Lysine and threonine plasma concentrations in Ivorian patients living with human immunodeficiency virus

Lydie Boyvin[1,2], Kipré Laurent Séri [1,2], Jeanne Armande Aké [1,2], Alexis Bahi Gnogbo [1,2] , **Yapi Guillaume Yayé [1,3]** *and Joseph Allico Djaman[1,2] ,*

1 Department of Clinical and Fundamental Biochemistry, Institut Pasteur of Côte d'Ivoire (IPCI) 01 BP 490
2 UFR Biosciences, University Félix Houphouët-Boigny (UFHB) Abidjan, 01 BP V34 Abidjan, Côte d'Ivoire
3 University Jean Lourougnon Guédé, Côte d'Ivoire, 01 BP 540 Abidjan 01 Côte d'Ivoire

Introduction

Côte d'Ivoire is one of the most affected countries in West Africa with HIV/AIDS, with a prevalence of 3.4%. Essential amino acids are needed by the organism as they play key roles in the immune system and they are supplied through diet.

The objective of this study was to determine the plasma lysine and threonine status for better medical and nutritional management of patients living with HIV.

Methods

This study involved 254 individuals: 127 HIV positive and 127 HIV negative (serving as controls) after confirmation of their HIV status through an HIV test (test DETERMINE® and GENIE II). Lysine and threonine were assayed using high performance liquid chromatography (HPLC) on plasma and CD4 lymphocyte count by the method of flow cytometry (FacsCalibur) from whole blood containing EDTA.

Ethical considerations

The study was conducted in accordance with the Helsinki Declaration 2000 on HIV and AIDS research conducted in poor countries and in accordance with the local legislation regarding the national program on treatment management for People Living with HIV/AIDS (Decree No. 411 of December 23, 2001). The blood samples were collected from HIV-positive patients monitored at the Institut Pasteur of Côte d'Ivoire (IPCI), a reference center for public health programs in Côte d'Ivoire supported by the global fund for HIV/AIDS/malaria/tuberculosis. However, for research purposes, written consent was obtained from patients for the use of their blood samples taken during biological monitoring

Statistical analysis

Statistical analyses were performed using Student's t-test for comparison of averages. The correlation between essential amino acid concentrations and CD4+ T lymphocytes count was determined by the Pearson test. A $P < 0.05$ value was considered to be statistically significant.

Results 1

This study showed that deficiency of lysine was more observed in male HIV infected individuals (66.7%) and threonine deficiency in female HIV infected individuals (17.1%) as compared to the controls subject. The amino acid concentrations as a measure of the degree of immunosuppression was significant for lysine ($P = 0.0006$) and not significant for threonine ($P = 0.8640$).

Relating to sex: Regarding deficiency, 66.7% (38/57) male HIV-positive had deficiency of lysine as compared to threonine; 0.0% (0/57 HIV-positive) (Figure 1a). On the other hand, in female PLHIV, 37.2% (26/70) had lysine deficiency as compared to threonine; 17.1% (12/70) of PLHIV (Figure 1b). Regarding excess amino acids, 74.1% (43/57) HIVpositive men had excess threonine and 0.0% (0/57) had excess lysine (Figure 1a). On the other hand, 50.0% (35/70) female HIV-positive have excess threonine and 12.8% have excess lysine (9/70) (Figure 1b). However, excess threonine was 100% in the male control subjects and 50.0% in women against total absence of excess in lysine in both sexes.

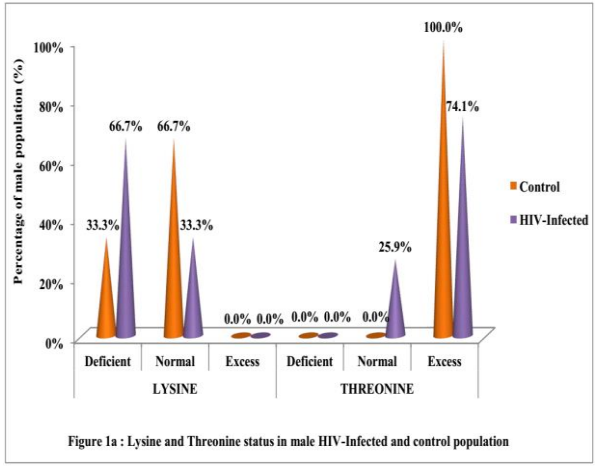

Figure 1a : Lysine and Threonine status in male HIV-Infected and control population

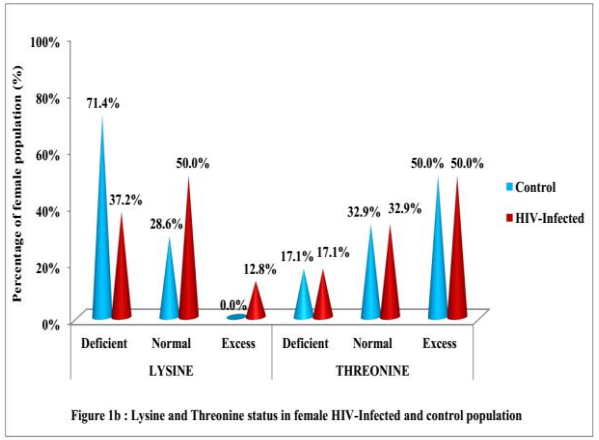

Figure 1b : Lysine and Threonine status in female HIV-Infected and control population

Figure 1: Lysine and Threonine status of subjects in this study according to sex

Results 2

In HIV infected male, mean concentrations of lysine and threonine were significantly lower, 97 ± 3.00 and 329 ± 27.36 µmol/L, respectively, as compared to the control (Table 1). However, in HIV infected females, average concentrations of lysine and threonine were respectively higher (173 ± 19.61 and 320 ± 49.05 µmol/L) as compared to the controls (83 ± 5.27 and 243 ± 36.32 µmol/L) with a significant difference for lysine ($P < 0.0001$) and non-significance for threonine ($P = 0.2101$) (Table 1).

Relating to HIV infection: Concerning lysine, 50.4% (64/127) of HIV-infected patients and 54.3% (69/127) of the control subjects had lysine deficiency. On the other hand, 9 (7.10%) samples from HIV patients had excess of lysine, as opposed to the control subjects that showed no excess in lysine concentration (Table 2). Concerning threonine, 9.5% of both HIV patients and controls (12/127) had threonine deficiency; however, 61.4% (78/127) of the HIV-infected patients and 72.4% (92/127) of the controls had excess threonine (Table 2). Finally, the number of HIV infected patients having lysine deficiency (64/127) was higher than those having threonine deficiency (12/127) (Table 2).

Relating to the WHO classification of CD4 lymphocytes: In HIV-infected female who had CD4 lymphocytes >500 and between 350 and 499 cells/mm3, the amino acid concentrations were normal for lysine (243 and 143 µmol/L, respectively) with a significant difference ($P < 0.05$) and higher for threonine (296 and 443 µmol/L) with no significant difference ($P > 0.05$) as compared to the

Lysine and threonine plasma concentrations in Ivorian patients living with human immunodeficiency virus

Lydie Boyvin[1,2], Kipré Laurent Séri [1,2], Jeanne Armande Aké [1,2], Alexis Bahi Gnogbo [1,2] , Yapi Guillaume Yayé [1,3] *and Joseph Allico Djaman[1,2]* ,

1 Department of Clinical and Fundamental Biochemistry, Institut Pasteur of Côte d'Ivoire (IPCI) 01 BP 490
2 UFR Biosciences, University Félix Houphouët-Boigny (UFHB) Abidjan, 01 BP V34 Abidjan, Côte d'Ivoire
3 University Jean Lourougnon Guédé, Côte d'Ivoire, 01 BP 540 Abidjan 01 . Côte d'Ivoire

normal reference values (lysine: 107 to 244 µmol/L; threonine: 74 to 175 µmol/L). However, when CD4 lymphocytes count was <200 cells/mm3 and between 200 and 349 cells/mm3, these values were lower for lysine (87 and 104 µmol/L, respectively). In the case of threonine, these values were higher (350 µmol/L) with a CD4 range of 200 to 349 cells/mm3 (P < 0.05) and lower (107 µmol/L) with a CD4 range < 200 cells/mm3 (P > 0.05) (Table 3a). In HIV-infected male, mean concentrations of lysine were normal (126 µmol/L) with CD4 range > 500 cell/mm3 and reduced with CD4 < 500 cells/mm3 (P > 0.05). The mean concentrations of threonine was high in any CD4 range with no significant difference in all cases (P > or = 0.05) (Table 3b). Finally, according to CD4 lymphocytes count, the correlation is significant for lysine (P = 0.0006) and not significant for threonine (P = 0.8640) (Table 4).

Table 1. Concentrations of L-lysine and L-threonine in HIV patients and control population according to gender

	Males			Females		
	PLIHIV	Control	P-values*	PLIHIV	Control	P-values*
L-lysine (107 – 244 µmol/L)	97 ± 3.00	115 ± 4.27	0.0012	173 ± 19.61	83 ± 5.27	< 0.0001
L-threonine (74 – 175 µmol/L)	329 ± 27.36	697 ± 23.31	< 0.0001	320 ± 49.05	243 ± 36.32	0.2101

The difference is significance for P < 0.05

Table 2. Distribution of PLHIV and controls based on mean concentrations in L-lysine and L-threonine

Essential amino acids	PLIHIV (n = 127)	Control (n = 127)
L-lysine		
< 107 µmol/L	64 (50.4%)	69 (54.3%)
107-244 µmol/L	54 (42.5%)	58 (45.7%)
> 244 µmol/L	9 (7.1%)	0 (0%)
L-threonine		
< 74 µmol/L	12 (9.5%)	12 (9.5%)
74-175 µmol/L	37 (29.1%)	23 (18.1%)
> 175 µmol/L	78 (61.4%)	92 (72.4%)

* The difference is significance for P < 0.05

Table 3a. Average concentrations of L-lysine and L-threonine in HIV-infected women according to CD4+ count

CD4+ Range	PLHIV female (n = 70)	L-lysine		L-threonine	
		Mean concentration (µmol/L)	Chi2 P*	Mean concentration (µmol/L)	Chi2 P*
> 500	35	243 ± 27.86	0.00	296 ± 27.86	0.87
499 – 350	17	143 ± 8.09	0.03	443 ± 67.76	0.70
349 – 200	07	104 ± 1.09	0.03	350 ± 3.57	0. 03
< 200	11	87 ± 0.49	0.64	107 ± 0.81	0.18

* The difference is significance for P < 0.05

Table 3b. Average concentrations of L-lysine and L-threonine in HIV-infected men according to CD4+ count

CD4+ Range	PLHIV male (n = 57)	L-lysine		L-threonine	
		Mean concentration (µmol/L)	Chi2 P*	Mean concentration (µmol/L)	Chi2 P*
> 500	20	126 ± 0.83	0.29	473 ± 18.84	0.05
499 – 350	11	96 ± 0.17	0.46	273 ± 6.69	0.38
349 – 200	13	92 ± 0.74	0.85	249 ± 20.42	0.72
< 200	13	83 ± 0.18	0.84	322 ± 1.13	0.47

The difference is significance for P < 0.05

Table 4: Correlation between CD4+T lymphocytes cells and plasma amino acids in HIV infected patients.

Amino acids	CD4+ T lymphocytes count	
	Correlation	P value
Lysine	r = 0.840	0.0006*
Threonine	r = 0.056	0.8640

r Value denotes degree of positive or negative correlation;
*P denotes statistically significant value; the difference is significant at P < 0.05

Conclusion

The deficiencies observed in HIV positive patients on antiretroviral therapy are therefore due to viral infection and insufficient nutritional intake of lysine. The threonine level depends on the degradation of the health condition of the subject. Therefore, effective early nutritional management of lysine and threonine is very essential to slow down viral replication in order to achieve a better quality of life for patients living with HIV.

References

1.Bender DA (2012). Amino Acids Synthesized from Aspartate: Lysine, Methionine (and Cysteine), Threonine and Isoleucine. In: Amino acid metabolism, 3rd ed, John Wiley & Sons, Ltd. pp. 225-277.
2. Bishop ML, Fody EP, Schoeff LE (2013). Amino acids and proteins. In: Clinical chemistry: Principles, Techniques, Correlations. 7th ed., Wolters Kluwer/Lippincott Williams & Wilkim, Philadelphia, USA. pp. 205-206.
3. Boyvin L, M'boh G, Aké-Edjème A, Soumahoro-Agbo MK, Séri KL, Djaman J (2013). Serum level of two antioxidant vitamins (A and E) in Ivorian (Côte d'Ivoire) people living with human immunodeficiency virus. Ann. Biol. Res. 4(11):48-54
4.Butorov EV (2013). Relationship between plasma L-lysine concentrations and levels of HIV-1 RNA. Virulence 4:646-653.
5.Faure M, Choné F, Mettraux C, Godin JP, Bécherau F, Vuichoud J, Papet I, Breuille D, Obled C (2007). Threonine utilization for synthesis of acute phase proteins, intestinal proteins, and mucins is increased during sepsis in rats. J. Nutr. 137(7):1802-1807.
6.Ghosh S, Smriga M, Vuvor F, Suri D, Mohammed H, Armah SM, Scrimshaw NS (2010). Effect of lysine supplementation on health and morbidity in subjects belonging to poor peri-urban households in Accra, Ghana. Am. J. Clin. Nutr. 92(4):928-939.

7. Hallen A, Jamie JF, Cooper AJ (2013). Lysine metabolism in mammalian brain: an update on the importance of recent discoveries. Amino Acids 45(6):1249-1272. Laforgerie