Journal of Diabetes Mellitus, 2023, 13, 45-57
https://www.scirp.org/journal/jdm
ISSN Online: 2160-5858
ISSN Print: 2160-5831

Short-Term Effects of Liraglutide versus Vildagliptin on Insulin Secretion and Sensitivity in Type 2 Diabetes: A Single Blinded Randomized Controlled Trial (LIRAVIS Study)

Martine Claude Etoa Etoga[1,2*], Estelle Amandine Well[1,2], Simeon Pierre Choukem[3,4], Mesmin Dehayem[1,2], Francine Mendane Mekobe[2,5], Anne Boli Ongmeb[1,6], Astasselbe Hadja Inna[7], Jean Claude Mbanya[1,2,8], Eugene Sobngwi[1,2,8]

[1]National Obesity Center, Yaoundé Central Hospital, Yaoundé, Cameroon
[2]Department of Internal Medicine and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon
[3]Department of Internal Medicine Faculty of Medicine and Pharmaceutical Sciences, University of Dschang, Dschang, Cameroon
[4]Health and Human Development (2HD) Research Network, Douala, Cameroon
[5]Internal Medicine, Essos Hospital Centre, Yaoundé, Cameroon
[6]Faculty of Health Sciences University of Bamenda, Bamenda, Cameroon
[7]Department of Internal Medicine, Faculty of Medicine and Biomedical Sciences, University of Garoua, Garoua, Cameroon
[8]Laboratory of Molecular Medicine and Metabolism, Biotechnology Center, University of Yaoundé 1, Yaoundé, Cameroon
Email: *claudetoa@yahoo.fr

How to cite this paper: Etoga, M.C.E., Well, E.A., Choukem, S.P., Dehayem, M., Mekobe, F.M., Ongmeb, A.B., Inna, A.H., Mbanya, J.C. and Sobngwi, E. (2023) Short-Term Effects of Liraglutide versus Vildagliptin on Insulin Secretion and Sensitivity in Type 2 Diabetes: A Single Blinded Randomized Controlled Trial (LIRAVIS Study). *Journal of Diabetes Mellitus*, **13**, 45-57.
https://doi.org/10.4236/jdm.2023.131005

Received: December 20, 2022
Accepted: February 7, 2023
Published: February 10, 2023

Abstract

Background: We aimed to evaluate the short-term metabolic effects of a GLP-1a, (liraglutide) versus a DPP-4i, (vildagliptin) in a group of sub-Saharan type 2 diabetes patients. **Methods:** We conducted a randomized controlled single blinded clinical trial in 14 uncontrolled type 2 diabetes patients (HbA1c ≥ 53 mmol/mol) with mean duration of diabetes of 8 [1 - 12] years and median age of 57 [49 - 61] years. Baseline treatment consisted of metformin in monotherapy or metformin plus sulfonylureas. Participants were randomly allocated to 2 groups of add-on 1.2 mg/day subcutaneous liraglutide in group 1 or 100 mg/day of oral vildagliptin in group 2 for 2 weeks. In all participants, insulin secretion in response to mixed meal tolerance test, insulin sensitivity by 80 mU/m^2/min hyperinsulinemic-euglycemic clamp, body composition, and lipid profile were measured before and after intervention. **Results:** At the end of intervention, insulin sensitivity remained unchanged both with liraglutide from 6.6 [4.2 - 7.9] to 6.9 [4.3 - 10.8] mg/kg/min; p = 0.61 and vildagliptin from 7.1 [5.3 - 9.0] to 6.5 [5.6 - 9.4] mg/kg/min (p = 0.86). The area under the C-peptide curve varied from 5.5 [1.0 - 10.9] to 14.9 [10.8 - 17.2] nmol/L/120min, p = 0.09 in group 1 and from 1.1 [0.5 - 14.1] to 13.0 [9.6 -

16.9] nmol/L/120min (p = 0.17) in group 2. LDL Cholesterol levels decreased significantly with liraglutide from 0.85 g/L [0.51 - 1.02] to 0.54 g/L [0.50 - 0.73] (p = 0.04) but not with Vildagliptin. Body weight tended to decrease in group 1 (−0.6 kg) versus modest increase in group 2 (+1.1 kg). **Conclusion:** Short-term metabolic effects of Liraglutide and Vildagliptin add-on therapy are comparable in sub-Saharan type 2 diabetes patients with a more favorable trend for Liraglutide on body weight, lipid profile, and insulin secretion.

Keywords

Insulin Sensitivity, Insulin Secretion, Liraglutide, Vildagliptin, Incretinomimetics

1. Introduction

Type 2 diabetes is a major public health threat with complex pathophysiology. The pharmacological management of type 2 diabetes has undergone recent changes that parallel the unravelling of its etiology [1]. Because of decrease of the incretin effect in type 2 diabetes [2], two classes of incretinomimetics were developed including exogenous Glucagon-Like Peptide analogs (GLP1a) such as Liraglutide, and the inhibitors of Dipeptidyl peptidase IV (DPP4i) that prolong the half-life of endogenous GLP1 such as Vildagliptin [3]. These two drugs are effective in terms of blood glucose control associated with a reduction of 0.8 to 1%, and both improve insulin sensitivity and secretion [4] [5] [6]. However, the time-to-appearance of the metabolic benefits of these two classes is not known. Also, it remains unclear which of the two strategies—GLP1 analogs or prolonging half-life of endogenous GLP1—have a better effect on insulin sensitivity and insulin secretion in people living with type 2 diabetes. Head-to-head studies comparing both treatment strategies on insulin secretion and sensitivity are scarce. Hence our aim was to assess the short-term effects of Liraglutide versus Vildagliptin on insulin sensitivity, insulin secretion, lipid profile, anthropometry and resting energy expenditure (REE) in an understudied population.

2. Methods

2.1. Research Participants

We carried out a single-blinded randomised controlled clinical trial at the Endocrinology and Metabolic disease unit of the Yaoundé Central Hospital of Cameroon for 7 months (October 2015 to May 2016). 14 uncontrolled type 2 diabetes patients on one or two oral anti-diabetic drugs, naïve of any incretinomimetic treatment were enrolled (HbA1c ≥ 7% or 53 mmol/mol) and randomly allocated to two groups. Patients with a previous history of pancreatitis, hepatic cytolysis or estimated glomerular filtration rate: eGFR < 30 ml/min/1.73m^2 (Modified Diet Renal Disease equation) were excluded, as well as patients with

acute complications of diabetes, anaemia pregnant and breastfeeding women.

The study was powered to detect a 20% change in insulin sensitivity using the following formula [7]: $N = (2/d^2) \times Cp$ where N = Sample size per group; d = Standardised difference = target difference/standard deviation; Cp = Power which is a constant. The calculated sample size was 9 subjects per group.

2.2. Randomization, Allocation and Intervention

Participants were randomized and allocated to 2 groups using the software random allocation 2.0. Due to the different presentations of the 2 drugs to be used, oral and injectable, the study was blinded only to the investigator but not the patient. In group 1, subcutaneous liraglutide (Victoza®) was administered at 0.6 mg/day for 1 week and increased to 1.2 mg the second week. In group 2, oral vildagliptin (Galvus®) was administered at 50 mg bid for two weeks. The study treatment was given as add-on therapy with no change in baseline treatment.

2.3. Outcomes

The primary outcome was the variation of insulin sensitivity from baseline, after 2 weeks of treatment. The secondary outcomes included the variation of insulin secretion, plasma glucose, body composition and parameters of the lipid profile after treatment.

2.4. Procedure

Data were collected using a pre-designed questionnaire. Clinical and anthropometric data, body composition analysis and metabolic explorations and indirect calorimetry were performed before intervention and repeated the day following the end of intervention period. Insulin sensitivity was assessed using a 2-hour euglycemic hyperinsulinemic clamp at 80 mU/m^2/min of insulin infusion rate. Resting energy expenditure (REE) was measured using indirect calorimetry. A mixed meal tolerance test with the assessment of plasma glucose and C-peptide at 0, 30, 90 and 120 minutes for the evaluation of insulin secretion. All side effects were also recorded.

Body composition analysis: This was evaluated using bio-electrical impedance. It consisted of using an impedancemeter TANITA BC 418 MA (TANITA®, TANITA Corporation 1-14-2 Maeno-cho, Itabashi-ku, Tokyo-Japan). This non-invasive test involves the placement of two electrodes under the person's feet and two electrodes in their hands. A low level, imperceptible electrical current is sent through the body. This device measures how this signal is impeded through different types of tissue. The weight is recorded automatically. The output variables include the percent body fat, fat mass, fat-free mass and bone mass with a coefficient of variation being between 3% and 4%.

Indirect calorimetry: The Korr® Reevue indirect calorimetry (Korr Medical Technologies, Inc. Salt Lake City, UT USA 84120) was performed after at least 3-hour fast. Participants were required not to smoke, drink alcoholic beverages

or exercise 24 hours prior to the exploration. They were installed supine and resting for 20 minutes. The calibrated calorimeter then recorded their breathing over 10 minutes and resting energy expenditure adjusted for total mass was obtained.

Euglycemic-hyperinsulinemic clamp: After an overnight fast, participants were admitted into the Clinical Research Facility of the Endocrine Unit of Yaoundé Central Hospital. Participants were required not to exercise one week prior to procedure.

Rapid insulin (Actrapid® HM Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark) concentrated at 100 mU/mL installed in a syringe pump (ALARIS® MEDICAL SYSTEMS UK Ltd., Basingstoke, RG22 4BS, UK) and 10% dextrose solution were infused via the right antecubital vein. Blood was sampled through the left antecubital vein. A priming dose of insulin was given over the first 10 minutes followed by a constant infusion rate of 80 mU/m^2/min up to the 120th minutes. The 10% dextrose solution was infused as from the 11th minute at variable rates modifiable every 5 minutes using an infusion pump (IVAC Corporation-Model 598, San Diego, California) with the aim of maintaining capillary blood glucose levels at 5.5 ± 0.5 mmol/L. Capillary blood glucose measurements were done with a glucometer and strips (ONE TOUCH® Ultra® 2, LifeScan Europe Division of Cilag GmbH International 6300 Zug, Switzerland). Blood samples were collected at baseline, and at the 100th, 110th and 120th min. Insulin sensitivity was estimated using the M-value (mg/min/kg) which represents the glucose disposal rate during insulin infusion. It was calculated as the space of glucose correction (SC) subtracted by the rate of glucose infusion, and adjusted to lean body mass. During the last 20 minutes of the hyperinsulinemic-euglycemic clamp, glycaemia was not always constant therefore, SC was adjusted for glycaemic levels and variations of glucose infusion rate. This was calculate using the difference of glucose levels from the beginning and to the end of the steady state period multiplied by 0.095.

Mixed meal tolerance test and insulin secretion measurement

This test was performed after an overnight fast the day before intervention and the day after the last dose of study treatment. The meal test consisted of a skimmed milk preparation containing 51 g of carbohydrates, 35 g of proteins and 0.8 g of fats to which we added 20 g of rice powder and 21 g of oil to obtain a total of 580 kcal and comparable nutrient composition as *Boost*. Blood samples were collected before, 30 minutes, 90 minutes, and 120 minutes after the ingestion of the meal for plasma glucose and C-peptide determination. Plasma glucose was measured using the glucose oxidase method. C-peptide was measured using the sandwich ELISA method with the ultrasensitive Mercodia test (Mercodia AB, Sylveniusgatan 8A, SE-754 50 Uppsala, Sweden). *Hs*-CRp was measured using the latex-enhanced immunoturbidimetric assay. Insulin secretion was estimated as Area Under the Curve (AUC) of glycemia and C-peptide using the Tai formula ($\mathrm{AUC} = 1/2 \sum_i^n = X_i - 1\left(y_i - 1 + y_i\right)$) [8].

2.5. Statistical Analysis

Data were entered, encoded and analysed using IBM SPSS for Windows, version 21.0 for Windows (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, version 23.0. Armonk, NY: IBM Corp.). Data are expressed as medians [interquartile range] for quantitative data and percentage for qualitative data. Comparisons were performed using non-parametric tests namely the Mann-Whitney test for difference between the two groups and Wilcoxon test for difference within the same group. Significant threshold was set at $p = 0.05$.

2.6. Ethical Considerations

The study protocol was approved by the institutional Ethical committee for Research of the Faculty of Medicine and Biomedical Sciences of Yaoundé I University. The study was performed in accordance with the Declaration of Helsinki. All eligible participants provided a signed informed consent. The study was registered at ClinicalTrial.gov (ClinicalTrial.gov identifier: NCT02832999).

3. Results

As shown in Figure 1, we obtained a total of 14 patients randomized into 2 groups of 7. The first group on liraglutide and the second group on vildagliptin. The median [interquartile range, IQR] age of the study participants was 57 [41 - 61] years with a median diabetes duration of 8 [1 - 12] years. The median HbA1c was 76 [67 - 97] mmol/mol and the median weight was 85.1 [71.0 - 94.9] Kg. Baseline characteristics were similar in both groups as shown in Table 1.

There was little difference on clinical parameters after intervention between the two groups, however, body weight decreased by −0.6 kg in the liraglutide group while it increased by +1.1 kg in the vildagliptin group ($p = 0.11$). Resting energy expenditure (REE) significantly decreased in the liraglutide group but not in the vildagliptin group (p-value = 0.02 vs 0.50) (Table 2).

Fasting blood glucose significantly dropped in both groups after intervention with a similar trend (Table 3), while the LDL Cholesterol level decreased in the liraglutide group (−37%) but not in the vildagliptin group. Conversely, *Hs*-CRp decreased in the vildagliptin group only (Table 3). Insulin sensitivity remained unchanged in both groups (Table 4). Concerning insulin secretion, the area under the curve of C-peptide (AUC) increased more in the liraglutide group than in the vildagliptin group, showing a non-significant trend towards improvement (Table 4). There was no significant change in the M-value (Table 4).

The most reported side effects were gastro intestinal (Table 5). All side effects were mild and subsided within the first week of intervention.

4. Discussion

This study aimed to compare the metabolic effects after 2 weeks of therapy by replacing endogenous GLP-1 by a GLP-1 analog (Liraglutide) on one side, and/or extending endogenous GLP-1 half-life using DPP4i (Vildagliptin). Both

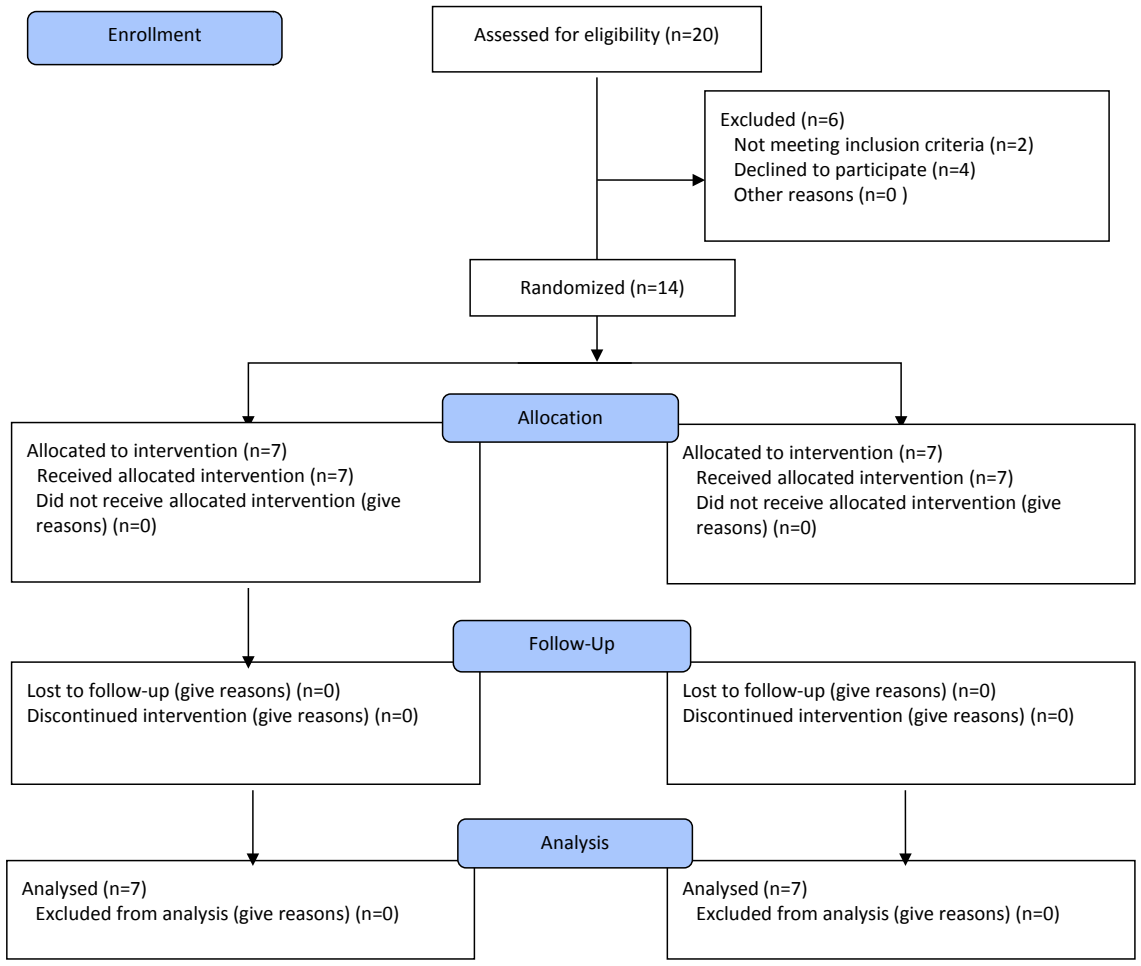

Figure 1. Flow diagram of patients.

Table 1. General characteristics of the study population.

Characteristics	Study population	Liraglutide	Vildagliptin	P
Age M [IQR]	57 [49 - 61.5]	57 [41 - 61]	51 [49 - 63]	0.74
Sex n (%)				0.56
Male	4	3 (42.9)	1 (14.3)	
Female	10	4 (57.1)	6 (85.7)	
Duration of diabetes				0.26
<10 ans	9	6 (85.7)	3 (42.9)	
≥10 ans	5	1 (14.3)	4 (57.1)	
Family history of diabetes				1.00
Yes	9	5 (71.4)	4 (57.1)	
No	5	2 (28.6)	3 (42.9)	
Initial treatment				1.00
Biguanides	9	5 (71.4)	4 (57.1)	
Biguanides and sulfonylureas	5	2 (28.6)	3 (42.9)	

Table 2. Changes in clinical characteristics before and after the intervention.

Characteristics	Liraglutide			Vildagliptin			P between group
	Before	After	P within group	Before	After	P within group	
SBP sitting (mmHg)	131 [121 - 139]	124 [114 - 127]	0.50	131 [120 - 143]	120 [115 - 131]	0.08	0.74
DBP sitting (mmHg)	77 [71 - 90]	77 [65 - 85]	0.67	81 [72 - 83]	70 [69 - 78]	0.07	0.60
SBP upright (mmHg)	130 [120 - 145]	118 [113 - 123]	**0.04**	134 [118 - 146]	120 [105 - 139]	**0.03**	0.94
DBP upright (mmHg)	88 [78 - 98]	80 [72 - 88]	0.12	80 [76 - 89]	79 [71 - 80]	0.31	0.24
HR (bpm)	78 [72 - 90]	89 [77 - 97]	0.13	91 [80 - 96]	85 [70 - 90]	0.08	0.40
Weight (kg)	91.7 [81.6 - 100]	91.1 [79.8 - 97.1]	0.07	77.5 [66.1 - 92.4]	78.6 [58.7 - 92.0]	0.87	0.11
BMI (kg/m^2)	29.6 [28.5 - 35.8]	28.9 [27.5 - 35.6]	0.06	30.3 [23.1 - 32.7]	30.7 [22.2 - 32.9]	0.87	0.56
WC (cm)	103 [94 - 109]	102 [90 - 108]	0.49	95 [81 - 98]	93 [77 - 98]	0.08	0.06
HC (cm)	110 [103 - 115]	110 [101 - 113]	0.34	111 [95 - 119]	105 [94 - 123]	0.92	0.44

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; WC: Waist circumference; HC: Hip circumference.

Characteristics	Liraglutide			Vildagliptin			P between groups
	Before	After	P within group	Before	After	P within group	
Waist-to-hip ratio	0.96 [0.81 - 0.97]	0.93 [0.79 - 0.98]	0.20	0.87 [0.83 - 0.89]	0.82 [0.81 - 0.89]	0.07	0.10
Fat mass (kg)	25.7 [24.3 - 38.2]	25.1 [23.2 - 38.7]	0.12	29.9 [17.4 - 44.0]	25.9 [16.5 - 43.8]	0.31	0.65
Lean mass (kg)	59.6 [53.4 - 66.7]	58.6 [52.3 - 69.8]	0.61	48.3 [41.0 - 53.3]	48.1 [42.2 - 54.0]	0.61	**0.03**
Total body fat percentage (%)	33.3 [29.5 - 41.7]	30.0 [26.6 - 42.3]	0.67	36.9 [26.4 - 47.6]	37.3 [26.5 - 47.7]	0.73	0.56
REE (Kcal/day)	1699 [1426 - 1771]	1454 [1377 - 1590]	**0.02**	1382 [154 - 1771]	1598 [1138 - 1714]	0.50	0.94

REE: resting energy expenditure.

Table 3. Biological characteristics of the study population before and after the intervention.

Characteristics	Liraglutide			Vildagliptin			P between groups
	Before	After	P within group	Before	After	P within group	
Fasting blood glucose (mmol/L)	13.6 [11.0 - 17.2]	6.9 [6.2 - 7.8]	**0.018**	15.7 [11.4 - 17.6]	8.8 [6.6 - 13.1]	**0.04**	0.11
Creatininemia (mg/L)	11.6 [9.3 - 12.0]	10.0 [9.3 - 11.0]	**0.046**	10 [9.1 - 11.0]	10 [7.3 - 11.0]	0.71	0.78
ALAT (UI)	12 [8 - 15]	15 [9 - 21]	0.46	17 [13 - 37]	17 [13 - 22]	1.00	0.44
Hs-CRp (mg/L)	3.3 [2.1 - 16.5]	3.0 [0.6 - 12.2]	0.13	4.3 [3.7 - 4.8]	1.0 [1.0 - 4.1]	**0.04**	0.48
Total Cholesterol (g/L)	1.49 [1.15 - 1.64]	1.18 [1.08 - 1.42]	0.09	1.44 [1.19 - 1.66]	1.38 [1.10 - 1.41]	0.31	0.79
HDL-C (g/L)	0.40 [0.35 - 0.46]	0.46 [0.44 - 0.48]	0.07	0.44 [0.43 - 0.52]	0.46 [0.42 - 0.48]	0.40	0.74
LDL-C (g/L)	0.85 [0.51 - 1.02]	0.54 [0.50 - 0.73]	**0.04**	0.84 [0.52 - 0.96]	0.60 [0.37 - 0.80]	0.23	0.84
TG (g/L)	1.13 [0.77 - 1.34]	0.73 [0.66 - 1.26]	0.31	0.83 [0.63 - 1.26]	1.20 [1.06 - 1.23]	0.13	0.14

Hs-CRp; highly sensitive C reactive protein, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TG: triglycerides.

Table 4. Change in insulin secretion, insulin sensitivity, glycaemia before and after treatment.

Characteristics	Liraglutide			Vildagliptin			P between groups
	Before	**After**	**P within group**	**Before**	**After**	**P within group**	
Baseline C peptide (nmol/L)	0.03 [0.02 - 0.10]	0.11 [0.09 - 0.17]	0.23	0.00 [0.00 - 0.13]	0.02 [0.00 - 0.17]	0.86	0.18
AUC glycaemia (nmol/L/120mn)	745.8 [617.5 - 935.8]	640.0 [541.6 - 746.6]	0.12	705.0 [525 - 1165]	720 [588.3 - 818.3]	0.49	0.48
AUC C peptide (nmol/L/120mn)	5.5 [1.0 - 10.9]	14.9 [10.8 - 17.2]	0.09	1.2 [0.5 - 14.1]	13.0 [9.6 - 16.9]	0.17	0.56
HOMA-IR	0.01 [0.01 - 0.08]	0.03 [0.01 - 0.06]	0.61	0.00 [0.00 - 0.06]	0.00 [0.00 - 0.05]	0.86	0.27
M-value (mg/kg/min)	6.6 [4.2 - 7.9]	6.9 [4.3 - 10.8]	0.39	7.2 [5.3 - 9.0]	6.5 [5.6 - 9.4]	0.61	0.84
M adjusted for lean mass (Mg/kg/min)	10.0 [7.0 - 13.5]	11.0 [7.5 - 14.9]	0.39	10.5 [8.4 - 14.9]	10.8 [9.9 - 13.1]	0.74	0.84

AUC: Area Under the Curve; HOMA-IR: Homeostasis model assessment-Insulin Resistance.

Table 5. Reported side effects.

Sides effects	Liraglutide N (%)	Vildagliptine N (%)	P
Nausea			
Yes	2 (28.6)	3 (42.9)	1.00
No	5 (71.4)	4 (57.1)	
Vomiting			
Yes	1 (14.3)	1 (14.3)	1.00
No	6 (85.7)	6 (85.7)	
Abdominal pain			
Yes	2 (28.6)	2 (28.6)	1.00
No	5 (71.4)	5 (71.4)	
Headache			
Yes	0 (0)	3 (42.9)	0.19
No	7 (100)	4 (57.1)	
Vertigo			
Yes	3 (42.9)	3 (42.9)	1.00
No	4 (57.1)	4 (57.1)	
Asthenia			
Yes	3 (42.9)	1 (14.3)	0.56
No	4 (57.1)	6 (85.7)	
Anorexia			
Yes	2 (28.6)	0 (0)	0.46
No	5 (71.4)	7 (100)	

classes used as add-on therapy exhibit similar short term metabolic effects in sub Saharan uncontrolled type 2 diabetes patients within the observation period. Liraglutide was more effective on LDL-C and body weight, while vildagliptin has a better effect on reducing inflammation (*Hs*-CRp). Both strategies tended to improve insulin secretion, but no change in insulin sensitivity was observed after 2 weeks of treatment.

Several studies have shown an improvement of insulin sensitivity using these molecules over much longer treatment periods [4] [6] [9]. This was explained by the anti-inflammatory effects of the two drugs [10] [11]. However, we noted a significant decrease in *Hs*-CRp only with Vildagliptin within two weeks of treatment suggesting that a reduction in insulin resistance could be expected earlier with Vildagliptin compared to Liraglutide.

Both drugs showed a trend towards an improvement of insulin secretion after 2 weeks of treatment. However, it seemed to be more favorable under Liraglutide as expected. In fact liraglutide like other GLP1a causes a higher, pharmacological increase in GLP-1 whereas vildagliptin like other DPP-IV inhibitors trigger a physiological GLP-1 increase [1]. The non-significant change found in our study may be explained by the sample size, as it was powered to detect changes in insulin sensitivity but not secretion.

Body composition analysis showed a tendency towards weight loss in the liraglutide group and weight gain in the vildagliptin group. In addition, we noted a downward trend in the body fat percentage only under liraglutide, showing early weight effects of liraglutide despite insufficient glycaemic control. In this sub-Saharan population, Liraglutide proves to have beneficial anthropometric effects observed elsewhere [12] [13] [14] [15] [16], and this occurs very early after the initiation of treatment.

Participants on liraglutide had a reduction of nearly 37% of LDL cholesterol in 2 weeks but not those on vildagliptin. This effect is equivalent to the decrease in LDL cholesterol observed after 6 weeks with atorvastatin 10 mg or simvastatin 20 mg [17]. The effect on lipids has been attributed to the action of liraglutide on the expression of the genes involved in lipogenesis [18]. The effects of Liraglutide on the weight and lipid profile have been described in clinical trials and they partly explain the cardiovascular benefit of this drug as demonstrated in the LEADER trial [19]. Both strategies have shown a comparable and significant efficacy on glycaemic control as described in the literature [20] [21] [22]. The difference in short-term variation in resting energy expenditure with liraglutide vs. vildagliptin could provide an explanation for the difference in the lipid profile and weight between the two molecules. This was a paradoxical decrease in REE under liraglutide and a non-significant increase under vildagliptin. This effect on the REE has not been found after 4 weeks of treatment with liraglutide and vildagliptin in earlier studies [23] [24].

Systolic blood pressure decreased significantly in both groups. This result is consistent with the results of the LEAD studies where a reduction of the SBP under Liraglutide is observed from the second week of treatment [13] [14] [15] [25] [26].

5. Conclusion

Liraglutide tends to have better metabolic effects than vildagliptin after two weeks of treatment, especially on insulin secretion and LDL cholesterol.

Ethical Considerations

This study was performed in accordance with the guidelines of the Helsinki Declaration and was approved by the Institutional Research Ethical Committee of the Faculty of Medicine and Biomedical Sciences of Yaoundé and by the institutional review board of the Yaoundé Central Hospital of Cameroon. All participants provided written informed consent.

Availability of Data and Material

The datasets generated and/or analyzed during the current study are available from the corresponding author upon request.

Authors' Contributions

MCEE, EAW, SPC, ES designed the research.

MCEE, EAW, SPC, MD, ES performed the research.

MCEE, EAW, ES analyzed the data; MCEE, EAW, and ES wrote the paper; All authors revised the manuscript.

ES is the guarantor of this work.

All the authors approved the final version of the manuscript.

Acknowledgements

We gratefully acknowledge all the patients who have accepted to take part in this study. We are grateful to Dr. Tankeu Aurel for manuscript revision and Mr. Djahmeni Eric for laboratory assistance.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Verspohl, E.J. (2012) Novel Pharmacological Approaches to the Treatment of Type 2 Diabetes. *Pharmacological Reviews*, **64**, 188-237. https://doi.org/10.1124/pr.110.003319

[2] Nauck, M.A. and Meier, J.J. (2016) The Incretin Effect in Healthy Individuals and Those with Type 2 Diabetes: Physiology, Pathophysiology, and Response to Therapeutic Interventions. *The Lancet Diabetes & Endocrinology*, **4**, 525-536. https://doi.org/10.1016/S2213-8587(15)00482-9

[3] Pratley, R.E. and Gilbert, M. (2008) Targeting Incretins in Type 2 Diabetes: Role of GLP-1 Receptor Agonists and DPP-4 Inhibitors. *The Review of Diabetic Studies*, **5**, 73-94. https://doi.org/10.1900/RDS.2008.5.73

[4] Jinnouchi, H., Sugiyama, S., Yoshida, A., *et al.* (2015) Liraglutide, a Glucagon-Like

Peptide-1 Analog, Increased Insulin Sensitivity Assessed by Hyperinsulinemic-Euglycemic Clamp Examination in Patients with Uncontrolled Type 2 Diabetes Mellitus. *Journal of Diabetes Research*, **2015**, Article ID: 706416. https://doi.org/10.1155/2015/706416

[5] Horie, A., Tokuyama, Y., Ishizuka, T., *et al.* (2014) The Dipeptidyl Peptidase-4 Inhibitor Vildagliptin Has the Capacity to Repair β-Cell Dysfunction and Insulin Resistance. *Hormone and Metabolic Research. Hormon-und Stoffwechselforschung. Hormones et metabolisme*, **46**, 814-818. https://doi.org/10.1055/s-0034-1382015

[6] Derosa, G., Ragonesi, P.D., Carbone, A., *et al.* (2012) Vildagliptin Added to Metformin on β-Cell Function after a Euglycemic Hyperinsulinemic and Hyperglycemic Clamp in Type 2 Diabetes Patients. *Diabetes Technology & Therapeutics*, **14**, 475-484. https://doi.org/10.1089/dia.2011.0278

[7] Eng, J. (2003) Sample Size Estimation: How Many Individuals Should Be Studied? *Radiology*, **227**, 309-313. https://doi.org/10.1148/radiol.2272012051

[8] Tai, M.M. (1994) A Mathematical Model for Determination of Total Area under Glucose Tolerance and Other Metabolic Curves. Diabetes Care, **17**, 152-154. https://doi.org/10.2337/diacare.17.2.152

[9] Azuma, K., Rádiková, Z., Mancino, J., *et al.* (2008) Measurements of Islet Function and Glucose Metabolism with the Dipeptidyl Peptidase 4 Inhibitor Vildagliptin in Patients with Type 2 Diabetes. *The Journal of Clinical Endocrinology & Metabolism*, **93**, 459-464. https://doi.org/10.1210/jc.2007-1369

[10] Krasner, N.M., Ido, Y., Ruderman, N.B. and Cacicedo, J.M. (2014) Glucagon-Like Peptide-1 (GLP-1) Analog Liraglutide Inhibits Endothelial Cell Inflammation through a Calcium and AMPK Dependent Mechanism. *PLOS ONE*, **9**, e97554. https://doi.org/10.1371/journal.pone.0097554

[11] Langlois, A., Dal, S., Vivot, K., *et al.* (2016) Improvement of Islet Graft Function Using Liraglutide Is Correlated with Its Anti-Inflammatory Properties. *British Journal of Pharmacology*, **173**, 3443-3453. https://doi.org/10.1111/bph.13575

[12] Henry, R.R., Buse, J.B., Sesti, G., *et al.* (2011) Efficacy of Anti Hyperglycemic Therapies and the Influence of Baseline Hemoglobin A1C: A Meta-Analysis of the Liraglutide Development Program. *Endocrine Practice*, **17**, 906-913. https://doi.org/10.4158/EP.17.6.906

[13] Nauck, M., Frid, A., Hermansen, K., *et al.* (2009) Efficacy and Safety Comparison of Liraglutide, Glimepiride, and Placebo, All in Combination with Metformin, in Type 2 Diabetes: The LEAD (Liraglutide Effect and Action in Diabetes)-2 Study. *Diabetes Care*, **32**, 84-90. https://doi.org/10.2337/dc08-1355

[14] Zinman, B., Gerich, J., Buse, J.B., *et al.* (2009) Efficacy and Safety of the Human Glucagon-Like Peptide-1 Analog Liraglutide in Combination with Metformin and Thiazolidinedione in Patients with Type 2 Diabetes (LEAD-4 Met+TZD). *Diabetes Care*, **32**, 1224-1230. https://doi.org/10.2337/dc08-2124

[15] Buse, J.B., Rosenstock, J., Sesti, G., *et al.* (2009) Liraglutide once a Day versus Exenatide Twice a Day for Type 2 Diabetes: A 26-Week Randomised, Parallel-Group, Multinational, Open-Label Trial (LEAD-6). *The Lancet*, **374**, 39-47. https://doi.org/10.1016/S0140-6736(09)60659-0

[16] Foley, J.E. and Jordan, J. (2010) Weight Neutrality with the DPP-4 Inhibitor, Vildagliptin: Mechanistic Basis and Clinical Experience. *Vascular Health and Risk Management*, **6**, 541-548. https://doi.org/10.2147/VHRM.S10952

[17] Welty, F.K., Lewis, S.J., Friday, K.E., Cain, V.A. and Anzalone, D.A. (2016) A Comparison of Statin Therapies in Hypercholesterolemia in Women: A Subgroup Anal-

ysis of the STELLAR Study. *Journal of Women's Health*, **25**, 50-56. https://doi.org/10.1089/jwh.2015.5271

[18] Decara, J., Arrabal, S., Beiroa, D., *et al.* (2016) Antiobesity Efficacy of GLP-1 Receptor Agonist Liraglutide Is Associated with Peripheral Tissue-Specific Modulation of Lipid Metabolic Regulators. *BioFactors* (*Oxford*, *England*), **42**, 600-611. https://doi.org/10.1002/biof.1295

[19] Marso, S.P., Daniels, G., Brown-Frandsen, K., *et al.* (2016) Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *The New England Journal of Medicine*, **375**, 311-322. https://doi.org/10.1056/NEJMoa1603827

[20] Blonde, L. and Montanya, E. (2012) Comparison of Liraglutide versus Other Incretin-Related Anti-Hyperglycaemic Agents. *Diabetes*, *Obesity and Metabolism*, **14**, 20-32. https://doi.org/10.1111/j.1463-1326.2012.01575.x

[21] Takeshita, Y., Takamura, T., Kita, Y., *et al.* (2015) Vildagliptin vs Liraglutide as a Second-Line Therapy Switched from Sitagliptin-Based Regimens in Patients with Type 2 Diabetes: A Randomized, Parallel-Group Study. *Journal of Diabetes Investigation*, **6**, 192-200. https://doi.org/10.1111/jdi.12269

[22] Li, C.-J., Yu, Q., Yu, P., *et al.* (2014) Efficacy and Safety Comparison of Add-On Therapy with Liraglutide, Saxagliptin and Vildagliptin, All in Combination with Current Conventional Oral Hypoglycemic Agents Therapy in Poorly Controlled Chinese Type 2 Diabetes. *Experimental and Clinical Endocrinology & Diabetes*, **122**, 469-476. https://doi.org/10.1055/s-0034-1374586

[23] Horowitz, M., Flint, A., Jones, K.L., *et al.* (2012) Effect of the Once-Daily Human GLP-1 Analogue Liraglutide on Appetite, Energy Intake, Energy Expenditure and Gastric Emptying in Type 2 Diabetes. *Diabetes Research and Clinical Practice*, **97**, 258-266. https://doi.org/10.1016/j.diabres.2012.02.016

[24] Heruc, G.A., Horowitz, M., Deacon, C.F., *et al.* (2014) Effects of Dipeptidyl Peptidase IV Inhibition on Glycemic, Gut Hormone, Triglyceride, Energy Expenditure, and Energy Intake Responses to Fat in Healthy Males. *American Journal of Physiology-Endocrinology and Metabolism*, **307**, E830-E837. https://doi.org/10.1152/ajpendo.00370.2014

[25] Russell-Jones, D., Vaag, A., Schmitz, O., *et al.* (2009) Liraglutide vs Insulin Glargine and Placebo in Combination with Metformin and Sulfonylurea Therapy in Type 2 Diabetes Mellitus (LEAD-5 met+SU): A Randomised Controlled Trial. *Diabetologia*, **52**, 2046-2055. https://doi.org/10.1007/s00125-009-1472-y

[26] Garber, A., Henry, R., Ratner, R., *et al.* (2009) Liraglutide versus Glimepiride Monotherapy for Type 2 Diabetes (LEAD-3 Mono): A Randomised, 52-Week, Phase III, Double-Blind, Parallel-Treatment Trial. *The Lancet*, **373**, 473-481. https://doi.org/10.1016/S0140-6736(08)61246-5

List of Abbreviations

AUC: Area Under the Curve, BMI: Body Mass Index; DBP: Diastolic Blood Pressure, DPP4i: Dipeptidyl Peptidase 4 Inhibitors, FPG: Fasting Plasma Glucose, GFR: Glomerular Filtration Rate, GLP1a: Glucagon Like Peptide 1 Analog, HDL: High Density Lipoprotein, HDL: High Density Lipoprotein, *Hs*-CRp: High Sensitive C Reactive Protein, IDF: International Diabetes Federation, LDL: Low Density Lipoprotein, NOC: National Obesity Center, REE: Resting Energy Expenditure, SBP: Systolic Blood Pressure, TG: Triglyceride.