African Journal of Biology and Medical Research
ISSN: 2689-534X
Volume 6, Issue 1, 2023 (pp. 24-34)
www.abjournals.org

EFFECT OF SEVEN ANTIRETROVIRAL COMBINATIONS ON BIOCHEMICAL PARAMETERS IN HIV POSITIVE PATIENTS AT THE NATIONAL BLOOD TRANSFUSION CENTER OF ABIDJAN

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Cite this article:

Tovi W.M., Abo Y., Minga K.A., Kouakou K. (2023), Effect of Seven Antiretroviral Combinations on Biochemical Parameters in HIV Positive Patients at the National Blood Transfusion Center of Abidjan. African Journal of Biology and Medical Research 6(1), 24-34. DOI: 10.52589/AJBMR-VLJJRYIM

Manuscript History

Received: 30 Nov 2022

Accepted: 20 Dec 2022

Published: 23 Jan 2023

ABSTRACT : *In order to contribute to the knowledge of the effects of antiretroviral drugs, a descriptive study was conducted on HIV patients who started antiretroviral therapy (ART). The 321 patients who were the subject of this study were selected from the cohort of HIV-infected patients followed at the Centre Médical de Suivi des Donateurs de Sang (CMSDS) in Abidjan (RCI), in the period from 2005 to 2012. These patients received regularly, according to their condition, seven (7) ARV therapeutic combinations which are AZT-3TC-EFV, AZT-3TC-NVP, AZT-3TC-NFV, AZT-3TC-LOP/RIT, DT4-3TC-EFV, DT4-3TC-NVP, and FTC-TDF-EFV. Biological check-ups performed every six (6) months allowed to follow these patients during 36 months of treatment and biological parameters were measured. The results on transaminases (GOT, GPT) and creatinine do not show toxicity of these different treatments on the hepatic and renal functions.*

KEYWORDS: arv, hiv, liver toxicity, renal toxicity.

Article DOI: 10.52589/AJBMR-VLJJRYIM
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INTRODUCTION

Since the discovery of the human immunodeficiency virus (HIV) (**Barré-Sinoussi F *et al.*, 1983**; **Barré-Sinoussi F *et al.*, 1985; Miedema F, 2008; Vahlne A, 2009; Agrawal S, Sawant S, & Shastri J, 2010)**, HIV-1 and HIV-2, both causative agents of the acquired immunodeficiency syndrome (AIDS), have spread throughout the world, causing a pandemic with tragic consequences. Despite the importance of the work done and the quality of the knowledge accumulated, AIDS remains a subject of justified universal concern.

Indeed, in the absence of a cure, antiretroviral therapy (ART) has emerged as an effective life-saving tool. Today, ART remains the best guarantee for a "normalization" of life for people living with HIV (PLHIV). Although they do not offer a cure, ARVs allow for the containing of the action of the virus by slowing down its proliferation in the body, preventing the evolution towards the AIDS stage, the ultimate stage of HIV infection. The objective of this work is to evaluate the impact of ARV treatment on two vital organs—the liver and the kidneys.

MATERIAL AND METHOD

Sampling

The study included a sample of 321 patients from the Centre Médical de Suivi des Donateurs de Sang (CMSDS) based at the Centre National de Transfusion Sanguine in Abidjan. Adult patients infected with HIV-1 and/or HIV-2, females and males, who started ART for the first time and were followed up in the above-mentioned recruitment center, in the period from 2005 to 2012, were retained (inclusion criteria). However, any HIV-positive patient under 16 years of age, female or male, or any untreated adult patient was not included (Exclusion criteria).

Treatment of Patients

The selected patients received thirty-six (36) months of first-line antiretroviral treatment (seven therapeutic combinations). They were followed up in the laboratory for six months; every six months, blood samples were taken for biological analysis.

Biochemical Analysis Technique

The apparatus used is the FULLY AUTOMATER. The FULLY consists of a computer and a set of numbered racks where the samples to be analyzed and the reagents are placed. Blood samples are collected in dry tubes and centrifuged. They are left to settle for 5 to 10 minutes and the serum is collected for analysis. The FULLY performs the determination of creatinine, blood sugar, transaminases, urea.

Statistical Analysis

Data processing was performed using Statistica version 10 software. Results were expressed as mean +/-SD (standard deviation). Student's t-test was used to compare means. The test was considered significant at a value of $P<0.05$.

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RESULTS

Effect of ARVs on Glutamic Oxaloacetic Transaminases (GOT)

The effects of the different combination therapies on the GOT level are reflected by a reduction in the initial GOT level as early as the 12th month of treatment, with the exception of the AZT 3TC LOP RIT and AZT 3TC NFV combinations (Figure 1).

The AZT 3TC EFV and AZT 3TC LOP RIT treatments reduced the GTT from 77.66±10.8 (M0) to 36.41±15 (M36) and from 29±8.3 (M0) to 26.66±15 (M36) respectively, following variations of 53.11% and 8.06%.

The four other therapeutic combinations—AZT 3TC NFV, AZT 3TC NVP, D4T 3TC NVP and FTC TDF EFV—after having induced a decrease in the rate of TGO, maintain this rate without significant variation until the 36th month of treatment.

AZT 3TC NFV and AZT 3TC NVP treatments induced respective decreases of 28.07% and 18.20%, bringing TG0 from 31.0±7 IU/L (M0) to 26±6.2 (M36) and from 40.93±4 IU/L (M0) to 33.48±3.3 IU/L (M36). Under D4T 3TC NVP treatment, OGTT decreased by 21.13% to 32.42±13.5 IU/L, whereas the level at M0 was 41.11±7.5 IU/L. With FTC TDF EFV treatment, OGTTs decreased from 47.22±12.8 IU/L (M0) to 35±10.7 IU/L (M36). The rate of change was 24.48%. With the D4T 3TC EFV combination, the decrease was delayed by 6 months and appeared after 18 months of treatment.

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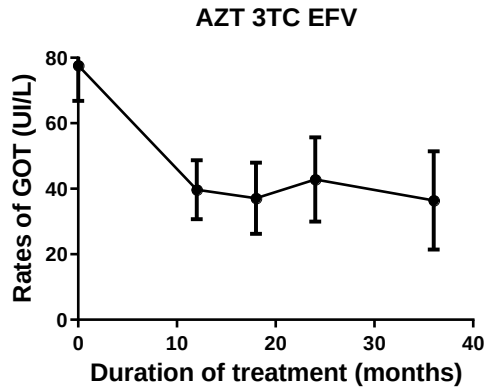

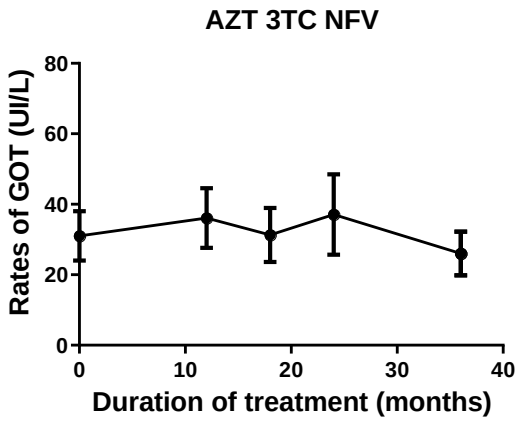

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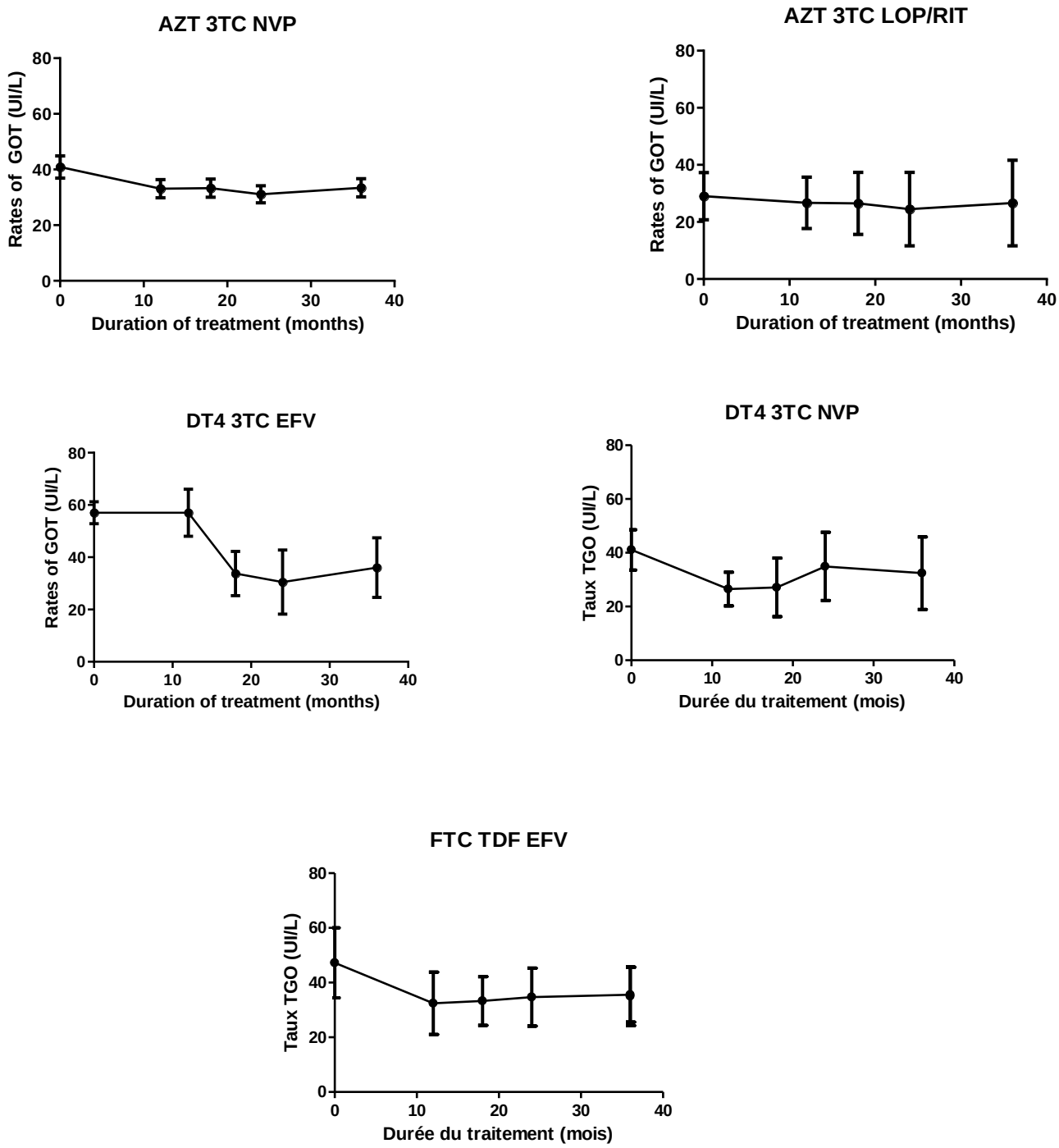

Figure 1: Effects of combination therapies on Glutamic Oxaloacetic Transaminases

* : P<0.05 **Normal values: 5 to 35 UI/l**

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Effect of ARVs on Glutamic Pyruvic Transaminases (GPT)

GTPs are hepatic enzymes that play a role in the transfer of amino acids during certain metabolic reactions. Unlike GOTs found in other cells such as heart and muscle cells, TGPs are more prevalent in the liver and better reflect the catalytic state of this organ. The average TGP values in a healthy person are between 5 IU/l and 40 IU/l.

Analysis according to the therapeutic combination administered allows us to note some differences, even if overall, the profiles of TGP levels are similar. Indeed, whatever the therapeutic combination, an increase appears at the 30th month of treatment followed at the 36th month by a decrease bringing the TGP value below the value at the initiation of the treatment (Figure 2).

Before the 30th month, the combination therapies AZT 3TC NVP, AZT 3TC NFV and FTC TDF EFV do not induce a significant change. The following values are measured:

6.94% (at M12), 9.21% (at M18), 19.18% (at M24), 10.79 (at M30), and 14.64% (at M36), for the AZT 3TC NVP combination, with a peak of 33.67±16IU/L (at M30)

- 14.81% (at M18), 9.27% (at M24), 19.55% (at M30), and 23.38% (at M36) for the AZT 3TC NFV combination, with a peak of 35.58±18IU/L (at M30)

- 8.16% (at M12), 7.27% (at M18), 7.27% (at M24), 38.11% (M30), and 5.34% (at M36), for the FTC TDF EFV combination, with a peak of 32.8±3.5IU/L (at M30)

In contrast, the AZT 3TC EFV, AZT 3TC LOP RIT, D4T 3TC EFV, and D4T 3TC NVP combinations initially induce a decline before the onset of the month 30 increase. The following values are measured:

- 18.98% (at M12), 13.32% (at M18), 11.68% (at M24), 28.93% (at M30), and 21.03% (at M36), for the AZT 3TC EFV combination, with a peak of 45.23±4.5 IU/L (at M30).

- 23.91% (at M12), 23.54% (at M18), 28.99% (at M24), 11.95% (at M30), and 29.77% (at M36) for the AZT 3TC LOP/RIT combination, with a peak of 24.44±2.4 IU/L (at M30)

- 24.44% (at M12), 38.11% (at M18), 55.91% (at M24), 19.11% (at M30), and 44.05% (at M36) for the D4T 3TC EFV combination, with a peak of 29.1±10 IU/L (at M30)

- 24.26% (at M12), 17.62% (at M18), 25.92% (at M24), 30.40% (at M30), and 9.08% (at M36) for the D4T 3TC NVP combination, with a peak of 31.44±15 IU/L (at M30).

After 36 months of treatment, each of the 7 combinations administered also yielded TGP levels below the baseline, with peak increases also at month 30.

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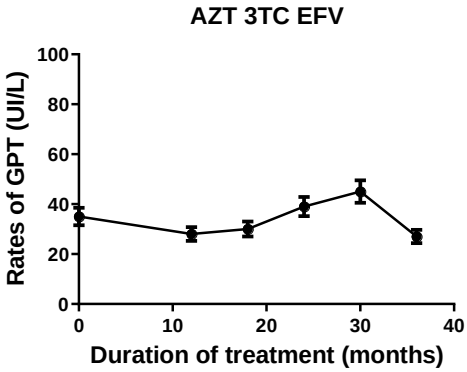

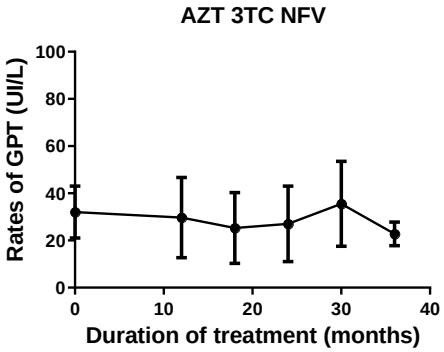

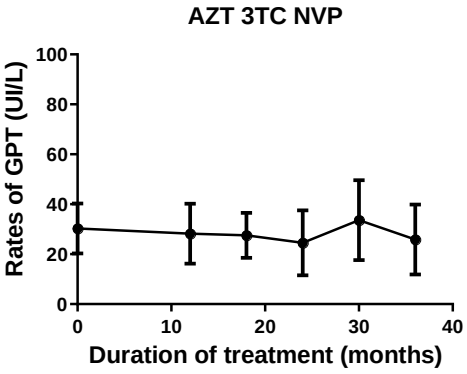

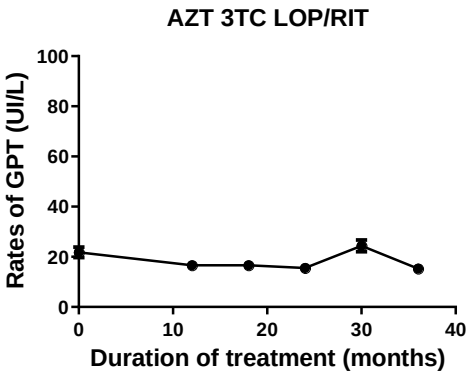

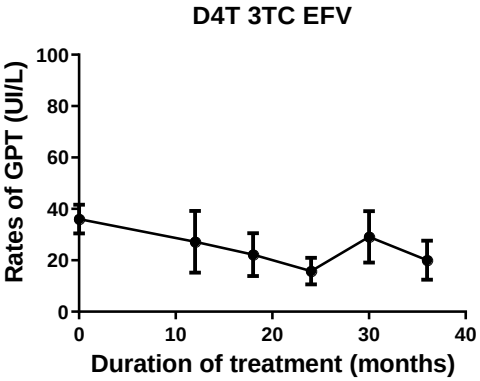

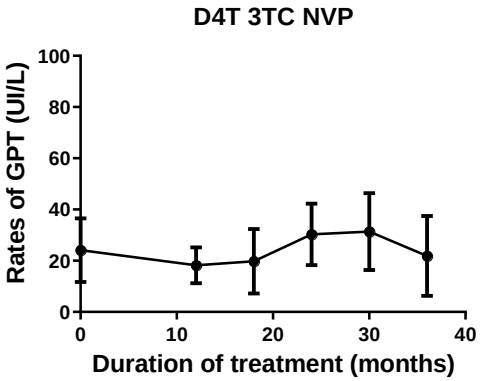

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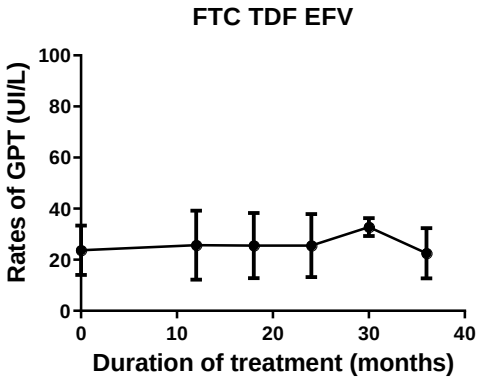


Figure 2: Effects of combination therapies on Glutamic Pyruvic Transaminases

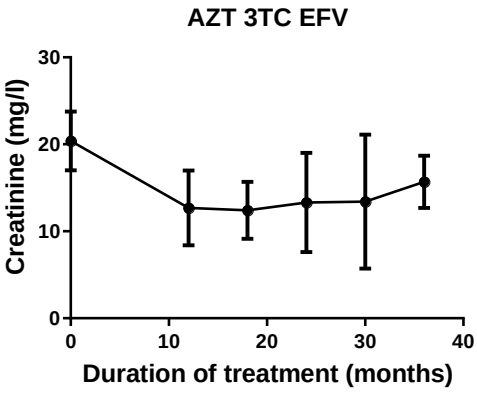
* : P<0.05 **Normal values: 5 to 40 UI/l**

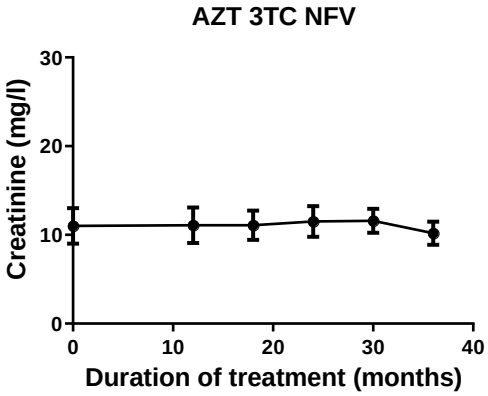
Effect of ARVs on Creatinine

Creatinine is a breakdown product of a molecule called creatine that is present in muscles and is used for energy production. Creatinine is carried in the blood and eliminated from the body by the kidneys through the urine. For a healthy person, creatinine levels are constant, within the range of 6 to 14 mg/L. An increase in creatinine levels in the blood goes hand in hand with an alteration in glomerular function (renal function).

Of the 7 combination therapies administered, 6 maintained creatinine levels measured at the start of treatment almost unchanged within a range of 10 to 12 mg/l from the first month to the 36th month.

Only the AZT 3TC EFV combination shows a notable difference in the evolution of this parameter. Indeed, at the initiation of treatment, the measured creatinine value was 20.4±3.4 mg/ml. After 12 months of treatment, there was a 37.35% drop, resulting in a measured level of 12.78±4.3 mg/ml (at M12). This value remained almost constant until the 30th month, when a non-significant increase was measured (Figure 3).





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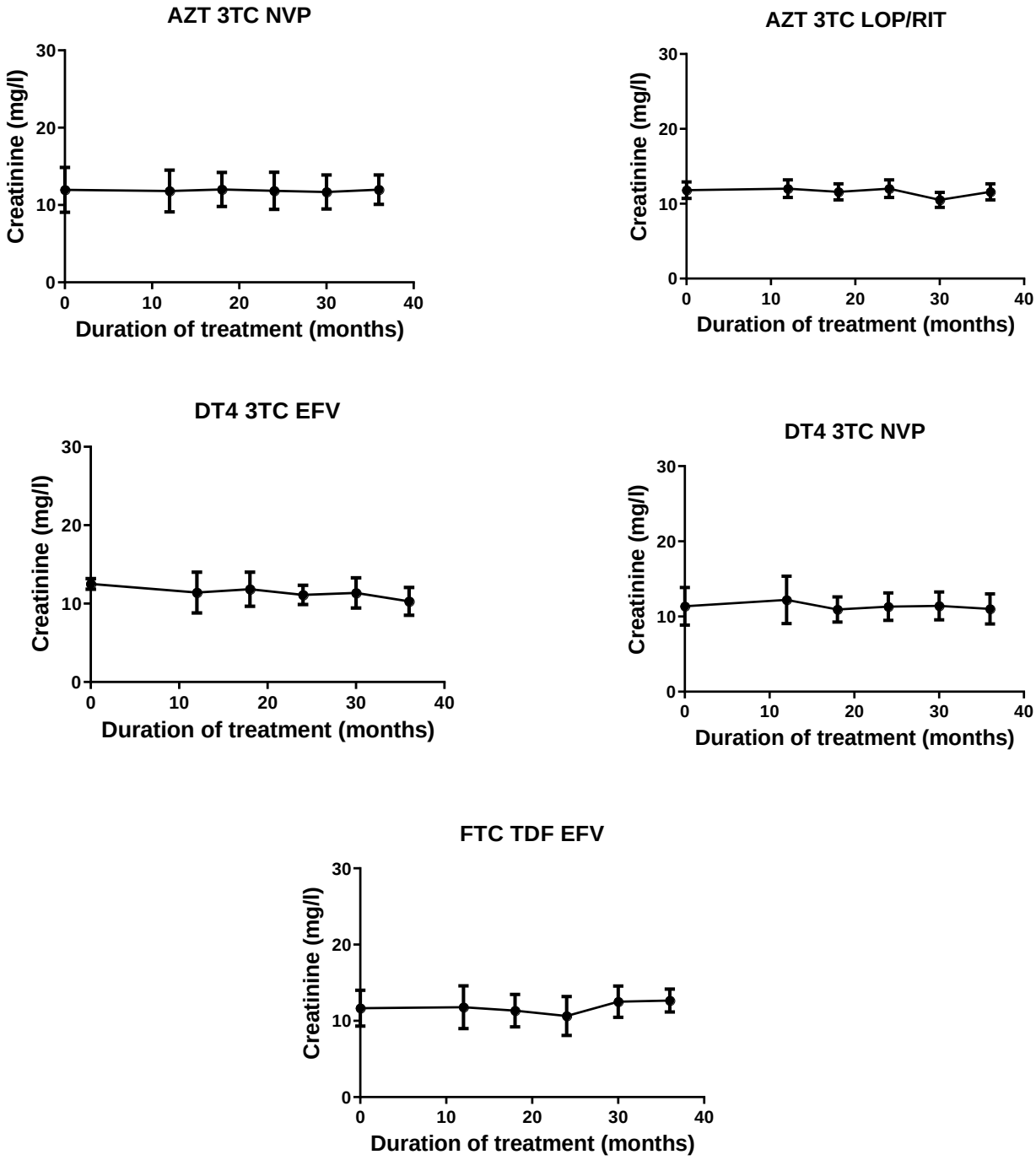

Figure 3: Effects of combination therapies on creatinine levels

Normal values: 6 to 14 mg/L

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DISCUSSION

In our study, whatever the treatment received, we have an overall stability of the patients' hepatic and renal functions. This is reflected by transaminase and creatinine levels within the norms.

However, the literature describes the existence of hepatic and renal disorders usually associated with ARV treatment.

Indeed, it is not uncommon to observe abnormalities of the liver balance in people living with HIV on ARVs. All classes of ARVs can induce hepatotoxicity (**Kontorinis N. & Dieterich D., 2003)**. Most often, this is an elevation of liver enzymes (transaminases), which is completely reversible and does not require the discontinuation of treatment. For example, the hepatotoxicity of nucleotide reverse transcriptase inhibitors described by **Gervais A. (2009)** is well known. For **Ollivon (2012)**, the ARVs most likely to induce hepatic abnormalities are NNRTIs and PI, because these drugs are mainly metabolized by the liver. In this class of ARVs, **Gervais (2009)** described the hepatotoxicity of efavirenz and nevirapine. Similarly, according to **Ollivon (2012)**, people living with HIV (PLHIV) have a 30–40% significant risk of steatosis (which is an accumulation of fat in the liver cells) that may be caused by NRTI use. Drug intolerance, which occurs during the first few weeks following the start of treatment, is most often incriminated in these anormalities (**Ollivon, 2012)**. The absence of this toxicity in our study could be justified by the fact that our patients tolerated the drugs prescribed to them well. However, this hypothesis should be taken with caution because, according to the same author, liver damage is often silent and symptoms take time to appear. They are often difficult to identify. This is why in patients with metabolic disorders and elevated transaminases, it is recommended to carry out complementary examinations such as ultrasound, liver biopsy, etc.

The literature also reports that antiretroviral drugs have a nephrotoxic potential (**Izzedine H., Launay-Vacher V. & Deray G., 2005**). Indeed, some ARVs can cause tubulopathy, a kidney damage that can lead to severe renal failure in some patients (**Mocroft A. *et al.,* 2010)**. This is the case of Fanconi syndrome, an impairment of the proximal tubule of the kidney, attributable to Tenofovir toxicity (**Harmouche H. *et al.,* 2005; Ondounda M. *et al.,* 2010)**, although studies on the renal toxicity of this molecule seem to be discordant (**Scherzer R. *et al*., 2012)**. Stavudine and Lamivudine have also been implicated in this condition.

Stavudine, for example, causes disabling neuropathy and sometimes severe mitochondrial toxicity, which in the long term leads to a loss of adherence to treatment and a risk of therapeutic failure (**Lazon, Gange S.J., Wilson T.E. *et al.,* 2007; Podsadecki T., Vrijens B., Tousset E. *et al*., 2007)**. Renal lithiasis is a possible complication of treatment with protease inhibitors such as Indinavir (**Traba-Villameytide M.L. & Fernandez-Guerrero M., 2004)**. While the renal toxicity of ARVs is well documented, our results reveal that after 36 months of treatment, patients' renal function is stable on ARVs. This overall stability in our study was assessed by measuring creatinine levels. Creatinine measurement is a very useful test in nephrology. Since creatinine levels are stable for a given person and all of it is eliminated by the kidney, creatinine is a good indicator of glomerular function. An increase in blood creatinine levels is associated with a reduction in renal function. In all our patients, this level was constant over the 36 months of observation, regardless of the combination received. It follows that none of the treatments altered the kidney function of the patients. One might also assume that these patients were free of all the risk factors for kidney damage, such as

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dehydration, pre-existing renal insufficiency and co-prescription of nephrotoxic drugs. However, if the good level of this parameter is a sign of the absence of toxicity of the treatments administered, this does not exclude vigilance in the patients by regularly monitoring this organ which could be the object of other anomalies that the sole determination of this parameter cannot reveal.

CONCLUSION

Research on the biological effects of seven first-line antiretrovirals (ARVs) commonly used at the National Blood Transfusion Center has shown that these ARVs do not show toxicity on the liver (TGO, TGP) and kidney (creatinine).

REFERENCES

Agrawal S, Sawant S, & Shastri J (2010). Prevalence of HIV-2 infection in Mumbai. India Journal of Dermatology Venereology Leprology, 76:709-710.

Barré-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, Gruet J, Dauguet C, Axler-Blin C, Vezinet-Brun F, Rouzioux C, Rozenbaum W, Montagnier L (1983). Isolation of a T-lymphotropic retrovirus from patient at risk of Acquired Immune Deficiency Syndrome (AIDS). Science, 220: 868-871.

Barré-Sinoussi F, Mathur-Wagh U, Rey F, Brun-Vazinet F, Yancovitz SR, Rouzioux, Montagnier L, Mildvan D, Chermann JC (1985). Isolation of lymphodenopathy-associated virus (LAV) and detection of LAV antibodies from US patients with AIDS. Journal of American Medical Association, 253: 1737-1739.

Gervais A (2009). Hépatotoxicité des antirétroviraux, John Libbey Eurotext (en ligne). Hépato-Gastro. Volume 16, Numéro 2, 93-9, mars-avril 2009, Mini-revue.

Harmouche H, Le Bras Ph, Bignani O, Delfraissy JF, Goujard C (2005). Insuffisance rénale aiguë avec diabète insipide et syndrome de Fanconi chez un patient infecté par le virus de l'immunodéficience humaine traité par Ténofovir. La Revue de Médecine Interne, 26(6): 522-523.

Izzedine H, Launay-Vacher V & Deray G (2005). Antiviral drug-induced nephrotoxicity. American Journal of Kidney Diseases 45(5):804-17

Kontorinis N. and Dieterich D (2003). Hepatotoxicity of antiretroviral therapy. AIDS, 5(1): 36-43.

Lazon, Gange SJ, Wilson TE et al (2007). Patterns and predictors of changes in adherence to highly active antiretroviral therapy: longitudinal study of men and women. Clinical infectious Disease, 45: 1377-1383.

Miedema F (2008). A brief history of HIV vaccine research: Stepping back to the drawing board. AIDS, 22: 1699-1703.

Mocroft A, Kirk O, Reiss P, De Wit S, Sedlacek D, Beniowski M, Gatell J, Phillips AN, Ledergerber B, Lundgren JD (2010). EuroSIDA Study Group. Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients. AIDS. 24(11) :1667-1678.

Article DOI: 10.52589/AJBMR-VLJJRYIM
DOI URL: https://doi.org/10.52589/AJBMR-VLJJRYIM

Ollivon C (2012). Surveillance hépatique chez les personnes vivant avec le VIH (PVVIH). infotraitements 212- mars-avril 2012. www.actions-traitements.org › *InfoTraitements*

Ondounda M, Tanon A, Ehui E, Ouattara I, Kassi A, Aba YT, Aoussi EF, Kakou AR, Eholié SP, Bissagnene E, Kadio A (2010). « Le syndrome de Fanconi induit par le ténofovir en Afrique : deux cas en Côte d'Ivoire ». Médecine et Maladies Infectieuses, édition en ligne du 15 Septembre 2010.

Podsadecki T, Vrijens B, Tousset E et al (2007). Decrease adherence to antiretroviral therapy observed prior to transient human immunodeficienty virus type 1 viremia. Journal of Infectious Disease, 196: 1773-1785.

Scherzer R, Estrella M, Li Y, Choi AI, Deeks SG, Grunfeld C, Shlipak MG (2012). Association of Tenofovir exposure with kidney disease risk in HIV infection. AIDS, 26:867–875.

Traba-Villameytide ML & Fernandez-Guerrero M (2004). « Idinavir and renal lithiasis ». Actas Urol Esp 28(7):523-526.

Vahlne A (2009). A historical reflection on the discovery of human retroviruses. Retrovirology, 6: 40-40.

Article DOI: 10.52589/AJBMR-VLJJRYIM
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