammatory protein-1-b, monocyte chemotactic protein 1 and granulocyte-macrophage colony-stimulating factor, and hepcidin.

Results: we included 18 patients, 10 of these resolved anemia (group A-GA, 13.25 g/dl) while 8 remained anemic (group B- GB, 11.95 g/dl) at T1.Among GB 62.5% were HCV-coinfected (30% in GA). cART improved $CD4^+$ and $CD4^+/CD8^+$ in all patients (statistically significant only for GA). Only patients of GA had mild iron deficiency at T0, resolved with cART. In GB, iron levels were normal at T0 and remained unchanged with cART **(Table 1)**. In general, cART decreased values of several inflammatory markers in all patients. All inflammatory marker were always higher in GB than in GA, except for hepcidin and IL 6 that were higher in GA at T0 even if not statistically significant. In this group these 2 markers decreased after cART while in GB cART increased hepcidin values **(Table 2)**.

Variables	Mean (min-max) Group A (n = 10) T0	Mean (min-max) Group A (n = 10) T1	*p*-value	Mean(min-max) Group B (n=8) T0	Mean(min-max) Group B (n=8) T1	*p*-value
Ferritina ng/ml	192.50	80.00	**0.0488**	149.00	9.50	0.1953
	(9.00-415.00)	(6.00-220.00)		(16.00-303.00)	(58.00-280.00)	
Sideremia µg/dl	54.00	71.00	**0.2408**	85.50	70.50	0.3828
	(32.00-91.00)	(24.00-160.00)		(42.00-112.00)	(42.00-156.00)	
Transferrina mg/dl	203.00	215.50	0.5533	184.50	184.50	0.7260
	(144.00-269.00)	(148.00-311.00)		(122.00-230.00)	(133.00-225.00)	
Transferrina,	21.41	29.83	0.2754	34.28	30.02	0.6406
saturazione %	(9.31-28.52)	(7.35-45.25)		(16.34-55.99	(16.69-55.21)	

Table 1: iron homeostasis markers in Group A and B, at T0 and T1; *p*-value<0.05

Variables	Mean *(min-max)* Group A (n = 10) T0	Mean *(min-max)* Group A (n = 10) T1	*p*-value	Mean*(min-max)* Group B (n=8) T0	Mean*(min-max)* Group B (n=8) T1	*p*-value
Epcidina ng/ml	4.41	2.71	0.7695	1.84	2.46	0.5469
	(0.50-22.93)	(0.33-11.38)		(0.52-3.87)	(0.72-6.92)	
IL-6 pg/ml	6.11	4.97	0.8457	4.52	4.23	1.000
	(3.73-9.83)	(3.49-11.91)		(3.29-8.50)	(2.91-7.05)	
IL-8 pg/ml	9.65	2.90	0.0756	19.50	16.00	0.3828
	(2.90-60.00)	(2.90-23.00)		(2.90-418.00)	(2.90-119.00)	
IL-18 pg/ml	282.50	149.50	0.1235	428.00	348.00	**0.0391**
	(145.00-466.00)	(119.00-808.00)		(145.00-868.00)	(111.00-533.00)	
MIP-1-beta pg/ml	175.50	125.50	0.4922	176.00	192.00	0.9453
	(113.00-286.00)	(30.00-981.00)		(83.00-687.00)	(72.00-620.00)	
MCP-1 pg/ml	160.00	116.50	0.0972	166.00	131.50	**0.0360**
	(43.50-606.00)	(43.50-288.00)		(93.00-489.00	(43.50-167.00)	

Table 2: inflammatory markers in Group A and B, at T0 and T1; *p*-value<0.05.

Conclusions: cART decreased values of inflammatory markers in all patients. We see that baseline mild anemia in HIV-infected patients cannot always be resolved with cART. These patients had normal values of serum iron and are frequently coinfected with HCV; furthermore, in these subjects, hepcidin doesn't play the main role in the inflammation. Understanding the mechanisms that mediate the inflammation/immune activation in HIV with suppressive cART is a challenger issue.