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Liraglutide and Dulaglutide Have Comparable HbA1c Reduction in Emirati Patients with T2DM

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Abstract

Glucagon like peptide-1 is responsible for the incretin effect after a meal or an oral glucose load. Patients with type 2 diabetes mellitus have impairment of secretion and action of glucagon like peptide-1. This impairment can be overcome through pharmacological doses of glucagon like peptide-1 analogues. **Aim of the Study:** This study aimed at evaluation of the effect of treatment with glucagon like peptide-1 analogues; liraglutide and dulaglutide, in Emirati patients with type 2 diabetes mellitus. Glycemic control was the primary end point while the secondary end point was the effect on body mass index, blood pressure, heart rate, serum creatinine, lipid profile and estimated glomerular filtration rate. **Patients & Methods:** This is a retrospective study including 54 patients with type 2 diabetes mellitus. Patients used Liraglutide or Dulaglutide as add on therapy to oral antidiabetic medications for one year. Thirty-four patients used liraglutide 1.8 mg once daily and 20 patients used dulaglutide 1.5 mg once weekly. All patients were older than 18 years and had estimated glomerular filtration rate (>90 ml/min/1.73 m^2). Body mass index, sitting blood pressure and heart rate were collected. Fasting plasma glucose, HbA1c, lipid panel and other biochemical parameters were also collected. Data were analysed before and at 6 and 12 months of glucagon like peptide-1 analogue treatment. **Results:** At 12 months of treatment, liraglutide significantly reduced fasting plasma glucose (11.3 ± 4 vs 7 ± 1.7, p < 0.001), HbA1c (8.55 ± 1.6 vs 7.18 ± 1.04, p < 0.001) and body mass index (39.4 ± 6.4 vs 37.6 ± 6.7, p < 0.0005). Dulaglutide did not significantly reduce fasting plasma glucose (15.4 ± 3.5 vs 9.5 ± 5.4 mmol/L, p = 0.053), significantly reduced HbA1c (8.84 ± 1.8 vs 7.5 ± 0.79, p = 0.007), body mass index (38.8 ± 6.8 vs 37.2 ± 6.6, p = 0.004) and estimated glomerular filtration rate

(123.6 ± 60 vs 104 ± 47.3, p = 0.008). Dulaglutide was more effective in reduction of body mass index than liraglutide. Both drugs did not show significant effect on blood pressure, heart rate or lipid profile. **Conclusion:** Over a period of one year, liraglutide and dulaglutide produced comparable reduction of HbA1c and hence diabetes control. Both drugs significantly reduced body mass index but this effect was more pronounced with Dulaglutide. Only liraglutide significantly reduced fasting plasma glucose. Dulaglutide significantly reduced estimated glomerular filtration rate. There was no significant effect of liraglutide or dulaglutide on blood pressure, heart rate or lipid profile.

Keywords

Liraglutide, Dulaglutide, HbA1c, eGFR, FPG, BMI

1. Introduction

Glucagon like peptide 1 (GLP-1) is a peptide hormone secreted from the L-cells in the lower gut; the distal jejunum, ileum, and colon, in response to ingestion of carbohydrates, lipids, and mixed meals [1] [2] [3]. GLP-1 increases glucose-dependent insulin synthesis and secretion in the pancreatic islets. It increases satiety and decreases appetite by acting on brain areas involved in regulation of food intake. It also delays gastric emptying, suppresses glucagon secretion and decreases hepatic glucose output (1). These effects explain the potential of GLP1 analogues as antidiabetic agents.

Patients with T2DM have impairment of secretion and effect of GLP-1. Pharmacological doses of GLP-1 in the form of GLP-1 analogues can overcome these underlying defects [2] [3].

Liraglutide has a close structural homology to native GLP-1 and is conjugated to a palmitic acid to prolong its half-life for daily administration. Dulaglutide is a recombinant fusion protein consisting of two GLP-1 peptides covalently linked to a human IgG4-Fc heavy-chain variant with more prolonged half-life making it suitable for weekly use [3].

Liraglutide was approved by the European Commission in July 2009 and by the Food and Drug Administration (FDA) in the United States in January 2010 for use in type 2 diabetes [4].

Dulaglutide was approved for use in September 2014 by the FDA and in November 2014 by the European Commission [5] [6] [7] [8].

Management of type 2 diabetes considers glycemic control as the major target. However, a comprehensive approach that includes diabetes associated comorbidities has been raised in recent years with appearance of new hypoglycemic agents that have extra benefits in addition to plasma glucose control [9].

GLP-1 analogues can be used as add on to other antidiabetic medications. Adverse effects of these agents are mainly gastrointestinal which may limit their

use. This is in addition to the need for subcutaneous administration and the high cost [9] [10] [11]. These agents showed a significant reduction in HbA1c with a favorable weight reducing effect. Hypoglycemic risk in this group is very low [12] [13].

They can be used as components of dual or triple therapy. They can be a good choice when weight control and avoidance of hypoglycemia are significant targets. Sometimes they are as effective as insulin. Gender, ethnicity, body weight and body mass index (BMI) do not require dose modification as they have no effect on the pharmacokinetics of GLP-1 analogues [14]. Effectiveness of GLP-1analogues in improving HbA1c and fasting plasma glucose (FPG) was clinically meaningful in patients with type 2 diabetes of recent onset as well as those harboring the disease for a long duration [15].

Liraglutide and dulaglutide are safely used in patients with severe renal impairment (eGFR ≥ 15 to <30 mL/min) without dose modification. However, they are not recommended in end-stage renal disease (eGFR < 15 mL/min/1.73m²) [16].

Liraglutide was effective in the secondary prevention of cardiovascular (CV) events in patients with type 2 diabetes [17] [18]. It significantly reduced all-cause death. Therefore, it is highly recommended in diabetes patients with atherosclerotic CV disease [11]. Cardiovascular safety of dulaglutide was evident in many randomized controlled trials as well as observational studies [19].

Patients with diabetes usually have concern about the use of medications that are administered by injection. Studies comparing patient's perception of the injection devices used with liraglutide and dulaglutide showed that dulaglutide device was more preferred by patients. The dulaglutide device and the weekly use made it easier and more convenient for some patients in comparison with the liraglutide device and its daily use [20].

As a class, the GLP-1 analogues are well tolerated. A physician has to explain to the patient about the gastrointestinal (GI) related adverse effects that may occur with initiation of therapy. These effects are usually transient and disappear with continuation of treatment. To overcome these GI associated symptoms, the patient may be advised to take smaller meals and to avoid spicy and high fat meals. Returning the patient to a lower GLP-1 analogue dose for about 1 week or more then re-increasing the dose can overcome the GI adverse effects [21].

Data about GLP-1 analogues in patients with type 2 diabetes in UAE and gulf area are very limited.

In the present study we investigated the effect of liraglutide and dulaglutide on glycemic control, as evaluated by FPG and HbA1c, in Emirati patients with type 2 diabetes. We also looked at their effects on clinical parameters such as BMI, blood pressure and heart rate as well as biochemical parameters such as serum creatinine, eGFR and plasma lipids.

2. Materials & Methods

This is a retrospective, cross-sectional observational study, analyzing data of type

2 diabetes patients who received liraglutide 1.8 mg injection once daily or Dulaglutide 1.5 mg injection once weekly as add on therapy to oral antidiabetic medications for 12 months.

The study proposal has been reviewed and approved by the MOHAP Research Ethics Committee, Sharjah (Research Approval Reference No. MOHAP/DXB-REC/OON/No. 42 2019). The ethics committee waived the need to obtain informed consent for this study. All methods were performed in accordance with the relevant guidelines and regulations of Zulekha Hospital, Sharjah (ZHS).

Two hundred files of type 2 diabetes patients who visited a single endocrinology clinic at Zulekha Hospital, Sharjah during 2018 and 2019 were screened. Fifty-four patients were eligible for the study. All patients had T2DM, age more than 18 years and normal kidney function (eGFR > 90 ml/min/1.73m^2, no microalbuminuria). Patients were using Liraglutide 1.8 mg injection daily or Dulaglutide 1.5 mg injection once weekly as add on therapy for the recent 12 months. Patients continued with stable lifestyle pattern all through the study period.

Patient exclusion was done if data were not enough or there was a change or adjustment in antidiabetic medication. Any condition that may affect the studied variables such as acute illness, hospitalization, anemia or steroid treatment, was also an exclusion criterion.

BMI was calculated as per the equation: BMI = weight in Kg/(height in meters)^2, sitting blood pressure and heart rate were collected. Fasting plasma glucose, HbA1c and lipid profile and other biochemical parameters e.g. creatinine, blood urea nitrogen (BUN), urine albumin creatinine ratio were traced from medical records of the patients when available. The Modification of Diet in Renal Disease (MDRD) study formula was used for calculation of eGFR [22].

As per laboratory protocol that is followed for patients including our study population, blood samples were collected from all participants, after an overnight fasting, using plain, EDTA and Lithium Heparin vacutainers. Sera were separated by centrifuging blood at 3500 rpm for 10 minutes and all samples were immediately processed.

Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured by Cobas 6000, Modular autoanalyzer, Roche Diagnostics, using an enzymatic colorimetric method [23] [24]. Low-density lipoprotein cholesterol (LDL-C) was directly measured [25]. Plasma glucose, urine albumin and urine creatinine were determined on the same instrument by enzymatic hexokinase, turbidimetric, immunoturbidimetric & kinetic Jaffe methods; respectively [26]. HbA1c was measured by turbidimetric inhibition immunoassay (TINIA) using COBAS INTEGTRA 400 plus machine; Roche Diagnostics. The final result was expressed as HbA1c percent and is calculated from the HbA1c/Hb ratio as follows: HbA1c (%) = (HbA1c/Hb) × 91.5 + 2.15 [27].

Primary endpoints were the changes in the fasting plasma glucose and HbA1c from baseline.

Secondary endpoints were the changes in BMI, blood pressure, heart rate,

eGFR, serum creatinine, and plasma lipids from baseline.

Statistical analysis

Sample size

Based on the AWARD-6 non-inferiority trial, group sample sizes of 20 patients with type 2 diabetes for Dulaglutide arm and another 20 patients for Liraglutide arm achieve 82% power to detect non-inferiority using a one-sided, two-sample t-test. The margin of non-inferiority is -0.6. The true difference between the means is assumed to be 0.1. The significance level (alpha) of the test is 0.050. The data were drawn from populations with standard deviations of 0.8 and 0.8. Sample size was calculated by PASS 15 Power Analysis and Sample Size Software (2017). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass [28].

Data were entered and analyzed using IBM-SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) Qualitative data were expressed as frequency and percentage and compared by Chi-Square test. Quantitative data were initially tested for normality using Kolmogorov-Smirnov and Shapiro-Wilk's test with data being normally distributed if $p > 0.050$. Presence of significant outliers (extreme values) was tested for by examining boxplots. Quantitative data were expressed as mean ± standard deviation (SD) if normally distributed or median and interquartile range (IQR) if not. To compare quantitative data between two groups, Independent-Samples t-Test (normally distributed data) or its non-parametric equivalent; Mann-Whitney U test (non-normally distributed data) were used. The two-way repeated measures ANOVA was used to determine if there is a statistically significant interaction effect between two within-subjects' factors (drug type and time) on a continuous dependent variable (*i.e.*, FPG, HbA1c, etc.). As there was no two-way interaction for any of the study parameters, main effects of group and time were examined. For any of the used tests, results were considered as statistically significant if p value ≤ 0.050.

3. Results

This study was carried out on 54 cases; 16 males (29.63%) and 38 females (70.37%). Liraglutide (Lira) group consisted of 34 patients and Dulaglutide (Dula) group consisted of 20 patients with median age (IQR) of 57 (41 - 61) and 60 (54 - 63) years, respectively. Baseline characteristics did not differ between both groups (Table 1).

At 12 months of treatment, liraglutide significantly reduced FPG (11.3 ± 4 vs 7 ± 1.7 mml/l, $p < 0.001$) while the reduction with Dulaglutide was statistically insignificant (5.4 ± 3.5 vs 9.5 ± 5.4 mmol/l, $p = 0.053$). A significant reduction in HbA1c was noticed with both drugs (Lira 8.55 ± 1.6 vs7.18 ± 1.04; $p < 0.001$, Dula 8.84 ± 1.8 vs7.5 ± 0.79; $p = 0.007$). BMI significantly decreased (Lira 39.4 ± 6.4 vs 37.6 ± 6.7; $p < 0.001$, Dula 38.8 ± 6.9 vs 37.2 ± 6.6; $p = 0.004$). Dulaglutide resulted in a significant reduction in eGFR from baseline to 6-months to 12 months of treatment (123.6 ± 60 vs 105.5 ± 46.3 vs 104.9 ± 47.3, $p = 0.008$). Liraglutide reduced

Table 1. Baseline clinical and laboratory characteristics of the two groups.

Characteristic	Group		P value
	Liraglutide (n = 34)	Dulaglutide (n = 20)	
Age (years)	57 (41 - 61)	60 (54 - 63)	0.113
Sex: Male: Female:	8 (23.5%) 26 (76.5%)	8 (40%) 12 (60%)	0.201
Weight (kg)	102.6 ± 18.3	100 ± 20.6	0.319
BMI (kg/m^2)	39 ± 6.3	38.8 ± 6.9	0.402
SBP (mmHg)	127.8 ± 13.3	127.4 ± 20.1	0.934
DBP (mmHg)	75.6 ± 7.8	74 ± 8.6	0.467
Pulse (bpm)	81.9 ± 11.3	86.5 ± 14	0.198
FPG (mmol/L)	10.8 ± 3.9	12.8 ± 4.9	0.281
HbA1C %	8.5 ± 1.6	8.6 ± 1.8	0.821
Serum Cr (mmol/L)	78.3 ± 23.5	79.8 ± 17.6	0.857
eGFR (ml/min/1.73m^2)	116 (96 - 150)	103.7 (85.8 - 127)	0.352
BUN (mmol/L)	5.8 ± 2.2	8.1 ± 3.9	0.217
ACR (mg/gm)	9.4 (5.5 - 39.4)	9.2 (8.5 - 20.4)	0.765
T-C (mmol/L)	4.3 ± 0.9	4.4 ± 1.97	0.946
LDL-C (mmol/L)	2.4 ± 0.85	2.8 ± 1.46	0.616
HDL-C (mmol/L)	1.3 ± 0.3	1.4 ± 0.3	0.638
TG (mmol/L)	1.5 ± 0.6	1.6 ± 0.98	0.872

Abbreviations: BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycosylated Haemoglobin, eGFR: estimated glomerular filtration rate, BUN: blood urea nitrogrn, T-C: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TG: triglycerides.

blood urea nitrogen (BUN) (p = 0.019) but did not affect the eGFR (p = 0.54). Neither liraglutide nor dulaglutide showed significant effects on blood pressure, heart rate, lipid profile or serum creatinine (Table 2, Figure 1).

Table 3 shows no statistically significant two-way interaction between within-subjects' factors (time and group) on all studied continuous dependent variables (BMI, FPG, HbA1c, BUN and eGFR). So, main effects of group and time were presented. For group, there were statistically significant differences for BMI (lower in dulaglutide vs liraglutide) and eGFR (lower in dulaglutide vs liraglutide). Estimated marginal means for BMI and eGFR in dulaglutide vs liraglutide were 33.4 vs 39.3 kg/m^2 and 111.3 vs 149 ml/min/1.73 m^2). For time, there was statistically significant difference between baseline reading and readings at 6 months and 12 months for BMI, FPG, HbA1c and e GFR but not for BUN. The difference was statistically significant between baseline reading and both 6-month and 12-month readings but not between the 6-month and 12-month readings for BMI and eGFR. The difference was statistically significant between

baseline and 6-month readings only for FPG. The test was statistically significant between baseline and 12-month readings only for HbA1c. Dulaglutide was more effective in reduction of BMI.

Table 2. Changes in clinical and biochemical variables at 6-month and 12-month of treatment with both medications.

Measurement	Liraglutide group				Dulaglutide group			
	Baseline	6-months	12-months	P value	Baseline	6-months	12-months	P value
BMI (kg/m^2)	39.4 ± 6.4	38.3 ± 6.5	37.6 ± 6.7	**<0.0005**	38.8 ± 6.8	37.9 ± 6.5	37.2 ± 6.6	**0.004**
SBP (mmHg)	128.9 ± 13.1	125.6 ± 12.9	123.3 ± 13.5	0.147	127.4 ± 20.1	129.1 ± 13.2	125.1 ± 15.7	0.625
DBP (mmHg)	75.5 ± 8.1	76.6 ± 9	77.5 ± 8.4	0.522	74 ± 1.9	76.5 ± 1.6	73.1 ± 2.1	0.292
Pulse (bpm)	82.3 ± 10.6	85.7 ± 11.8	82.7 ± 11.4	0.332	86.5 ± 14	89.6 ± 14.1	87.9 ± 11.6	0.495
RPP	10629 ± 1487	10800 ± 1949	10278 ± 1860	0.396	11049 ± 2629	11507 ± 1866	11003 ± 2066	0.480
FPG (mmol/l)	11.3 ± 4	8.7 ± 3.5	7 ± 1.7	**<0.001**	15.4 ± 3.5	10.1 ± 5.3	9.5 ± 5.4	0.053
HbA1C %	8.55 ± 1.6	7.98 ± 1.6	7.18 ± 1.04	**<0.001**	8.84 ± 1.8	8.23 ± 1.5	7.5 ± 0.79	**0.007**
Serum Cr (mmol/l)	76.95 ± 23.8	73.62 ± 17.8	74.14 ± 21.0	0.425	79.75 ± 17.6	86.5 ± 20.4	85.75 ± 19.8	0.086
BUN (mmol/dl)	6.76 ± 1.8	6.86 ± 1.7	5.14 ± 1.6	**0.019**	8.5 ± 4.4	7.2 ± 2	5.4 ± 0.7	0.368
eGFR (ml/min/1.73m^2)	125.3 ± 45.9	122 ± 40.2	120.4 ± 38.2	0.540	123.6 ± 60	105.5 ± 46.3	104.9 ± 47.3	**0.008**
ACR (mg/gm)	35.6 ± 57.5	-	42.8 ± 60	0.232	31.6 ± 52.6	-	33.2 ± 61	0.677
T-C (mmol/l)	4.38 ± 0.93	-	4.01 ± 0.74	0.241	3.7 ± 2.3	-	3.2 ± 1.3	0.558
LDL-C (mmol/l)	2.53 ± 0.88	-	2.37 ± 0.72	0.645	1.99 ± 1.82	-	1.57 ± 0.86	0.557
HDL-C (mmol/l)	1.28 ± 0.34	-	1.27 ± 0.37	0.916	1.21 ± 0.3	-	1.17 ± 0.24	0.373
TG (mmol/l)	1.6 ± 0.6	-	1.5 ± 0.5	0.499	1.3 ± 0.9	-	1.7 ± 1.1	0.293

Abbreviations: bpm: beat per minute, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, RPP: rate pressure product, FPG: fasting plasma glucose, HbA1c: glycosylated Haemoglobin, eGFR: estimated glomerular filtration rate, Serum Cr: serum creatinine, BUN: blood urea nitrogen, ACR: albumin creatinine ratio, T-C: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TG: triglycerides.
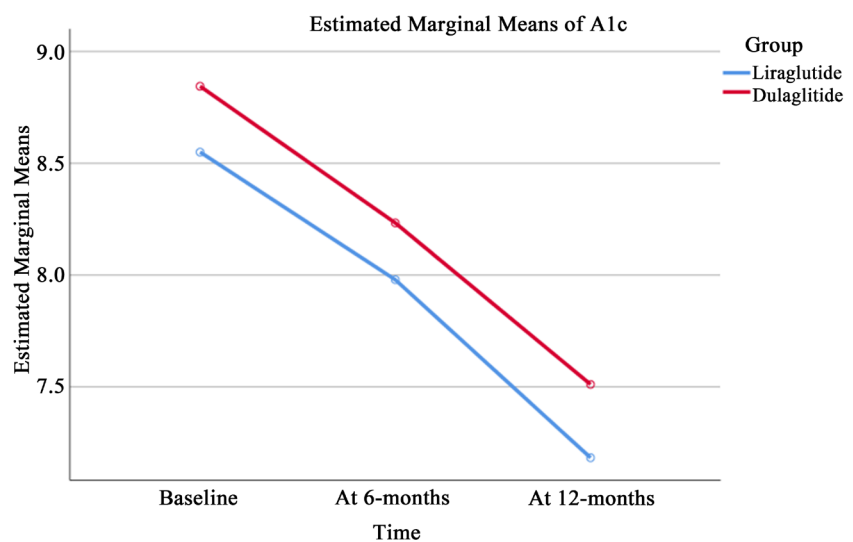

Figure 1. Reduction of HbA1c in both groups, dulaglutide and liraglutide, over one year.

Table 3. The interaction between time and group for any of the studied variables.

Parameter	Interaction: Time*Group			Main effect: Group			Main effect: Time		
	F	P	Partial η^2	F	P	Partial η^2	F	P	Partial η^2
BMI kg/m²	2.669	0.088	0.057	4.901	**0.045**	0.274	21.372	**<0.0005**	0.327
FPG mmol/l	1.310	0.282	0.086	0.976	0.504	0.194	19.150	**<0.0005**	0.578
HbA1c %	0.012	0.988	0.000	0.225	0.650	0.031	16.664	**<0.0005**	0.350
BUN mmol/dl	0.552	0.590	0.084	1.278	0.376	0.190	4.629	**0.032**	0.435
eGFR ml/min/1.73 m²	1.990	0.164	0.066	49.043	**<0.0005**	0.860	4.953	**0.024**	0.150

Abbreviations: bpm: beat per minute, BMI: body mass index, FPG: fasting plasma glucose, HbA1c: glycosylated Haemoglobin, eGFR: estimated glomerular filtration rate, BUN: blood urea nitrogen.

4. Discussion

In accordance with clinical guidelines, GLP-1 analogues are not currently considered first-line therapy for type 2 diabetes mellitus. They are, however, considered as second-line therapy in combination with oral antidiabetic drugs or insulin [11].

GLP-1 analogues lower both fasting and postprandial plasma glucose, and each formulation differs in the extent to which it lowers the glucose level. Short-acting analogues predominantly lower the postprandial plasma glucose mainly by delaying gastric emptying while long-acting analogues such as liraglutide and dulaglutide lower both fasting and postprandial plasma glucose by increasing insulin and reducing glucagon secretion. They differ in terms of their formulations, indications (monotherapy and/or combined therapy), injection devices, dosages, precautions and use in special patient populations. These agents also differ in terms of their effects on CV risk factors and GI tolerability [29] [30].

Across the AWARD studies, dulaglutide demonstrated a significant improvement in glycaemic control irrespective of gender, duration of diabetes, or baseline HbA1c. Dulaglutide was well tolerated, with a safety profile similar to other GLP-1 analogues [31] [32]. In another study, dulaglutide significantly reduced HbA1c regardless of β-cell function, HbA1c, or BMI at baseline [33] [34] [35]. This was evident in several other studies with other GLP1 analogues including liraglutide [36] [37] which indicates that GLP1 analogues can be effective in patients with long duration of diabetes. Mean duration of diabetes in our study population was 11.76 ± 5.79 years indicating the effectiveness of the studied GLP-1 analogues in patients with long duration of diabetes (Table 1).

The average reduction of HbA1c by GLP-1 analogues is approximately 1% - 1.5% as demonstrated in several studies and meta-analyses [38] [39]. In our study the mean reduction of HbA1c with dulaglutide 1.5 mg was 1.0% (0.25% - 2.65%) and 1.25% (0.625% to 2.1%) with liraglutide after one year of treatment (Table 2, Figure 1).

Some studies demonstrated that both dulaglutide and liraglutide have comparable HbA1c reduction but weight loss is greater with liraglutide [11] [40] [41].

In a retrospective study in Indian patients with type 2 diabetes, patients poorly controlled with metformin and sodium glucose transporter-2 inhibitors (SGLT-2i), liraglutide was found to lower HbA1c by 0.9% to 1.5% whereas dulaglutide lowered HbA1c by 0.9% to 1%, both in a dose-dependent fashion after 12 months of treatment [42] [43] [44] [45] [46]. This is comparable to our reports in the current study.

In his study, Ghosal *et al.* [47], reported comparable metabolic effects of both dulaglutide and liraglutide as regard to HbA1c, FPG and BMI. In a study of Japanese type 2 diabetes patients, dulaglutide was superior to liraglutide in glycemic control and comparable to it in reduction of body weight [48].

In Grunberger's study, body-weight reduction with dulaglutide was dose-dependent but was not significant when compared to placebo and was not associated with a significant change of blood pressure [5].

In our study, dulaglutide was more effective than liraglutide in reduction of BMI (Table 3).

Some studies also demonstrated that GLP-1 analogues have positive chronotropic effect by increasing the heart rate [49] [50] [51]. In several reviews, meta-analyses and studies including LEAD studies, liraglutide reduced SBP by 2 to 6 mm Hg with a small (2 - 4 bpm) increase in heart rate [14] [45] [46]. In Ghosal's study, only liraglutide was associated with a significant reduction in systolic blood pressure (10.23 ± 2.36 mm of Hg; p < 0.001) while dulaglutide did not show a significant effect [47]. Blood pressure effects of GLP-1 analogues were found to be independent of weight loss or concomitant antihypertensive medications [52]. Dulaglutide 1.5 mg was also reported to significantly reduce the mean 24-hour SBP at 16 and 26 weeks when compared with placebo [50] [51] [53].

However, none of the trials was conducted to specifically evaluate the effects of GLP-1 analogues on blood pressure. Interestingly in those studies, GLP-1 analogues did not reduce BP in normotensive subjects [50] [51].

In our study no reduction of blood pressure or change in heart rate was observed in patients treated with either liraglutide or dulaglutide (Table 2).

In the AWARD-10 study, a modest reduction in LDL-C was noticed with dulaglutide [31]. In another study, liraglutide improved total cholesterol, LDL-C and triglycerides. Total cholesterol levels decreased from baseline by 0.13 mmol/L, and Low-density by 0.20 mmol/L [54].

In our study, neither liraglutide nor dulaglutide had an effect on the measured serum lipids; total cholesterol, LDL-C, HDL-C or triglycerides. Similar to our study, Peradze *et al* did not find a significant effect of liraglutide on plasma lipids. No significant change was noticed in HDL-C, LDL-C or triglycerides [55].

A meta-analysis of large outcome trials of people with type 2 diabetes, reported that plasma glucose control reduced the hazard of renal outcomes by 20% [56] [57].

In our study, there was a significant reduction of eGFR with dulaglutide. Our

patients had baseline eGFR with a mean value of 123.6 ± 60 ml/min/1.73m^2 that was reduced to 104.9 ± 47.3 ml/min/1.73m^2. In short-term studies, it was found that dulaglutide did not change eGFR in type 2 diabetes patients with normal kidney function. It reduced microalbuminuria in patients with chronic kidney disease and eGFR of 38.3 ± 12.8 mL/min/1.73m^2 who had urine albumin-to-creatinine ratio > 300 mg/g with less decline in eGFR [58]. However, the effect of dulaglutide on HbA1c cannot account for all of its effect on the renal outcome. Absence of any effect of dulaglutide on the eGFR during the first year of therapy in some studies suggests that this is an unlikely mechanism [59] [60].

Noteworthy mentioning that none of our patients had microalbuminuria or low eGFR. Instead, the mean eGFR was more than 120 ml/min/1.73m^2 and with reduction it reached a mean that was within the range of normal eGFR and at the same time no change or elevation of serum creatinine was noticed. This observation may support the renal protective effect of dulaglutide as the high eGFR at the start of the study may indicate early involvement of the kidney in diabetic nephropathy characterized by hyperfiltration [61].

Liraglutide did not show a significant effect on eGFR or serum creatinine (Table 2).

Limitations of our study are the retrospective analysis, the small number of patients and lack of a placebo group.

5. Conclusion

We conclude that both dulaglutide and liraglutide have significant and comparable glycemic control in Emirati patients with diabetes mellitus. Dulaglutide significantly reduces eGFR in patients with mean eGFR above normal which may indicate a renoprotective effect in early incipient stages of nephropathy with hyperfiltration and elevated eGFR. Dulaglutide produces more reduction of BMI in comparison with liraglutide. Liraglutide produces significant reduction of fasting plasma glucose while the reduction induced by dulaglutide is statistically insignificant.

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Conflicts of Interest

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

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