Health Sciences & Disease
The Journal of Medicine and Biomedical Sciences

Original Article

Clinical, Biochemical and CT-Scan Characteristics of Obesity Onset in Patients Under Dolutegravir in Comparison With Low-Dose-Efavirenz: A Pilot Study in Cameroon

Clinical, biochemical and CT-scan characteristics of obesity onset in patients under Dolutegravir in comparison with Low-dose-Efavirenz: a pilot study in Cameroon

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Keywords: HIV; Dolutegravir; Efavirenz; Insulin resistance; Diabetes; Visceral adiposity
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ABSTRACT

Background. Dolutegravir is an HIV drug, which belongs to the class of integrase inhibitors. In June 2018, WHO recommended the usage of this drug as the first line treatment, in combination with Tenofovir and Lamivudine for the treatment of HIV. This drug has shown a better profile with regard to viral suppression, immunological recovery and more important, a great genetic barrier to resistance, unlike Efavirenz. However, recent data show a higher obesity rate among people on Dolutegravir than on Efavirenz. The aim of this study was to characterize obesity in these two groups, and to investigate whether it would be associated with other metabolic complications. **Methods.** A pilot study was carried out from march 2020 to July 2020 in three hospitals in Cameroon.. The study populations were made up of HIV-positive people who became obese on protocol including Dolutegravir and those on protocol including Efavirenz. We looked for socio-demographic data, risky eating habits and described the glycemic and lipid profiles under these two protocols. The homeostatic model (HOMA-IR) was used to assess insulin sensitivity, with an insulin resistance threshold defined as 2.1 or greater. The measurement of visceral adiposity (v) and subcutaneous adiposity (s) was made using CT scans passing through the navel. a v/s ratio to assess the metabolic risk was determined. The significance threshold was set at 5%. **Results**. We enrolled 22 participants, in this study. They were 11 for the Dolutegravir and 11 for the Efavirenz. We found a 50 % prevalence of android type obesity among our various participants; it was 87,5 % in the Dolutegravir group, and 40 % in the Efavirenz group p = 0.06 (Table 1). Regarding Insulin resistance, it was present in 22.7 % of our participants, that is 45.5% for the Dolutegravir arm and 0 % for Efavirenz arm p = 0.07 (Table 2); however, we did not observe any case of diabetes nor glucose intolerance for both participants. The study of fat distribution with CT scan showed that adipose tissue was preferentially located in the subcutaneous space. We had a mean of 268.6 cm^3 for subcutaneous adiposity, and 97.9 cm^3 for visceral adiposity in the Dolutegravir group while in the Efavirenz group, the mean for subcutaneous adiposity was 240.8 cm^3 and 75.1 cm^3 for visceral adiposity. The estimated metabolic risk ratio (v/s) was 0.42 for all the participants. **Conclusion.** There is a significant difference between the waist over hip circumference suggesting that obesity under Dolutegravir is of Android type. We found no case of diabetes in our two groups. Insulin resistance is present in 45% of people on Dolutegravir compared to 0% in people on Efavirenz and Fat is more located in the subcutaneous space.

RÉSUMÉ

Background. Dolutegravir is an HIV drug, which belongs to the class of integrase inhibitors. In June 2018, WHO recommended the usage of this drug as the first line treatment, in combination with Tenofovir and Lamivudine for the treatment of HIV. This drug has shown a better profile with regard to viral suppression, immunological recovery and more important, a great genetic barrier to resistance, unlike Efavirenz. However, recent data show a higher obesity rate among people on Dolutegravir than on Efavirenz. The aim of this study was to characterize obesity in these two groups, and to investigate whether it would be associated with other metabolic complications. **Methods.** A pilot study was carried out from march 2020 to July 2020 in three hospitals in Cameroon.. The study populations were made up of HIV-positive people who became obese on protocol including Dolutegravir and those on protocol including Efavirenz. We looked for socio-demographic data, risky eating habits and described the glycemic and lipid profiles under these two protocols. The homeostatic model (HOMA-IR) was used to assess insulin sensitivity, with an insulin resistance threshold defined as 2.1 or greater. The measurement of visceral adiposity (v) and subcutaneous adiposity (s) was made using CT scans passing through the navel. a v/s ratio to assess the metabolic risk was determined. The significance threshold was set at 5%. **Results**. We enrolled 22 participants, in this study. They were 11 for the Dolutegravir and 11 for the Efavirenz. We found a 50 % prevalence of android type obesity among our various participants; it was 87,5 % in the Dolutegravir group, and 40 % in the Efavirenz group p = 0.06 (Table 1). Regarding Insulin resistance, it was present in 22.7 % of our participants, that is 45.5% for the Dolutegravir arm and 0 % for Efavirenz arm p = 0.07 (Table 2); however, we did not observe any case of diabetes nor glucose intolerance for both participants. The study of fat distribution with CT scan showed that adipose tissue was preferentially located in the subcutaneous space. We had a mean of 268.6 cm^3 for subcutaneous adiposity, and 97.9 cm^3 for visceral adiposity in the Dolutegravir group while in the Efavirenz group, the mean for subcutaneous adiposity was 240.8 cm^3 and 75.1 cm^3 for visceral adiposity. The estimated metabolic risk ratio (v/s) was 0.42 for all the participants. **Conclusion.** There is a significant difference between the waist over hip circumference suggesting that obesity under Dolutegravir is of Android type. We found no case of diabetes in our two groups. Insulin resistance is present in 45% of people on Dolutegravir compared to 0% in people on Efavirenz and Fat is more located in the subcutaneous space.

INTRODUCTION

The human immunodeficiency virus (HIV) is a virus that targets the immune system and weakens the body's defense systems against infection. In 2018, An estimated 37.9 million people worldwide were living with HIV, of which 36.2 million are adults and 1.7 million are children under the age of 15[1]. The African region remains the most affected according to UNAIDS, with 25.6 million people living with HIV in 2018. In Cameroon the HIV prevalence was 2.7 % among adults (between 15 and 49 years old) in 2018[2].

Despite all the efforts to combat this HIV infection, the disease still accounts for a high proportion of morbidity, with consequences for individuals, households and families. In addition to prevention, efforts are being made to make effective medicines available to all those in need. Between 2004 and 2009, the number of people living with HIV and receiving antiretroviral treatment (ART) in developing countries increased by 20-fold. In June 2019, around 24.5 million people living with HIV had access to antiretroviral treatment[1]. As a result, mortality has decreased and the life expectancy of those affected is increasing. meanwhile, long-term exposure to ARVs is associated with the development of resistance to treatment. In East Africa, rates of resistance to ARVs such as Nevirapine or Efavirenz have recently been observed[3]. Therefore, the development of new drugs remains a key factor for controlling viral replication, and for ensuring effective control of infection.

Integrase inhibitors (INIs) represent a class of drugs in the therapeutic arsenal, and are active against viruses resistant to other classes of drugs[4]. Since June 2018, the World Health Organization (WHO) recommended that Dolutegravir (integrase inhibitors class of drugs), should be used in the first line treatment in combination with two nucleoside reverse transcriptase inhibitors (NRTIs). This molecule has a more favorable profile with regard to prolonged viral suppression as well as immunological recovery[5].

Moreover, long-term use of this antiretroviral (ARV) treatment is linked to the occurrence of a higher proportion of obesity compared to other therapies. This is the case observed in a cohort study conducted in Cameroon in 2019 in three sites, which showed greater weight gain in a group of HIV patients taking Dolutegravir with an incidence of obesity of 12.3% against 5.4% for patients taking Efavirenz[6]. Giving this new drug whose viral effectiveness has been proven, but which makes to gain weight, a question arises as to whether this obesity is not metabolically noxious. Given that, little data in the international literature is available on the characterization of obesity under this protocol, we decided to conduct a study to assess the clinical, biochemical and CT characteristics of obesity with Dolutegravir and Efavirenz.

METHODS

Study design

This was a pilot study from March 2020, to July 2020 in three hospitals in Cameroon. We recruited participants of the NAMSAL ANRS 12313 trial who became obese after 48 weeks of trial treatment, with no clinical Cushing nor medical history of hypothyroidism. The New Antiretroviral and Monitoring Strategies in HIV-Infected Adults in Low-Income Countries (NAMSAL) ANRS 12313 trial, is an open-label, randomized phase 3 trial to evaluate Dolutegravir compared with Efavirenz 400, both combined with Tenofovir disoproxil fumarate and Lamivudine, as first-line ART for HIV-1-infected adults in low-and middle-income countries. The trial comprises 613 participants, in which 310 were assigned and received the Dolutegravir-based regimen and 303 received to the low-dose Efavirenz-based regimen. The trial begun in July 2016. Approval from the Cameroon National Ethics Committee was obtained in November 2015. All the participants provided written inform consent before any trial-specific procedures were performed. An independent data and safety monitoring committee performed separate reviews of unblinded efficacy and safety data during the trial. Participants and investigators were unaware of the results of these interim analyses. The trial drugs were paid for by Unitaid; no commercial support for drugs or tests was provided.

Visit procedures

We used a standardized and pre-tested questionnaire to collect sociodemographic data like age and gender, risky eating habits, history of HIV infection including duration since diagnosis, and type of HIV virus.

Weight was measured to the nearest 0.1 kg using an electronic scale (CAMRY, Hong Kong, China); with the participant standing up on the scale without shoes and heavy clothing, looking straight ahead, arms stretching along the body. Height was measured to the nearest 0.1 cm using a stadiometer, with the participant standing up without shoes and hat, looking straight ahead, arms stretching along the body. Body Mass Index (BMI) was then derived as weight (kg)/height*height (m^2), and participants grouped into 4 categories: underweight (< 18.5), normal (18.5-24.9), overweight (25.0-29.9) or obese (≥30.0)[7]. waist and hip circumferences were measured to the nearest 0.1 cm using a measuring tape; the waist-to-hip ratio (WHR) was then calculated. We used an electronic sphygmomanometer (Omron M5-1, Omron Healthcare, Kyoto, Japan) for blood pressure measurement. Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 and/or self-reported history of ongoing antihypertensive medication use[8].

Laboratory procedures

Blood samples were aseptically collected after a 12-h overnight fasting, by venipuncture of the brachial vein in a 5 ml sodium fluoride tube and a 5 ml dry tube without a tourniquet. Thereafter, they were immediately transported to National Obesity Center laboratory where plasma and serum specimen were separated accordingly, by centrifugation at 4.000 rpm for 15 min. Fasting plasma glucose (FPG) and lipids including total cholesterol (TC), triglycerides (TG) and HDL-C were assayed without delay using standard colorimetric methods. The Friedwald's formula, was calculated when TG levels were below 4 mmol/L, and measured when

TG values were over 4 mmol/L[9]. serum was aliquoted and stored at -20 ◦C for further measurement of C-Peptide. C-peptide was measured within 6 weeks using a previously validated sandwich immunoassay method[10].

Dyslipidemia was considered in the presence of elevated levels of TC (> 6.2 mmol/L) and/or an elevated levels of LDL-C (> 4.1 mmol/L) and/or a low HDL-C level (< 1.04 mmol/L in men and 1.29 mmol/L in women) and/or an elevated level of TG (≥ 1.7 mmol/L)[11]. Diabetes was define whenever a patient had at least 2 FPG levels ≥ 7.0 mmol/L on two occasions at least 48 h apart, or self-reported history of antidiabetic medications after the diagnosis was made in a health facility[12].

We used an HOMA-IR like index for insulin sensitivity assessment, it was determined by the HOMA-IR formula: FPG (mmol/L) x insulin (mU/L) /22.5[13]; where the insulin level was replaced by the C-peptide level. The C-peptide measurement was use to access insulin level base on their equimolar secretion in blood. In fact, the measurement of insulin would have not been easy according to our facilities; however, we decided to measure the C-peptide because it is co-secreted in equimolar concentration with insulin, it is not metabolized by the liver and does not undergo any extraction during the first hepatic passage[14]. therefore, it can be indirectly measured to access insulin secretion[14]. insulin resistance was defined by value of the HOMA-IR like index equal or above 2.1; this threshold was defined in an HIV-infected population in Peru[15].

CT-Scan procedures

CT scans (Siemens Somaton Emotion) were performed with all subject's supine, a tube voltage of 110 kVp, and tube current set to 100 mA. The CT images of abdominal adipose tissue were obtained with the following parameters: scan FOV, large body; rotation time, 0.5 second; section thickness, 2.5 mm; and inter-slice interval, 10 mm. Eight 2.5-mm-thick original transaxial images were centered at the umbilical region and were used to reconstruct four 5.0 mm-thick images, which in turn were used to reconstruct two 10.0 mm-thick images for estimating abdominal SAT and VAT areas. The SAT was defined as the extra-peritoneal fat between skin and muscles with attenuation ranging from -190 to -30 HU (Hounsfield units) on one of the constructed images at the umbilical plane [16]. the VAT was defined by intraperitoneal fat with the same density as the SAT layer **(figure 3).** To assess the inter-rater reproducibility and intra-rater repeatability of adipose measurement with the Syngo Program, two well-trained radiologist doctors, performed the post-processing measurements. The VFA-to-SFA ratio (v/s) were calculated with visceral obesity threshold defined as equal or greater than 0.4[17].

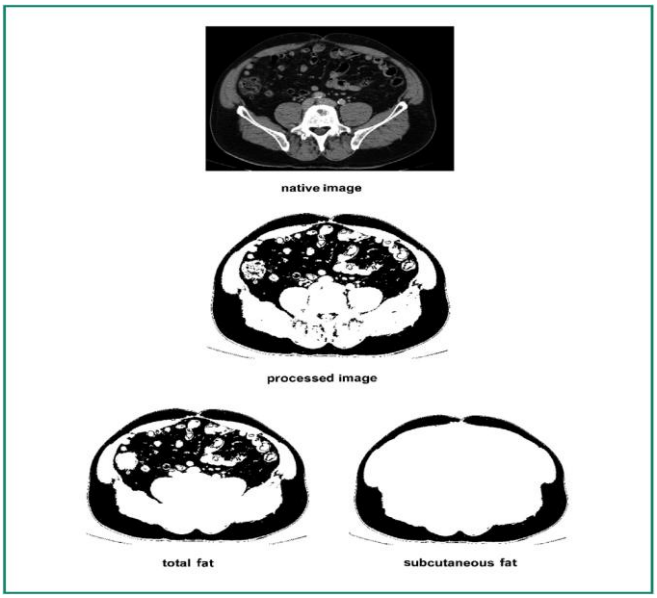

Figure 3: Computed tomography image in axial slice passing through the navel showing the different steps in the calculation of the total fat and subcutaneous fat after segmentation of the fat density pixels (−190 HU to −30 HU) with syngo software. The visceral fat is obtained by subtraction.

Statistical analysis

Data were analyzed using SPSS v. 23 (IBM Corporation, Chicago, Illinois, USA). Results are presented as count (percentage) for categorical variables, and mean ± standard deviation (SD) or median (25^{th}-75^{th} percentiles) for quantitative variables. The Student t-test, chi-square test or equivalents served for groups comparison. A p-value < 0.05 was used to characterize statistically significant results.

RESULTS

Participants

Of the 613 participants of the NAMSAL ANRS 12313 trial, that is 310 for the Dolutegravir arm and 303 for the Low-dose-Efavirenz arm; they recorded after 48 weeks of treatment an incidence of 12.3 % obesity for the Dolutegravir arm (36 participants) and an incidence of 5.4 % for the Low-dose-Efavirenz arm (15 participants) **(figure 1)**. Overall, we included 22 participants in this study, that is 11 for the Dolutegravir arm and 11 for the Efavirenz arm **(figure 2)**. 5 participants refused to participate in the study, 9 did not come back for exams due to the ongoing coronavirus pandemic and 18 where no more included in the trial **(figure 2)**. The mean age of the participants was 42 ± 10 years. 81.8% of the participants were female. The median duration of treatment was 144 weeks ± [144-165] **(table 1)**.

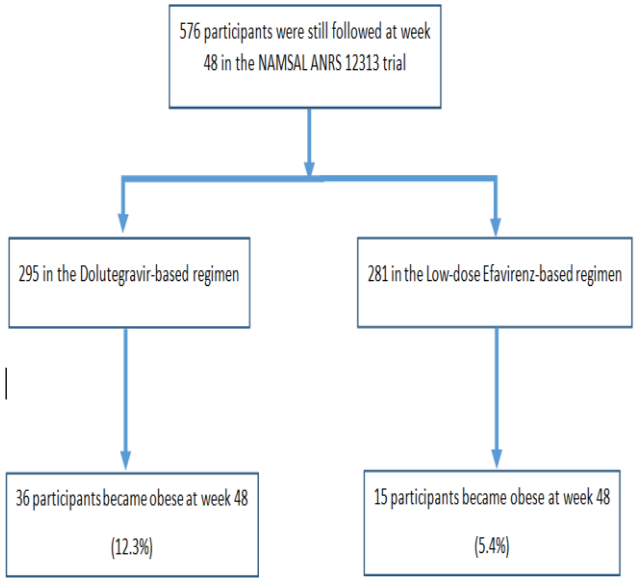

Figure 1: Study population determination

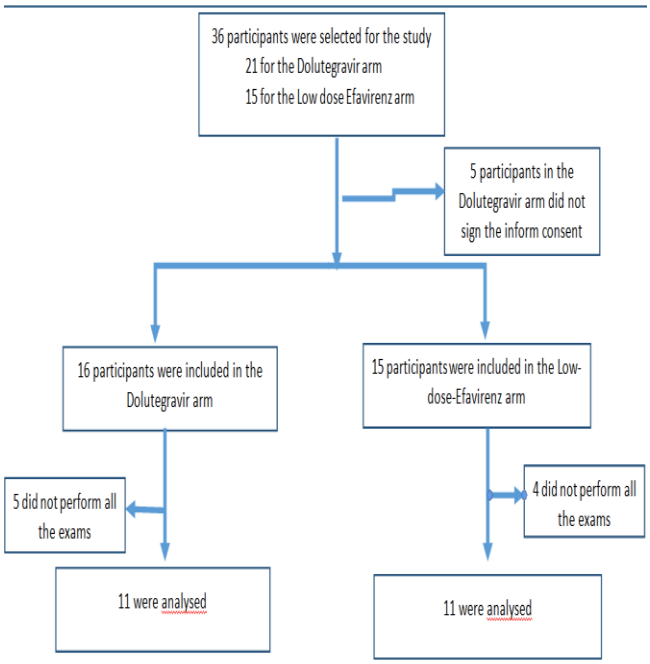

Figure 2: Repartition and analysis of study participants

Table 1: Baseline characteristics

Characteristic	**DTG 50 (N=11)**	**EFV 400 (N= 11)**	**Total (N= 22)**
Sex			
Female sex-no (%)	8 (72.7 %)	10 (90.9 %)	18 (81.8 %)
Age			
Moyenne ans ± (ET)	48 ± (9)	36 ± (8)	42 ± (10)
Week treatment			
Median week ± (IQR)-wk	144 (144-165)	144 (144-165)	144 (144-165)
Lieu de résidence			
Urban-n (%)	**8 (72.7 %)**	**9 (81.8 %)**	**17 (77.3 %)**
Rural –n (%)	3 (27.3 %)	2 (18.2 %)	5 (22.7 %)
Marital status			
Married	2 (18.2 %)	0 (0.0 %)	2 (9.1 %)
Single	1 (9.1 %)	**6 (54.5 %)**	**7 (31.8 %)**
Divorced	1 (9.1 %)	0 (0.0 %)	1 (4.5 %)
Cohabitation	3 (27.3 %)	3 (27.3 %)	6 (27.3%)
Widow	**4 (36.4 %)**	2 (18.2 %)	6 (27.3%)
Region of origine			
Center	**6 (54.5 %)**	**7 (63.6 %)**	**13 (59.1 %)**
Littoral	1 (9.1 %)	0 (0.0 %)	1 (4.5 %)
West	3 (27.3 %)	1 (9.1 %)	4 (18.2 %)
Eastern	0 (0.0 %)	1 (9.1 %)	1 (4.5 %)
South	1 (9.1 %)	2 (18.2 %)	3 (13.6 %)

Anthropometric profile

The average weight of our participants was higher in the DTG arm compared to the EFV arm **(table 2)**. The average body mass index of our participants was higher in the DTG arm compared to the EFV arm **(table 2)**.

Lipid and glycemic profile

The prevalence of lipid abnormalities was higher in the DTG arm compared to the EFV arm **(table 2)**. No cases of diabetes were recorded in the groups **(table 2)**. The mean blood glucose two hours after the glucose tolerance test was 1.02 ± (0.15) in the DTG arm and 0.93 ± (0.16) in the EFV arm p-value 0.19 **(table 2)**. The area under the glucose curve was 111.86 in the Dolutegravir arm and 101.44 ± (15.55) in the Efavirenz ± (13.3) arm p-value 0.13 **(table 2)**.

Table 2: Clinical and biochemical characteristics

	DTG 50 (N= 11)	EFV 400 (N= 11)	P
Clinical characteristics			
Weight kg	75.7 ± (13.1)	72.8 ± (11.3)	0.58
Height cm	164.5 ± (7.9)	163.9 ± (3.9)	0.84
BMI kg/m^2	28.1 ± (4.5)	27.1 ± (3.5)	0.58
Fat Mass*	38.4 ± (7.1)	34.9 ± (4.9)	0.24
WC cm	95.6 ± (10.1)	87.7 ± (8)	0.06
HC cm	103.9 ± (10.3)	103.3 ± (9.4)	0.88
WHR	0.92 ± (0.1)	0.85 ± (0.04)	0.01
Android Obesity* n (%)	7 (87.5 %)	4 (40 %)	0.06
Biochemical characteristics			
Mean total cholesterol (g/l)	1.64 ± (0.4)	1.57 ± (0.3)	0.67
Mean HDL cholesterol (g/l)	0.55 ± (0.2)	0.56 ± (0.2)	0.92
Mean LDL cholesterol (g/l)	0.83 ± (0.3)	0.86 ± (0.3)	0.83
Mean Triglycérides (g/l)	1.22 ± (0.9)	0.72 ± (0.3)	0.08
Hypercholesterolemia ; n (%)	2 (18.2 %)	1 (9.1 %)	0.5
Hypertriglyceridaemia ; n (%)	2 (18.2%)	0 (0.0 %)	0.24
High LDL cholesterol ; n (%)	0 (0.0 %)	0 (0.0 %)	
Low HDL ; n (%)	5 (45.5 %)	5 (45.5 %)	0.66
Any dyslipidemia ; n (%)	6 (54.5 %)	6 (54.5 %)	1.00
OGTT g/l			
T0	0.95 ± (0.2)	0.95 ± (0.2)	0.98
T60	1.25 ± (0.3)	1.09 ± (0.2)	0.16
T120	1.02 ± (0.6)	0.93 ± (0.2)	0.19
IASC$_{0\text{-}120}$ (mg h/dl)	111.9 ± (15.6)	101.4 ± (13.3)	0.13
Diabetes n (%)	0 (0.0 %)	0 (0.0 %)	
Median C-Peptide mIU/l	7.9 ± (3.7)	6.2 ± (2.5)	0.19
Median HOMA-IR like index	1.6 ± (0.8)	1.2 ± (0.5)	0.36
Insulin resistance n (%)	5 (45.5 %)	0 (0.0 %)	0.07

* : female population
*WC : waist circumference
*HC : hip circumference
*BMI : body mass indes
LDL: low density lipoproteins
HDL: high density lipoproteins
WHR: waist over hip ratio
OGTT: oral glucose tolerance test

Insulin resistance

We had a 22.7% prevalence of insulin resistance in all of our participants. All cases of insulin resistance were found in the DTG arm (45.5%) while there were no cases in the EFV arm (0%) p-value at 0.07**(table 2)**.

Fat distribution at CT-scan

The mean visceral adiposity was 86.5 cm3 in all of our participants. It was higher in the DTG arm (97.9 ± 50.7) compared to the EFV arm (75.1 ± 27.5) p-value 0.27**(table 3)**. The mean ratio was (0.44 ± 0.3) in the DTG group and (0.41 ± 0.3) in the EFV group, with no significant difference **(table 3)**.

Table 3: Abdominal fat distribution at CT-Scan

	DTG 50 (N= 11)	EFV 400 (N= 11)	p
Total fat	366.5 ± (165.3)	315.9 ± (149.9)	0.52
Visceral fat **cm^3**	97.9 ± (50.7)	75.1 ± (27.5)	0.27
Sub-cutaneaous fat **cm^3**	268.6 ± (130.7)	240.8 ± (128.6)	0.66
V/S ratio	0.44 ± (0.3)	0.41 ± (0.3)	0.85
Liver Density **UH ± (ET)**	63 (4)	63 (4)	0.55
Spleen Density **UH ± (ET)**	52 (2)	51 (2)	0.89
Metabolic risk **n(%)**	3 (27.2 %)	4 (36.3 %)	0.18
Hepatic steatosis **n(%)**	6 (54.5 %)	8 (72.8 %)	0.30

*** V : visceral adiposity**
*** S : sub-cutaneaous adiposity**

DISCUSSION

Weight gain when initiating antiretroviral therapy during HIV was considered to be a parameter for the patient's good progress and recovery. The aim of this study was to characterize this weight gain in two groups of patients respectively according to their protocol. We were interested in the anthropometric profile, the lipid and glycemic profile, insulin sensitivity, and abdominal fat distribution. As essential findings, it emerges that there is a significant different between the waist over the hip circumference suggesting that, obesity under Dolutegravir is of android type, fat is more localized in the subcutaneous space, we found no significant

difference between the lipid profile and glycemic profile in both groups, and finally insulin resistance is predominant in the Dolutegravir group.

We realized a pilot study, which main advantage was that it was carried in a reference population where the follow-up as well as the therapeutic adherence of the participants were effective. On the other hand, this study is one of the first to study the abdominal fat distribution under Dolutegravir, using abdominal CT-scan, a reference method and very good reflection of intra-abdominal adiposity. C-Peptide was assayed by the ELISA method, a method validated in Cameroon[10]. We assessed the blood glucose levels of our participants after a glucose tolerance test, which not only allowed us to diagnose diabetes but also assessed impaired glucose tolerance (IGT) states of our various participants. For total adiposity, we used BMI. BMI had a major advantage in its simplicity and reproducibility[18].

As limits of this study, we can note the fact of having used the HOMA-IR index for the determination of insulin resistance. Indeed, the euglycemic hyper insulinemic clamp is the gold standard for assessing insulin sensitivity[19]. However, several indices including the HOMA-IR calculated from fasting samples have been developed to facilitate this evaluation and is recommended when the realization of the clamp is impossible or restrictive[20].

Regarding the characteristics of our participants, the majority were female 81.8 % **(table 1)**, which was in agreement with the report of the Cameroon Demographic Health Survey, which estimated that, overall the percentage of women infected with HIV is higher than that of men, whatever the age group[2] **(table 1)**. This is explained by the high prevalence of HIV among women, but also by access to testing through prenatal consultation programs which make women more visible than men[21]. The average age of our participants was 42 years, consistent another study in Cameroon who found that the most affected age group in Cameroon was between 35 and 44 years old [22] **(table 1).**

Regarding the anthropometric profile, we found an average weight of 74.3 kg among our participants. It was higher in the Dolutegravir group compared to the Efavirenz group **(table 2)**. A study in the United States, showed that people taking Dolutegravir gain significantly more weight at 18 months than people starting NNRTI-based regimens [23]. One possible explanation was the rapid drop in viral load with INI-based regimens, and the correlation between virologic suppression and lower energy expenditure[24]. The prevalence of android obesity was about twice as high in the Dolutegravir group than in the Efavirenz group, with a non-significant p at 0.07 **(table 2)**. This could be explained by the high rate of sedentary lifestyle found in this group.

After the measurements of the adiposity with the CT-scan, we found that the fat was more localized in the subcutaneous space in the 2 groups. This can be explained by the dystrophic distribution of adipose tissue caused by HAART in HIV patients[25]. We calculated the ratio of visceral to subcutaneous fat. This showed an average ratio greater than 0.4 in the 2 groups, with no significant difference **(table 3)**. However, there is a relation between a high (V/S) ratio and metabolic risk[26].

No cases of diabetes were recorded in the two treatment arms. The area under the curve was calculated after the glucose tolerance test. This resulted in an average of 111.86 mg h / dl for the Dolutegravir group and 101.44 mg h / dl for the Efavirenz group, p-value at 0.13 **(table 2)**. These values were below the thresholds for impaired glucose tolerance set at 290 mg h / dl[27]. This could be explained by the distribution of abdominal fat which was predominantly subcutaneous, and therefore was a lower risk in metabolic complications.

People on Dolutegravir had an increase in the mean CT compared to those on Efavirenz **(table 2)**. These results were contrary to those found in the Single study in the United States, which showed that people on Efavirenz had higher values compared to those on Dolutegravir [28]. This could be explained by the difference in the duration of treatment which was 48 weeks in the Single study and 144 weeks in our study. Differences were also observed in LDL-C, the highest values being recorded in the Efavirenz arm **(table 2)**. This was similar with the observations of the Spring study in the United States[29]. Mean plasma HDL-C concentrations were slightly increased in both arms, which was consistent with the findings in the Spring study[29]. TG levels were twice high in the Dolutegravir group than in the Efavirenz group **(table 2)**.

Regarding insulin resistance, we had a prevalence of 22.7% in all of our participants. All cases of insulin resistance were found in the DTG group (45.5%) while there were no cases in the EFV group (0%) **(table 2)**. This difference may be due to the intrinsic properties of this drug, which could interfere with insulin receptors and thus cause increased secretion of insulin by the pancreas to allow glucose to enter cells. Other authors have suggested a relationship between advanced age and obesity in this group of patients, which can lead to activation of inflammatory cells, particularly monocytes / macrophages, by producing soluble markers sCD163 and would be correlated with insulin resistance[30].

CONCLUSION

At the end of this research work, which main objective was to describe obesity under Dolutegravir, and compare the metabolic risk to Efavirenz, we can conclude by saying that, there is a significant difference between the waist-to-hip ratio (WTH) in people on Dolutegravir and Efavirenz, suggesting a tendency to android obesity in people on Dolutegravir protocol. Regarding diabetes and glucose intolerance, we found no cases in both groups. Insulin resistance was present in 45% of people on Dolutegravir versus 0% in people on Efavirenz and the study of fat distribution showed that fat is preferentially localized in the subcutaneous tissue.

ACKNOWLEDGMENTS

The authors greatly thank all the personnel of the NAMSAL ANRS 12313 trial at the Yaounde Central Hospital, for their assistance during recruitment, all the personnel the National Obesity Center at the Yaounde Central Hospital, and all the personnel of the Radiology and Imagery service of the Yaounde Central Hospital for their help and assistance during biochemical and Ct-scan measurements. The authors are also grateful to all participants who have voluntarily accepted to be enrolled in this study.

Patient consent

Obtained

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interests

The authors declare that they have no competing interests in this section

Data confidentiality

The authors declare having followed the protocols in use at their working center regarding patient's data publication.

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