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Effects of the Therapeutic Diagrams on the Biological Parameters of the Patients under Antiretroviral Treatment during the Monitoringin Integrated Centre for Bioclinical Research of Abidjan (Côte d'Ivoire)

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Abstract: ***In treatment of the HIV/AIDS, the tri-therapy prescribes to the patients is generally made up of two therapeutic classes which are 2NRTIs+1NNRTI and 2NRTIs + 1IP.To evaluate the effect of these various therapeutic classes (2NRTIs+1IP and 2NRTIs+1NNRTI) on the biological monitoring parameters, a study was conducted on people infected by HIV. To do this, blood samples were taken from 45 subjects at the beginning of treatment up to 12 months. The results of our investigations showed that the 2NRTIs+1NNRTI therapeutic class was the most used during treatment with 84.44%, 80% and 75.56% respectively at M0, M06 and M12. At the erythrocyte level, anemia was very common among patients under the therapeutic class 2NRTIs+1IP, which with a rate of 28.6% at M0 increased to 33.3% at M06 and 45.5% at M12.In the same view, a significant increase of 27% in the prevalence of CD4 in the sixth month compared to the average rate at the beginning (respectively 28.6% and 55.6%) was observed. On the other hand, from M0 to M12, this rate dropped without a significant difference of 1.1%. Concerning the other parameters the majority of the subjects being under the two therapeutic classes had normal rates. This study shows that the different therapeutic classes had an effect on the biological parameters of our subjects.***

Keywords: Therapeutic classes; HIV; biological monitoring parameters; Abidjan (Côte d'Ivoire)

1. Introduction

More than a public health problem, HIV / AIDS is today a development and security problem that concerns the world. It is the main cause of death in sub-Saharan Africa[1]. The fight against this pandemic is undoubtedly one of the major challenges of the 21st century to ensure the harmonious development of our nations and guarantee the quality of life of the people[2].

Indeed, in this fight, a highly active antiretroviral therapy has significantly improved the health of patients since the introduction of antiretroviral combination therapies, combining nucleoside reverse transcriptase inhibitors with the new therapeutic class of protease inhibitors, then that of non-selective inhibitors nucleosides[3].

Côte d'Ivoire, which remains one of the most affected countries in the West African sub-region with a prevalence of 2.7%, has adopted a government action that allowed the majority of HIV-positive people to benefit from free combination of antiretroviral therapy since August 2008 [3, 4,5]. Investigations over the years have made it possible to assess the effectiveness of the various treatment regimens prescribed to patients. But, the trip-therapy used in some patients living with HIV is sometimes poorly supported because of its high toxicity and can even lead to their death. Therefore, some authors recommend monitoring blood parameters from the initiation of different therapeutic classes [6,7,8,9].

However, very few studies were carried out on the influence of different treatment regimens on the biological parameters of patients receiving antiretroviral therapy during their monotoring. Therefore, this study aims to evaluate the evolution of biological parameters according to the therapeutic class used during 12 months of monitoring with patients at the Abidjan Integrated Center for Bioclinical Research; a center specialized in the treatment people living with HIV/AIDS. Specifically, we will study the evolution of biological parameters according to the 2NRTIs + 1IP and 2NRTIs + 1NNRTI therapeutic classes.

2. Material and Methods

2.1 Study population

This was a monitoring study that took place from January 5, 2015 to January 8, 2016 in the Integrated Center for Bioclinical Research Abidjan (CIRBA). After obtaining authorizationfrom the CIRBA authorities and patient consent, we recruited 150 HIV-positive people onantiretroviral therapy who were followed in the center.Only 45 of the 150 HIV-positive people (30%) who started antiretroviral therapy for up to oneyear (M 12) were

included in the study.These seropositive subjects were screened through three types of HIV serology tests(Détermine Test, STAT-PAK and Test GénieIII (HIV-1 / HIV-2).

2.2 Characteristics of the subjects

The socio-demographic characteristics of our sample are presented in Table 1. It revealed that out of the 45 patients in our study, 27 or 60% were female versus 18 or 40% for the male gender. These patients are 18 to 35 years old with an average of 26.1 ± 0.7 years. In this same table, there is a low proportion (13.3%) of adolescents compared to subjects whose age is physiologically normal (86.7%). The body mass index was abnormal (underweight and overweight) in 46.7%. For our investigations, the patients had a good level of education. In our study, 91.1% of patients were infected with HIV type 1 against 8.89% infected with HIV type 2. Most of these selected HIV-positive people come from different municipalities in the city of Abidjan.

Table 1: Characteristics and HIV types of study population

Social characteristics and HIV types	*Numbers (N) N=45*	*Percentages (%)*
Sex		
Men	18	40
Women	27	60
Age (years)	**26.1 ± 0.7**	
18-19	6	13.3
20-35	39	86.7
BMI (kg/m^2)	**25.18±0.4**	
< 19.8	5	11.1
19.8 – 26	24	53.3
> 26	16	35.6
Education attainment		
Uneducated	5	11.1
Primary school	20	44.4
Secondary school	13	28.9
Superior	7	15.6
Residence		
Abidjan	42	93.3
suburban	3	6.7
Type de VIH		
HIV-1	41	91.1
HIV-2	4	8.9

N: Total number of each subject group; BMI: Index of Body Mass

Blood samples and assays of biological parameters

In each of the recruited patients, three types of blood samples collected in dry tubes, graytubes and purple tubes of 5 ml each were taken on an empty stomach, in the morning on the first day of the initiation of treatment, then six and twelve months later. The whole blood collected on purple tubes with anticoagulant (EDTA) made it possible to carry out the determination of CD4 (by flow cytometry with Fascalibur®) and the hemogram by an automaton the SysmexXt 2000L.The collected blood in the gray and dry tubes was centrifuged at 1107 Newton for fiveminutes. The serum obtained in the dry tubes was used to determine HIV serology andbiochemical data. On the other hand, the plasma obtained in the gray tubes made it possible todetermine the glycaemia.For HIV serology, the most used method in treatment centers is the successive use of threetests (Détermine, Stat Pak and Gen III HIV-l/HIV-2).Quantitative determination of biochemical parameters (glucose, creatinine, ALAT) is basedon a colorimetric technique available on COBAS INTEGRA 400 PLUS.

Statistical analysis of biological parameters studied

The results were expressed as means associated with their standard error. For the exploitationof the different parameters of the study, several statistical tests are used. A significance of theanalyses is defined for a probability threshold p less than 5%.

Comparisons of average biological parameters of people living with HIV on treatment duringfollow-up were performed by variance testing (Anova 1). They allowed to appreciate thebehaviour of the blood parameters during the follow-up of our subjects. In theseanalysis, thedependent variables (Data Explained) are the 17 biological parameters. The three samplingperiods (M0, M06 and M12) constituted the independent data (explanatory variables).

The different observed proportions of the biological blood indicators were compared by thetest of likelihood G or test log likehood ratio with the Windows version R.2.0.1 software.

3. Results

3.1 Distribution of therapeutic classes

The results of our study showed no statistically significant difference ($p < 0.05$) between class prevalence throughout treatment. However, the therapeutic class 2NRTIs + 1NNRTI was the most used during treatment, with 84.44 %; 80 and 75.56 % respectively at M0, M06 and M12 (Table 2).

Table 2: Distribution of molecules according to therapeutic classes

	M0		***M06***		***M12***		
Therapeutic classes	***n***	***%***	***n***	***%***	***n***	***%***	***p***
2NRTIs + 1IP	7	15.6	9	20	11	24.4	0.2 (NS)
2NRTIs+1NNRTI	38	84.4	36	80	34	75.6	0.07 (NS)
TOTAL	45	100	45	100	45	100	

NRTIs : nucleoside reverse transcriptase inhibitors ; NNRTI : non-nucleoside-reverse transcriptase inhibitor ; IP : protease inhibitor ; n : Observed subjects' number in each group ; M0 : Day of antiretroviral therapy starting, M6 : Month 6 of antiretroviral therapy, M12 : Month 12 of antiretroviral therapy ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

3.2. Distribution of treatment regimens

Table 3 summarizes the proportions of the different treatment regimens according to the molecules used during the treatment. According to this table, the triple therapy made of AZT+ 3TC + EFV, TDF + 3TC + EFV and DT4 + 3TC + EFV molecules were the most used treatment regimens in the majority of cases. Among these three treatment regimens triple therapy AZT + 3TC + EFV was the most commonly used regimen in M0, M06 and M12 with 44.67 %, 40 % and 31.11 %, respectively. After this

class, the therapy made of the molecules TDF + 3TC + EFV used in M06 and M12 comes in second place with respectively 26.67 % and 28.89 %. Finally, the therapy made of the molecules DT4 + 3TC + EFV more used in M0 than in M6 and M12 comes in third position with respectively 28.89 %, 2.22 % and 2.22 %.

Table 3: Distribution of treatment regimens according to the molecules used from M0 to M12

Association of the molecules used	*M0*		*M06*		*M12*		*p*
	n	%	n	%	n	%	
AZT+3TC+NVP	2	**4.4**	5	**11.1**	4	**8.89**	0.2 (NS)
AZT+3TC+EFV	21	**44.7**	18	**40**	14	**31.1**	0.09 (NS)
AZT+3TC+LPV/r	-	-	2	**4.4**	2	**4.4**	0.03 (NS)
ABC+TDF+AZT	-	-	-	-	1	**2.2**	0.09 (NS)
TDF+3TC+EFV	-	-	12	**26.7**	13	**28.9**	9.10^{-11} (S)
TDF+3TC+LPV/r	1	**2.2**	6	**13.3**	7	**13.3**	0.003 (S)
TDF+3TC+AZT/r	-	-	-	-	1	**2.2**	0.09 (NS)
ABC+3TC+LPV/r	1	**2.2**	1	**2.2**	2	**4.4**	0.5 (NS)
DT4+3TC+EFV	13	**28.9**	1	**2.2**	1	**2.2**	9.10^{-10} (S)
DDI+TDF+NVP	1	**2.2**	-	-	-	-	0.09 (NS)
3TC+DT4+NVP	1	**2.2**	-	-	-	-	0.09 (NS)
DT4+ABC+LPV/r	1	**2.2**	-	-	-	-	0.09 (NS)
AZT+3TC+IDV	3	**6.7**	-	-	-	-	0.09 (NS)
DDI+TDF+NVP	1	**2.2**	-	-	-	-	0.09 (NS)
3TC+DT4+NVP	1	**2.2**	-	-	-	-	0.09 (NS)
TOTAL	45	**100**	**45**	**100**	**45**	**100**	

AZT : Zidovudine ; 3TC : Lamivudine ; NVP : Nevirapine; EFV : Efavirenz ; LPV/r : Lopinavir ; ABC : Abavaci; TDF : Tenofovir ; DT4 : Stavudine; DDI : Didanosine ; IDV : Indinavir ; n : Observed subjects' number in each group ; M0 : Day of antiretroviral therapy starting, M6 : Month 6 of antiretroviral therapy, M12 : Month 12 of antiretroviral therapy ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05.

3.3. Evolution of the biological parameters according to therapeutic classes 2NRTIs + 1IPand 2NNTIs+1NNRTI

3.3.1. Erythrocyte parameters and thrombocyte levels

Table 4, showing the proportions of erythrocyte parameters and thrombocyte levels as according totherapeutic class 2NRTIs + 1NNRTI, indicated that no significant difference (p >0.05) was observed between the proportions blood cells, hemoglobin, hematocrit, thrombocytes, MCV, MCH, and MCHC. On the other hand, significant (p < 0.05) and highly significant (p < 0.001) differences were observed between the proportions of other erythrocyte parameters during follow-up.

Table 4: Proportions of erythrocyte parameters and thrombocyte rate according to the therapeutic class 2NRTIs + 1NNRTI

Erythrocytes and thrombocytes parameters	*M0*		*M06*		*M12*		*p*
	n	%	n	%	n	%	
Red blood cells (10^{12}/l)							
< 4 ou< 4.5	16	**42.1**	15	**41.7**	18	**52.9**	0.1 (NS)
4-5.4 ou 4.5-6	21	**55.3**	20	**55.6**	16	**47.1**	0.1 (NS)
> 5.4 ou 6	1	**2.6**	1	**2.9**	-		0.1 (NS)
Hemoglobin (g/dL)							
< 12 ou< 13	18	**47.4**	14	**38.9**	14	**41.2**	0.2 (NS)
12-16 ou 13-18	20	**52.6**	22	**61.1**	20	**58.8**	0.1 (NS)
Hematocrit (%)							
< 35	11	**28.9**	11	**30.6**	8	**23.5**	0.3 (NS)
35-47	27	**71.1**	25	**69.4**	26	**76.5**	0.1 (NS)
MCV (fL)							
< 85	11	**28.9**	9	**25**	10	**29.4**	0.3 (NS)
85 – 95	15	**39.5**	10	**27.8**	5	**14.7**	0.001 (S)
> 95	12	**31.6**	17	**47.2**	19	**55.9**	0.01 (S)
MCH (pg)							
< 27	9	**23.7**	9	**25**	9	**26.5**	0.4 (NS)
27-31	16	**42.1**	8	**22.2**	5	**14.7**	0.0003 (S)
> 31	13	**34.2**	19	**52.8**	20	**58.8**	0.01 (S)
MCHC (g/dl)							
< 32	23	**60.5**	16	**44.4**	14	**41.2**	0.03 (S)
32-36	14	**36.9**	19	**52.8**	20	**58.9**	0.01 (S)
> 36	1	**2.6**	1	**2.8**	1	**2.9**	0.9 (NS)
Thrombocytes (10^3/mm^3)							
< 150	3	**7.9**	5	**13.9**	3	**8.8**	0.3 (NS)
150-500	34	**89.5**	31	**86.1**	31	**91.2**	0.1 (NS)
> 500	1	**2.6**	-	-	-	-	0.05 (NS)

MCV : Mean corpuscular volume ; MCH : Mean corpuscular hemoglobin ; MCHC : Mean corpuscular hemoglobin concentration ;M0 : Day of antiretroviral therapy starting ; M6 : Month 6 of antiretroviral therapy ; M12 : Month 12 of antiretroviral therapy ; n : Observed subjects' number in each group ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

Table 5 shows the proportions of erythrocyte parameters and thrombocyte levels according to2NRTIs + 1IP therapeutic class. According to this table, no significant difference (p >0.05) was observed between the proportions of normal and abnormal haematocrit values, normal values of MCV and abnormal MCHC during follow-up. In contrast, a significant difference (p < 0.05) was observed between the proportions of below normal and normal values of red blood cell, hemoglobin, MCHT, and thrombocyte levels.

In addition, a significant difference (p < 0.05) was observed between the proportions of al MCHC values and subnormal and above normal values of MCV. This table indicates, a significant increase in the rate of anemia during follow-up. It also indicates a decrease in M06 and M12 microcytosis relative to M0 and hypochromia during follow-up.

Table V: Proportions of erythrocyte parameters and thrombocyte rate according to the therapeutic class 2NRTIs + 1IP

Erythrocyte parameters and thrombocyte rate	**M0**		**M06**		**M12**		p
	n	%	n	%	n	%	
Redsbloodscell (10^{12}/l)							
< 4 ou < 4.5	3	**42.9**	2	**22.2**	4	**36.4**	0.01 (S)
4-5.4 ou 4.5-6	4	**57.1**	7	**77.8**	7	**63.6**	0.02 (S)
> 5.4 ou 6	-	-	-		-	-	
Hemoglobin (g/dL)							
< 12 ou < 13	2	**28.6**	3	**33.3**	5	**45.5**	0.04 (S)
12-16 ou 13-18	5	**71.4**	6	**66.7**	6	**54.5**	0.04 (S)
Hematocrit (%)							
< 35	2	**28.6**	2	**22.2**	2	**18.2**	0.2 (NS)
35-47	5	**71.4**	7	**77.8**	9	**81.8**	0.1 (NS)
MCV (fL)							
< 85	3	**42.9**	2	**22.2**	3	**27.3**	0.01 (S)
85 – 95	2	**28.6**	3	**33.3**	3	**27.3**	0.3 (NS)
> 95	2	**28.6**	4	**44.4**	5	**45.4**	0.03 (S)
MCH (pg)							
< 27	3	**42.9**	1	**11.1**	1	**9.1**	$7.1.10^{-8}$ (S)
27-31	1	**14.3**	4	**44.4**	5	**45.5**	$9.6.10^{-6}$ (S)
> 31	3	**42.9**	4	**44.4**	5	**45.5**	0.3 (NS)

MCHC (g/dl)							
< 32	2	**28.6**	1	**11.1**	1	**9.1**	0.001 (S)
32-36	5	**71.4**	7	**77.8**	10	**90.9**	0.03 (S)
> 36	-	-	1	**11.1**	-	-	$4.6.10^{-6}$ (S)
Thrombocytes (10^3/mm^3)							
< 150	1	**14.3**	-	-	1	**9.1**	$3.5.10^{-5}$ (S)
150-500	6	**85.7**	9	**100**	10	**90.9**	0.04 (S)
> 500	-		-	-	-	-	

MCV : Mean corpuscular volume ; MCH : Mean corpuscular hemoglobin ; MCHC : Mean corpuscular hemoglobin concentration ;M0 : Day of antiretroviral therapy starting ; M6 : Month 6 of antiretroviral therapy ; M12 : Month 12 of antiretroviral therapy ; n : Observed subjects' number in each group ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

3.3.2. Leukocyte parameters and CD4 count

In Table 6, comparing the proportions of leukocyte parameters and CD4 levels according to therapeutic class 2NRTIs + 1NNRTI, no significant difference (p > 0.05) was observed in the proportions of the lower and normal values, leukocytes, abnormal eosinophilic polynuclearvalues, basophil values, CD4 lymphocyte values. In contrast, leukocytosis was present only in patients with M0. Neutropenia decreased significantly from M0 to M06 and increased slightly to M12 (60.5 %, 41.7 % and 58.8%). The prevalence of eosinophilic polynuclear normal values was 81.6% at M0 and dropped to 58.3% in the sixth month and then increased to 82.4 % in the twelfth month of treatment. Also, the prevalence of lymphocytosis that was 76.6 % at M0 dropped to 58.3% M06 and increased significantly from 82.4 % to M12.

Table 6: Proportions of leukocyte parameters and the rate of CD4 according to therapeutic class 2NRTIs+1NNRTI

Leukocyte parameters and the rate of CD4	***M0***		***M06***		***M12***		***p***
	n	%	n	%	n	%	
Leukocytes (10^3/mm^3)							
< 4	13	**34.2**	11	**30.6**	9	**26.5**	0.2 (NS)
4 – 10	23	**60.5**	25	**69.4**	25	**73.5**	0.07 (NS)
< 10	2	**5.3**	-	-	-	-	0.003 (S)
Neutrophils (%)							
< 40	23	**60.5**	15	**41.7**	20	**58.8**	0.02 (S)
40–70	15	**39.5**	21	**58.3**	14	**41.2**	0.03 (S)
> 70	-	-	-	-	-	-	
Eosinophils (%)							
<1	1	**2.6**	2	**5.6**	1	**2.9**	0.5 (NS)
1–5	31	**81.6**	21	**58.3**	28	**82.4**	0.01 (S)
> 5	6	**15.8**	13	**36.1**	5	**14.7**	0.001(S)
Basophils (%)							
0-1	37	**97.4**	34	**94.4**	33	**97.1**	0.05 (NS)
> 1	1	**2.6**	2	**5.6**	1	**2.9**	0.5 (NS)
Lymphocytes (%)							
< 15	-	-	-	-	-	-	
15–40	9	**23.7**	15	**41.7**	6	**17.6**	0.002 (S)
> 40	29	**76.3**	21	**58.3**	28	**82.4**	0.01 (S)
Monocytes (%)							
2 –10	15	**39.5**	16	**44.4**	14	**41.2**	0.2 (NS)
> 10	23	**60.5**	20	**55.6**	20	**58.8**	0.2 (NS)
Lymphocytes TCD4(/mm^3)							
< 200	7	**18.4**	4	**11.1**	6	**17.6**	0.2 (NS)
200 – 499	16	**42.1**	16	**44.4**	12	**35.3**	0.2 (NS)
≥ 499	15	**39.5**	16	**44.4**	16	**47.1**	0.2 (NS)

M0 : Day of antiretroviral therapy starting ; M6 : Month 6 of antiretroviral therapy ; M12 : Month 12 of antiretroviral therapy ; n : Observed subjects' number in each group ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

Table 7 compared the different leucocyte proportions and CD4 levels according to the 2NRTIs+ 1IP therapeutic class during follow-up of people living with HIV.This table shows a highly significant reduction in leukopenia from 71.4 % at MO to 55.6 % and 36.4 % at six (6) and 12 months, respectively. At the level of neutrophils, neutropenia was present only at M0. This table showed a significant (p < 0.001) increase in the prevalence of eosinophilic neutrophils during follow-up (57.1 %, 66.7 % and 81.8 %, respectively, at M0, M06 and M12). Basophilia was observed only in patients during the twelfth month of treatment. As for the prevalence of lymphocytosis, the 2NRTIs + 1IP class was most indicated at the beginning of treatment and at the twelfth month of treatment. In addition, the prevalence of monocytosis decreased significantly throughout the follow-up (28.6 %, 44.4 % and 54.5 % respectively at M0, M06 and M12).

Table 7: Proportions of leukocyte parameters and the rate of CD4 according to therapeutic class 2NRTIs + 1IP

Leukocyte parameters and the rate of CD4	**M0**		**M06**		**M12**		p
	n	%	n	%	n	%	
Leucocytes (10^3/mm^3)							
< 4	5	**71.4**	5	**55.6**	4	**36.4**	0.001 (S)
4 – 10	2	**28.6**	4	**44.4**	7	**63.7**	0.0003 (S)
< 10	-	-	-	-	-	-	
Neutrophils (%)							
< 40	2	**28.6**	2	**22.2**	4	**36.4**	0.07 (NS)
40–70	4	**57.1**	7	**77.8**	7	**63.6**	0.03 (NS)
> 70	1	**14.3**	-	-	-	-	$1.3.10^{-7}$ (S)
Eosinophils (%)							
<1	1	**14.3**	-	-	1	**9.1**	$6.7.10^{-7}$ (S)
1–5	4	**57.1**	6	**66.7**	9	**81.8**	0.01 (S)
> 5	2	**28.6**	3	**33.3**	1	**9.1**	0.0001 (S)
Basophils (%)							
0-1	7	**100**	9	**100**	10	**90.9**	0.04 (S)
> 1	-	-	-	-	1	**9.1**	$4.2.10^{-5}$ (S)
Lymphocytes (%)							
< 15	1	**14.3**	-	-	-	-	$1.3.10^{-7}$ (S)
15–40	2	**28.6**	6	**66.7**	6	**54.6**	$6.4.10^{-5}$ (S)
> 40	4	**57.1**	3	**33.3**	5	**45.4**	0.01 (S)
Monocytes (%)							
2 –10	5	**71.4**	5	**55.6**	5	**45.5**	0.01 (S)
> 10	2	**28.6**	4	**44.4**	6	**54.5**	0.004 (S)
Lymphocytes TCD4 (/mm^3)							
< 200	4	**57.1**	2	**22.2**	1	**9.1**	$1.2.10^{-6}$ (S)
200 – 499	2	**28.6**	5	**55.6**	6	**54.5**	0.001 (S)
≥ 499	1	**14.3**	2	**22.2**	4	**36.4**	0.003 (S)

M0 : Day of antiretroviral therapy starting ; M6 : Month 6 of antiretroviral therapy ; M12 : Month 12 of antiretroviral therapy ; n : Observed subjects' number in each group ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

3.3.3. Biochemical parameters

Table 8 represents the evolution of biochemical parameters according to the therapeutic class 2NRTIs + 1NNRTI. This table revealed that for all proportions of biochemical parameters, with the exception of abnormal glucose levels (< 0.7 g / L, > 1.1 g/L), no statistically significant difference (p > 0.05) was observed between the proportions of the parameters. However, all prevalence of normal values for biochemical parameters in patients under the

2NRTIs + 1NNRTI therapeutic class were elevated throughout the follow-up.

Table 8: Evolution of biochemical parameters according to therapeutic class 2NRTIs + 1NNRTI

Biochemical parameters	***M0***		***M06***		***M12***		*p*
	n	%	n	%	n	%	
Glycemia (g/L)							
< 0.7	2	**5.3**	1	**2.8**	-	-	0.02 (S)
0.7-1.10	35	**92.1**	33	**91.6**	33	**97.1**	0.05 (NS)
> 1.10	1	**2.6**	2	**5.6**	1	**2.9**	0.01(S)
Creatinemia (g/L)							
<5.5 ou<6.5	7	**18.4**	7	**19.4**	6	**17.6**	0.5 (NS)
5.5-11 ou 6.5-12.5	28	**73.7**	25	**69.4**	25	**73.5**	0.1 (NS)
> 11 ou>12.5	3	**7.9**	4	**11.1**	3	**8.8**	0.6 (NS)
ALAT (UI/L)							
<5	-	-	-	-	1	**2.9**	0.05 (NS)
5-40	34	**89.5**	29	**80.6**	26	**76.5**	0.05 (NS)
> 40	4	**10.5**	7	**19.44**	7	**20.6**	0.09 (NS)

ALAT : Amino-Transférase Alanine ; M0 : Day of antiretroviral therapy starting ; M6 : Month 6 of antiretroviral therapy ; M12 : Month 12 of antiretroviral therapy ; n : Observed subjects' number in each group ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

Table 9 compares the different proportions of the biochemical parameters according to the 2NRTIs + 1IP therapeutic class. The results indicated that for all proportions of biochemical parameters, with the exception of creatinine values, no statistically significant difference (p >0.05) was observed between the proportions of biochemical parameters. However, the prevalence of normal serum creatinine levels increased significantly (p < 0.001). This prevalence, which ranged from 57.14 to M0, increased to 88.9 % M06 and 100 % to M12. In addition, from M0 to M06 100 % of patients had normal blood glucose. In fact, most patients on this regimen had normal ALAT levels throughout the follow-up.

Table 9: Frequencies of biochemical parameters according to therapeutic class 2NRTIs + 1IP

Biochemical parameters	M0		M06		M12		p
	n	%	n	%	n	%	
Glycemia (g/L)							
< 0.7	-	-	-	-	-	-	
0.7-1.10	7	**100**	9	**100**	11	**100**	0.05 (NS)
> 1.10	-	-	-	-	-	-	
Creatinemia (g/L)							
<5.5 ou<6.5	2	**28.57**	1	**11.11**	-	-	$1.3.10^{-9}$ (S)
5.5-11 ou 6.5-12.5	4	**57.14**	8	**88.89**	11	**100**	0.0001 (S)
> 11 ou>12.5	1	**14.29**	-	-	-	-	$1.3.10^{-7}$(S)
ALAT (UI/L)							
<5	-	-	-	-	-	-	
5-40	6	**85.71**	8	**88.89**	10	**90.91**	0.06 (NS)
> 40	1	**14.29**	1	**11.11**	1	**9.09**	0.2 (NS)

ALAT : Amino-Transférase Alanine ; M0 : Day of antiretroviral therapy starting ; M6 : Month 6 of antiretroviral therapy ; M12 : Month 12 of antiretroviral therapy ; n : Observed subjects' number in each group ; S : Statistically different for p value < 0.05; NS : Not statistically significant for p value > 0.05

4. Discussion

Our study, which focuses on the effects of treatment regimens on the biological parameters of patients receiving antiretroviral therapy during monitoring, was conducted in the Integrated Center for Bioclinical Research in Abidjan (CIRBA). This center has a unit specializing in the care and monitoring of people living with HIV. This study involved 45 people living with HIV in the center. The average age of patients was 26.1 ± 0.7 years with extremes ranging from 18 to 45 years. This result is lower than that described by Nadembaega *et al.*who observed an average age of 35.87 ± 7.55 years[10]. Our sample was dominated by women with 60% of cases versus 40% of men. This female prevalence was found in the majority of the studies undertaken on the VIH, in particular those of Mouhari-Touré *et al.*and Tovi *et al.* [11,12]. Here, HIV-1 was the most common type with 91.1%. This high prevalence is roughly equal to that of Mouhari-Touré *et al.* (2011) and Cissé *et al.* (2013) who observed respectively 97.5% and 97.07% of HIV-1[11,13]. This predominance of HIV1 is explained by the fact that it is the most widespread virus, the most virulent and most transmissible in the world[13].

Indeed, for the fight against HIV in recent years, the ARV treatment used is a tri therapy generally combining two nucleoside reverse transcriptase inhibitors (NRTIs) with a non-nucleoside reverse transcriptase inhibitor (NNRTI) or an inhibitor of protease (IP).
In this study, the 2NRTIs + 1NNRTI therapeutic class was the most used during treatment with 84.44%, 80% and 75.56% respectively at M0, M06 and M12. Okome*et al.* (2007)and Karfo*et al*(2018) reported such regimens in 90.1% and 74.5%, respectively[14,15].

Furthermore, in our study, the 2NRTIs + 1IP regimen was prescribed at 15.6%, 20% and 24.4% of our subjects respectively at M0, M06 and M12. Our results are not the same with those obtained by Tanon*et al.* (2010:)[7].These authors observed a prevalence of 58% prescription of this class to patients.

This high prevalence of the prescription of the class (2NRTIs + 1NNRTI) is explained by the fact that it is used as a first-line regimen in a subject who is naive to any antiretroviral treatment.

Indeed, the decrease in the prevalence of the 2NRTIs + 1NNRTI class during follow-up may bedue to the use of the second-line regimen (2NRTIs + 1IP) after first-line therapeutic failure[16].

According to our study, triple therapy with zidovudine, lamivudine and efavirenz (AZT +3TC + EFV) was the most widely used regimen for M0, M6 and M12 with 44.67%, 40%, and31.11%, respectively. These prevalence are close to those observed by N'Guessan*et al.*(2012) who observed in their study that the combination AZT / 3TC / NVP accounted for halfof the prescriptions (53.8%)[17].

The main results of our investigations revealed the effects of these therapeutic classes 2NRTIs+ 1IP and 2NRTIs + 1NNRTI on the biological parameters of people living with HIV.

It emerges from this study that at the level of the prevalence of erythrocyte parameters, forthe therapeutic class 2NRTIs + 1NNRTI, a non-significant decrease in the

rate of anemia duringthe follow-up is observed. This prevalence, which is 47.4% at M0, passed to 38.9% at M06before increasing not significantly to 41.2% at M12. These same observations were made byKamagaté*et al*. (2016)[9]. In their study, the prevalence of anemia, which was 51.1% on theinitial balance sheet, increased to 42.2% in the sixth and 40% in the twelfth month oftreatment. But, unlike this study, these authors did not distinguish between the effects ofdifferent therapeutic classes on biological parameters.

In contrast, for the 2NRTIs + 1IP therapeutic class, a significant increase in the prevalence ofanemia is observed. The latter, which is 28.6% in M0, has risen to 33.3% in M06 and 45.5%in M12. These high prevalence of anemia result in significant proportions of mcrocytosis anda significant decrease in hypochromia during follow-up.

These observed prevalence of anemia in our study could be due to antiretroviral constitutingthis therapeutic class prescribed to our subjects. According to some authors, anemia is theresult of certain antiretroviral [18, 19, 20]. At the level of patients under the therapeutic classes 2NRTIs + 1NNRTI and 2NRTIs + 1IP, theprevalence of thrombocytopenia were low. Some authors have indicated these lowprevalence of thrombocytopenia in their work[9, 15].

During our work, at the level of the prevalence of leukocyte parameters and the level of CD4as a function of the therapeutic class 2NRTIs + 1NNRTI, a non-significant increase in this level ofM0 to M06 was observed before falling not significantly from M06 to M12. These sameobservations were made by Kamagaté*et al.* (2016)[9].

But in patients under the therapeutic class 2NRTIs + 1IP, a significant 27% increase in theprevalence of CD4 count in the sixth month compared to the average rate at initiation(respectively 28.6% and 55.6%) and from the sixth month to the twelfth month, this ratedecreased not significantly by 1.1% (respectively 55.6% and 54.5%). This increase in CD4observed in our study of M0 to M12 is higher than the rates obtained by some authors. Indeed,Van Dijk*et al*. (2011) and Okomo*et al*. (2012), Kamagaté*et al*. (2016) observed a 13%,10.3% and 6.7% increase in CD4 cell counts, respectively[21, 22, 9].

This increase in CD4 count in our study may be due, on the one hand, to the properties ofthese antiretroviral to restore immunity and, on the other hand, to good compliance.

In this study, the majority of biochemical parameters did not experience a statisticallysignificant change, except for the prevalence of normal creatinine values for subjectsundergoing 2NRTIs + 1IP treatment. This prevalence increased from 57.1% to 88.9% from M0to M06 and from 88.9% to 100% from M06 to M12. Our results are close to those of Kamagaté*et al.* (2016) who also did not notice a significant change in the rate of biochemicalparameters[9].Overall, the biological abnormalities observed in our study are not only due to the directaction of HIV itself, but also to antiretrovirals.

5. Conclusion

At the end of our study, it emerged that in the treatment of HIV there are two therapeutic classes 2NRTIs + IP and 2NRTIs + 1NNRTI that are used in the treatment of people living with HIV. This study revealed that the 2NRTIs + 1NNRTI therapeutic class was the most used class. The study of the effect of these different therapeutic classes on biological monitoring parameters indicated a non-significant decrease in the rate of anemia during monitoring for the 2NRTIs + 1NNRTI therapeutic class. For the 2NRTIs + 1IP therapeutic class, a significant increase in the prevalence of anemia was observed. In terms of leukocyte parameters, a significant increase in this rate was observed only for the 2NRTIs + 1IP therapeutic class. This study also reveals that at the level of biochemical parameters the majority of the subjects being under the two therapeutic classes had normal rates. This work must be continued by a comparative study of the effect of these two therapeutic classes on the blood parameters of these patients.

6. Conflicts of interest

The authors attest that there is no conflict of interest.

7. Thanks

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