Int J Clin Exp Med 2021;14(10):2435-2445
www.ijcem.com /ISSN:1940-5901/IJCEM0133065

Original Article

Relationship between exposure to liraglutide and weight loss: a cross-sectional study in Riyadh, Saudi Arabia

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Received March 12, 2021; Accepted October 13, 2021; Epub October 15, 2021; Published October 30, 2021

Abstract: Liraglutide treatments have recently been approved for obese diabetic and prediabetic patients. This study aimed to investigate the relationship between liraglutide and weight loss of these patients. This cross-sectional study was conducted at the King Khalid University Hospital outpatient clinics. The participants were over 18 years old, treated with 1.8 mg liraglutide (Victoza®, Novo Nordisk, Bagsvaerd, Denmark) daily over a 12-month period. Patients' data were extracted from electronic medical records. Body weight after 12 months of liraglutide treatment was evaluated to determine the relationship between the exposure to this drug and the changes in body weight. Glucose control parameters, blood pressure, and lipid profiles were measured and compared at baseline and a year after treatment. A multiple regression model was used to eliminate any effects of potential confounders (sex-, age-, ethnicity- and weight-related clinical variables). Sixty-eight patients were included with the majority were diabetic treated with antidiabetic medications. Significant decrease was seen in the mean body weight (delta from baseline) -3.82 ± 5.17 kg ($P < 0.001$), body mass index -1.41 ± 1.90 kg ($P < 0.001$), levels of glycated hemoglobin -0.58 ± 1.82% ($P < 0.014$), total cholesterol -0.38 ± 0.67 mmol/L ($P < 0.001$) and low-density lipoprotein -0.33 ± 0.65 mmol/L ($P < 0.001$). The results supported that liraglutide was associated with weight reduction as well as other metabolic parameters in the patients attended King Khalid University Hospital.

Keywords: Glucagon-like peptide 1, liraglutide, Victoza, weight loss, obesity, diabetes

Introduction

Obesity is a chronic, multifactorial disease, affecting over 1.1 billion individuals around the globe [1]. The World Health Organization (WHO) has defined obesity as an abnormal accumulation of fatty tissue in excessive amounts. It can be measured as body mass index (BMI), with a BMI of 30.0 kg/m^2 or above is considered obese [2]. Obesity can be influenced by genetic, cultural, environmental, socioeconomic, pharmacological, and psychological factors [3].

According to the data of the USA Centers for Disease Control and Prevention (CDC) in 2016 [4], around 40% of American adults are obese. In the Kingdom of Saudi Arabia (KSA), overweight and obesity affect more than 60% of the total population [5].

Obesity is considered a key risk factor for many diseases including sleep apnea, some types of cancers and cardiovascular diseases (CVD), which cover coronary heart disease, hypertension, dyslipidemia, and type 2 diabetes (T2D) [6]. The correlation of BMI with blood glucose, blood pressure (BP), and level of blood lipid was confirmed in previous studies [7-9]. It has been shown that with each unit increase of BMI above the 22 kg/m^2, the risk of developing coronary heart disease and T2D increased by 14%, and 12.1%, respectively. Similarly, there is a risk of increasing the overall BP level by 0.8 to 1.7 mmHg [6, 10, 11]. Treatment of obesity and its associated comorbidities is a significant economic burden on health care systems [12]. The global economic impact of obesity was estimated to be two trillion US dollars in 2014 [13].

In developed countries, obesity alone may cost 2-7% of all health care budget [14].

Management of obesity involves intensive lifestyle interventions, bariatric surgeries, and pharmacological interventions [15]. Lifestyle interventions are considered the first line in the management plan and can cause a clinically significant weight loss (≥5%). However, the relapse rate is high. More than half of the patients regain their lost weight within a year [16]. On the other hand, surgical interventions can cause dramatic weight loss and significant improvement in all other comorbidities. However, the invasive nature of this type of intervention, patient preferences, and lack of resources can limit its utility [17]. Most of the published guidelines from stringent entities recommend pharmacotherapy as the second line of obesity management [18-20]. Liraglutide is one of the pharmacological treatments for obesity, which is administered as a subcutaneous injection once daily. It is a glucagon-like-peptide-1 (GLP-1) receptor agonist [21]. As an antidiabetic medication, liraglutide regulates glucose metabolism in a dose varing between 1.2 mg to 1.8 mg (Victoza®; Novo Nordisk). Meanwhile, liraglutide can be used for weight reduction at higher doses (Saxenda®, Novo Nordisk) [22], leading to reduction of energy intake and suppression of appetite [23]. Because of this dual effects, it is mainly used to manage obese diabetic patients [24]. There is a meta-analysis of 28 randomized control trials (RCTs) that compared five anti-obesity medications in the USA in terms of effectiveness, and liraglutide showed the highest efficiency causing ≥5% weight loss when compared with a placebo [25].

Liraglutide injection has shown to be an effective and tolerable medication and changes the weight-related comorbidities and the quality of life [26-28]. However, there is a lack of literature about liraglutide in different ethnic groups. Studies in the Japanese population showed that liraglutide monotherapy resulted in a significant reduction of body weight [29]. On the contrary, when co-administered with other oral antidiabetic agents, no change in body weight was observed [30]. A study on the Emirati population [31], showed a mean weight reduction of 2.5 kg, which was less than that observed in the RCTs [32]. However, these studies were either on a non-therapeutic dose (≤1.2 mg) or a short follow-up period (≤12 months). Among the Saudi population, there were two recent cohort studies about the effects of liraglutide treatment among diabetic obese patients [33, 34]. The result are quite different in terms of weight loss in comparison with the baseline values after 12 months of treatment, although both studies were either underpowered with a low sample size or had a short follow-up period.

The prevalence of obesity is rising at an alarming rate in KSA [35]. Studies among the Saudi population in a real clinical practice were limited and with conflicting findings. The present study aims to address the relationship between liraglutide and changes in body weight among the Saudi Arabia population.

Material and methods

Study design and setting

A cross-sectional study was conducted at KKUH, one of the largest tertiary teaching hospitals with a 1,200-bed capacity located in Riyadh, Saudi Arabia. The patient population is comprised of citizens and legal residents, who live in the capital city, Riyadh. Moreover, it serves as a referral hospital for all of the KSA.

Study population

The study population included adult patients (≥18 years old), who attended KKUH outpatient clinics and were prescribed an 1.8 mg liraglutide (Victoza®, Novo Nordisk) daily for over 12 months. The main exposure of the study was treatment with 1.8 mg liraglutide over 12 months. These patients were obese with uncontrolled hyperglycemia. The main outcome of the study was the mean change in body weight (kg) since commencing the drug. The weight and height measurements at baseline and after 12 months from the index date were required for each eligible patient. There were no strict exclusion criteria except gestational diabetes patients, type 1 diabetes patients or any patients who underwent any type of bariatric surgery (i.e. gastric sleeve, gastric bypass, gastric balloon, and gastric band).

Data sources

Data was extracted from the electronic medical records (EMRs) for all patients on liraglutide

(1329 patients) attending outpatient clinics at KKUH between September 2015 and October 2019; then collated by the primary author in an Excel datasheet. Data was crosschecked to ensure quality. Since all the study data were from the EMRs, there was no direct involvement of any patients in the study; the individual patient's informed consent was not required because of the anonymized nature of patient records. However, patient confidentiality was maintained. This study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines. The institutional review board (IRB) at KKUH (IRB number: E-19-3888) approved this study.

Measurements

Study variables

The variables at baseline were demographic data, which includes age, sex, and nationality. The date of the first prescription of liraglutide and duration of the treatment were documented. Clinical characteristics were recorded at baseline and after 12-month follow-up visits. These variables include anthropometric parameters and cardiovascular (CV) risk factors. We also recorded the concomitant use of medications that affect body weight, including insulin and Metformin (antidiabetic medications), and Orlistat, a medication approved for weight loss. In addition, diagnosis of T2D and hypothyroidism were recorded. Other chronic comorbidities, including hypertension and dyslipidemia were not considered. Baseline measurements for individuals were determined as the closest value from the index date measured (within 14 days before the index date to up to 7 days after).

Anthropometric parameters

Body weight was recorded in kg and height in cm. BMI was calculated as kg/m^2 and we grouped the participants according to their BMI; overweight if BMI was 25-29.9 kg/m^2, obese class I if BMI was 30-34.9 kg/m^2, obese class II if BMI was 35-39.9 kg/m^2 and obese class III if BMI was ≥40 kg/m^2.

Cardiovascular risk factors

Data about common CV risk factors including T2D, BP, and lipid profile were collected. In addition to the diagnosis of T2D, glucose control measurements included glycated hemoglobin (HbA1c), random blood glucose (RBG), and fasting plasma glucose (FPG) levels. Other CV risk factor measurements, including systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and triglycerides (TG) were collected.

Outcome variables

Difference in weight

Primary outcome: Weight loss. The main outcome investigated in this study was the weight change among recruited patients. The body weight after 12 months of commencing liraglutide treatment was used to examine the relationship between the exposure to this drug and the change in body weight. It was also used to calculate the mean weight change, percentage of body weight lost and proportions of patients achieving ≥5% reduction in body weight since commencing liraglutide.

Secondary outcome: We calculated the mean and mean difference (delta from baseline) for glucose control parameters and CV risk factors. Then we assessed the differences between males and females in terms of weight loss and the other parameters.

Statistical analysis

The results were presented as mean ± standard deviation (SD) for continuous variables and as numbers and percentages for categorical variables. Male and female characteristics were compared at the baseline using an independent sample t-test for continuous variables and the Chi-square test for categorical variables. Comparisons were performed to study the differences between baseline visits and 12-month visits using the paired Student's t test. The percentage of body weight lost was computed as mean weight loss/baseline weight * 100. Mean weight reduction between males and females was compared using the independent sample t-test. For cross-sectional associations, multiple linear regression models were used to assess the associations between weight loss (dependent variable) and the exposure to 1.8 mg liraglutide. The model was adjusted for the possible confounders sex, age,

Table 1. Baseline characteristics for participants before commencing liraglutide

Measurements	Total (n = 68)	Males (n = 31)	Females (n = 37)	*p*-value
Age (years)	54.41 ± 9.48	52.58 ± 8.5	55.94 ± 10.08	0.146
Ethnicity	n (%)	n (%)	n (%)	
Saudi	55 (80.90%)	25 (80.60%)	30 (81.10%)	0.964
Non-Saudi	13 (19.10%)	6 (19.40%)	7 (18.90%)	
Height (cm)	165.34 ± 11.12	173.33 ± 7.65	158.65 ± 8.97	< 0.001
Body weight (kg)	107.78 ± 21.26	114.58 ± 18.53	102.08 ± 21.96	0.015
BMI (kg/m^2)	39.51 ± 7.33	38.15 ± 5.78	40.65 ± 8.32	0.164
BMI groups	n (%)	n (%)	n (%)	
27-29.9: overweight	6 (8.8%)	1 (3.2%)	5 (13.5%)	0.030
30-34.9: obese class I	13 (19.1%)	9 (29%)	4 (10.8%)	
35-39.9: obese class II	18 (26.5%)	11 (35.5%)	7 (18.9%)	
≥40: obese class III	31 (45.6%)	10 (32.3%)	21 (56.8%)	
Cardiovascular risk factors				
Hba1c (%)	8.54 ± 1.97	8.56 ± 1.69	8.53 ± 2.2	0.954
RBG (mmol/L)	9.21 ± 3.77	9.24 ± 3.22	9.18 ± 4.25	0.947
FPG (mmol/L)	9.71 ± 3.22	10.04 ± 2.95	9.54 ± 3.46	0.770
Systolic BP (mmHg)	133.73 ± 14.26	131.32 ± 11.62	135.75 ± 16.01	0.204
Diastolic BP (mmHg)	76.20 ± 9.04	77.48 ± 9.47	75.13 ± 8.64	0.290
Total cholesterol (mmol/L)	4.89 ± 0.95	4.34 ± 0.78	4.61 ± 1.01	0.253
LDL cholesterol (mmol/L)	2.46 ± 0.89	2.38 ± 0.76	2.52 ± 1	0.513
HDL cholesterol (mmol/L)	1.20 ± 0.32	1.02 ± 0.19	1.36 ± 0.33	< 0.001
TG (mmol/L)	1.81 ± 0.93	2.06 ± 0.95	1.60 ± 0.87	0.045
Baseline comorbidities	n (%)	n (%)	n (%)	
T2D	59 (86.8%)	28 (90.3%)	31 (83.8%)	0.428
Hypothyroidism	7 (10.3%)	2 (6.5%)	5 (13.5%)	0.340
Baseline medications	n (%)	n (%)	n (%)	
Insulin	22 (32.4%)	9 (29%)	13 (35.1%)	0.592
Metformin	57 (83.8%)	27 (87.1%)	30 (81.1%)	0.502
Orlistat	3 (4.4%)	2 (6.5%)	1 (2.7%)	0.453

BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBG, random blood glucose; TG, triglycerides; T2D, type 2 diabetes. Data are means ± SD, unless otherwise noted.

nationality, and clinical variables, including medications, treatment, comorbidities, BMI, blood lipids, and blood sugar levels. *P*-values < 0.05 were considered statistically significant. Analyses were performed using SPSS software version 21 (IBM® SPSS® Statistics 21, Armonk, NY, USA).

Sample size

The sample size for this study was calculated to be 185 patients based on an estimated proportion of 33.3% of adult subjects expected to lose ≥5% from their baseline weight [36]; with a 5% margin of error and an 85% confidence interval. The sample size was calculated by the formula: $n = Z^2 [p(1-p)]/d^2$ where, n = Sample size; Z-score = 1.44 for confidence level 85%; P = expected proportion (percentage of body weight loss); d = precision (margin of error). Substituting the above values: $N = (1.44)^2 [0.333(1-0.333)]/0.05^2 = 185$ patients with only 80 medical records were reviewed and 68 eligible participants.

Results

Subjects characteristics

The baseline demographics and clinical characteristics of the 68 participants are shown in **Table 1**. The mean age of the participants was

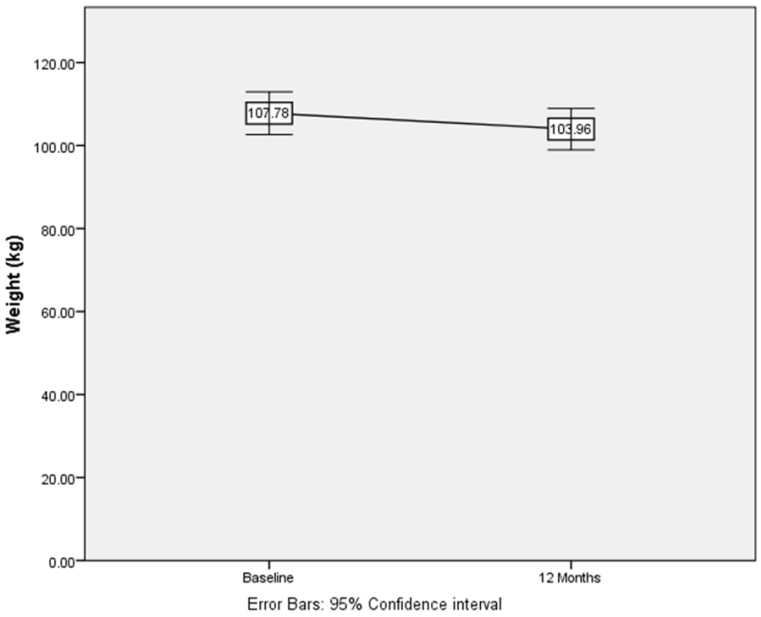

Figure 1. Mean weight at baseline and after 12 months of treatment with liraglutide (P < 0.001).

54.41 ± 9.48 years and mean body weight was 107.78 ± 21.26 kg with a BMI of 39.51 ± 7.33 kg/m^2. The study sample included almost the same number of males and females of similar ages. The majority were Saudis representing about 81% of the study population. In addition, most of the participants were diabetic (86.8%) with a mean HbA1c level of 8.54 ± 1.97%, FPG 9.71 ± 3.22 mmol/L, and RBG 9.21 ± 3.77 mmol/L. Baseline systolic blood pressure (SBP) and diastolic blood pressure (DBP) were 133.73 ± 14.26 mmHg and 76.2 ± 9.04 mmHg, respectively. Before initiating liraglutide, 10.3% of the patients had hypothyroidism, most of the patients were concomitantly treated with Metformin (83.8%), and a lower proportion of patients were concomitantly treated with insulin (32.4%) and Orlistat (4.4%). At baseline, there were statistically significant differences between males and females in height (P < 0.001), body weight (P < 0.015), distribution of study subjects between BMI categories (P < 0.030), and HDL levels (P < 0.001).

Changes in body weight and other related factors

The progression of body weight, from baseline to 12 months after commencing liraglutide is shown in **Figure 1**. **Table 2** shows changes in all clinical parameters as delta from baseline. Pairwise comparisons showed significant reductions in body weight (-3.82 ± 5.17 kg, P < 0.001) and BMI (-1.41 ± 1.90 kg/m^2, P < 0.001). The weight loss (Δ weight) in male and female participants was -4.36 ± 5.22 kg and -3.36 ± 5.15 kg (P < 0.431), respectively. Approximately a third of the study participants reduced ≥5% of their initial body weight.

The CV risk factors showed a similar pattern. There was a significant reduction in the blood markers of T2D among patients using liraglutide. HbA1c reduced by -0.58 ± 1.82% (P < 0.014) and FPG by -2.46 ± 1.38 mmol/L (P < 0.037); although there was reduction in the level of RBG, it did not reach statistical significance (-1.03 ± 4.19 mmol/L, P < 0.67). Concurrently, decreases were observed in the means of CV parameters; SBP -2.03± 15.7 mmHg (P < 0.298), DBP -1.06 ± 10.39 mmHg (P < 0.410), total cholesterol -0.38 ± 0.67 mmol/L (P < 0.001), LDL cholesterol -0.33 ± 0.65 mmol/L (P < 0.001), HDL cholesterol -0.01 ± 0.18 mmol/L (P < 0.730), and triglycerides -0.09 ± 0.76 mmol/L (P < 0.385) (**Table 2**). However, the observed reductions did not reach statistical significance except in total cholesterol and LDL. Similarly, there was no statistically significant difference between males and females for weight reduction (**Figure 2**).

Correlation of body weight with other metabolic factors

Multiple regression analysis was performed to examine whether baseline characteristics have an independent effect on body weight reduction (**Table 3**). Possible confounders including sex, nationality, age, comorbidities, concomitant use of medications, and initial weight, BMI, HbA1c, total cholesterol, and LDL were adjusted. The overall regression model was not significant. The 13 parameters together explained 21.5% of the variance of weight loss (F (13.52) = 1.07, P = 0.401, R^2 = 0. 215). The decline of weight from baseline to 12 months was posi-

Table 2. Variations in clinical parameters after 12-month liraglutide treatment initiation

	Mean ± SD	Delta from Baseline, (Mean ± SD)	*p*-value compared with baseline	Males		Females		*p*-value
				Mean ± SD	Delta from Baseline (Mean ± SD)	Mean ± SD	Delta from Baseline, (Mean ± SD)	
Weight (kg)	103.96 ± 20.70	-3.82 ± 5.17	< 0.001	110.21 ± 18.13	-4.36 ± 5.22	98.72 ± 21.49	-3.36 ± 5.15	0.431
BMI (kg/m^2)	38.12 ± 7.13	-1.41 ± 1.90	< 0.001	36.69 ± 5.647	-1.46 ± 1.81	39.29 ± 8.06	-1.36 ± 2.00	0.831
HbA1c (%)	8.05 ± 2.06	-0.58 ± 1.82	< 0.014	7.90 ± 1.72	-0.61 ± 1.96	8.19 ± 2.34	-0.559 ± 1.71	0.903
FPG (mmol/L)	7.95 ± 1.24	-2.46 ± 1.38	< 0.037	11.56 ± 6.86	-0.92 ± 1.10	8.13 ± 1.44	-2.97 ± 1.12	0.255
RBG (mmol/L)	8.06 ± 3.71	-1.03 ± 4.19	0.671	8.35 ± 3.70	-0.63 ± 3.64	7.83 ± 3.74	-1.37 ± 4.64	0.513
Systolic BP (mmHg)	131.64 ± 15.09	-2.03 ± 15.7	0.298	130.33 ± 15.16	-0.76 ± 13.79	132.72 ± 15.16	-3.08 ± 17.26	0.555
Diastolic BP (mmHg)	74.91 ± 10.61	-1.06 ± 10.39	0.410	77.17 ± 10.62	-0.2 ± 10.60	73.03 ± 10.37	-1.77 ± 10.3	0.543
Total cholesterol (mmol/L)	4.06 ± 0.81	-0.38 ± 0.67	< 0.001	3.91 ± 0.81	-0.41 ± 0.60	4.20 ± 0.80	-0.36 ± 0.74	0.769
LDL (mmol/L)	2.10 ± 0.81	-0.33 ± 0.65	< 0.001	1.97 ± 0.78	-0.39 ± 0.65	2.22 ± 0.82	-0.26 ± 0.65	0.432
HDL (mmol/L)	1.2 ± 0.31	-0.01 ± 0.18	0.730	1.03 ± 0.19	0 ± 0.12	1.35 ± 0.32	-0.016 ± 0.23	0.726
TG (mmol/L)	1.68 ± 1.09	-0.09 ± 0.76	0.385	1.99 ± 1.39	-0.028 ± 0.98	1.37 ± 0.57	-0.14 ± 0.46	0.566

BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; RBG, random blood glucose; SD, standard deviation; TG, triglycerides.

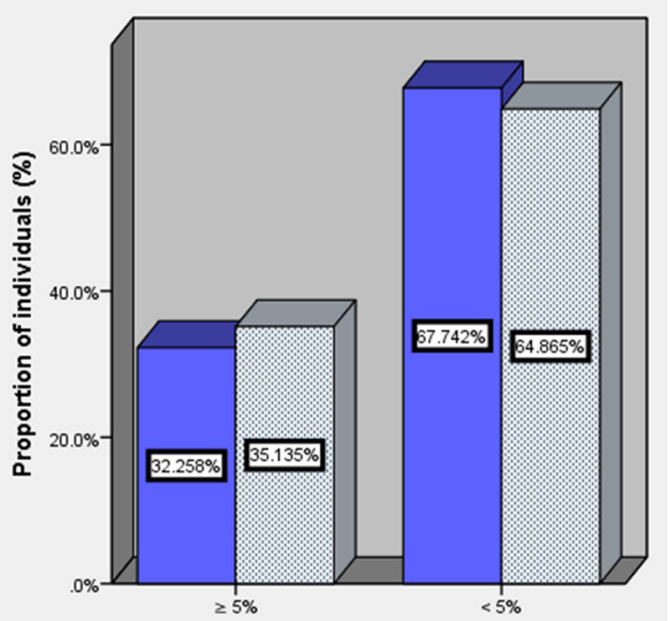

Figure 2. Proportion of participants who lost > 5% weight (P < 0.803).

tively correlated with the patients' baseline weight, age, levels of triglycerides, and negatively correlated with baseline BMI, Hba1c, and LDL levels.

The relative changes in body weight and HbA1c from baseline to month 12 after liraglutide initiation are represented as scatterplots in **Figure 3**. Overall, the majority of the study subjects were located in the lower left quadrant, i.e. body weight and HbA1c decreased for these individuals.

Discussion

In this cross-sectional study, we explored the relationship between exposure to 1.8 mg liraglutide per day and weight loss over a 12-month period among KKUH patients. Our findings showed that liraglutide significantly reduced body weight, HbA1c, total cholesterol, and LDL. These results were similar to the results from the RCTs with minor variations with respect to the different study designs and settings [26].

Several studies observed weight reduction after one year treatment with liraglutide [37-39]. In these studies, the weight loss ranged from 2% (2.2 kg) to 6% (6.4 kg) depending on the dose of liraglutide. In our study, one year of treatment with liraglutide resulted in a significant reduction in body weight and BMI. Compared to the baseline, the mean body weight was significantly reduced by almost 4 kg (3.42%, P < 0.001). The health benefit of moderate weight loss among obese and overweight individuals, can be observed on the risk reduction of developing T2D [39]. An analysis done by Richard F. Hamman [40], reported that for every kg of weight lost, there was a 16% reduction in risk of developing T2D among patients with impaired glucose tolerance. Furthermore, a large RCT conducted as part of the Diabetes Prevention Program in the USA, showed that this proportion of weight reduction could reduce the incidence of T2D by 58% among Americans adults with impaired glucose tolerance [41].

As described previously in the literature, weight reduction has a significant impact on minimizing the risk of developing CVDs [42]. Treatment with liraglutide was associated with a significant reduction of SBP compared to the placebo (-2.68 mmHg, P < 0.02). On the contrary, DBP did not differ significantly (-0.19 mmHg, P < 0.81) [27]. In a recent study, 40 obese Italian patients reported a BP reduction. After 5 years of treatment with 1.8 mg liraglutide, the SBP and DBP decreased from 132.9 ± 15.9 mmHg to 127.5 ± 18.9 mmHg; P < 0.128 and 72.9 ± 9.2 mmHg to 72.2 ± 10.1 mmHg; P < 0.983, respectively [36]. This reduction in BP might be underestimated as most of the participants were older adults with coexisting CVDs, which are associated with arterial stiffening and subsequent high BP. Our finding was consistent with that of the Italian cohort. There was a reduction in both SBP and DBP compared to the baseline readings. Despite the reduction observed, it did not show a statistically significant difference. This variation could be explained by the small sample size and the fact that the participants were middle-aged adults with a mean baseline BP of 131.64/74.9 mmHg, which is considered a mild elevation

Table 3. Patient characteristics and clinical determinants of weight reduction using a multiple linear regression model*

Variables	β coefficient (95% CI)	*p*-value
Constant	-4.58 (-20.74 to 11.58)	0.572
Females	2.1 (-1.77 to 6.01)	0.279
Ethnicity (Saudi)	3.73 (7.35 to 0.10)	0.044
Weight (kg)	0.05 (-0.09 to 0.20)	0.456
Body mass index (kg/m^2)	-0.24 (-0.63 to 0.16)	0.233
Age (years)	0.04 (-0.12 to 0.19)	0.644
Glycated hemoglobin (HbA1c%)	-0.28 (-1.17 to 0.61)	0.528
Total cholesterol	0.88 (-2.72 to 4.47)	0.628
Low-density lipoprotein (mmol/L)	-0.87 (-4.78 to 3.04)	0.655
Type 2 diabetes	0.10 (-5.77 to 5.98)	0.972
Hypothyroidism	-0.41(-5.19 to 4.36)	0.862
Concomitant treatment with insulin	1.37 (-1.80 to 4.53)	0.390
Concomitant treatment with Metformin	-1.45 (-5.82 to 2.93)	0.509
Concomitant treatment with Orlistat	-4.64 (-11.04 to 1.77)	0.152

*Change in weight from baseline to 12 months of liraglutide treatment as the dependent variable. Adjusted R2 was 0.215.

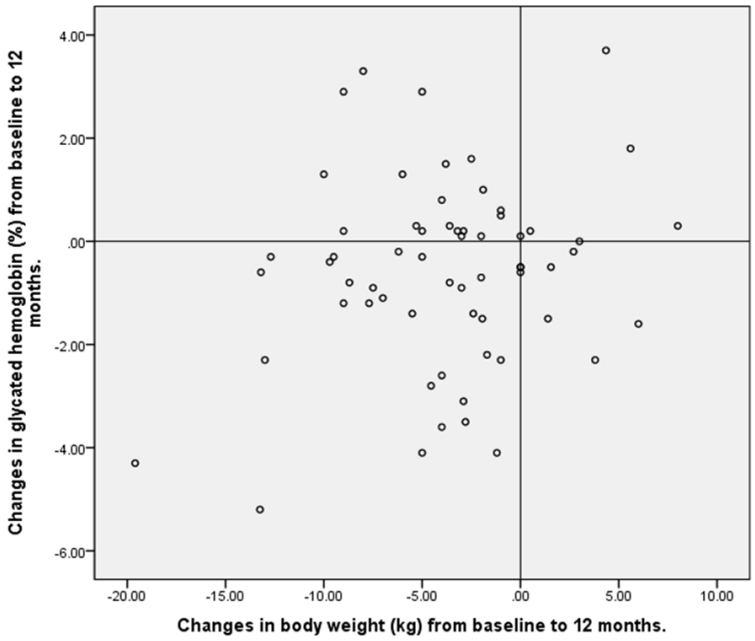

Figure 3. Scatterplot of changes in body weight (kg) and glycated hemoglobin (%).

[43], and possibly on antihypertensive medications.

Additional CV benefits of liraglutide that have been observed are improvement in the T2D and lipid profile. In a systemic review of 124 observational studies [44], they reported a data from baseline reduction in HbA1c (-0.6% to -2.26%) after treatment with liraglutide. While our finding was consistent with the lower limit reduction (-0.58%), this variation can be attributed to the high baseline level (8.54%) reported in our sample. However, a -0.58% reduction in HbA1c is considered clinically significant [45]. Treatment with 1.8 mg liraglutide was associated with improvement of the lipid profile. Significant reductions were observed in TG ($P < 0.001$) and total cholesterol ($P < 0.004$), and no significant changes were found in LDL and HDL cholesterol levels [46]. Another observational study found that after 12 months of treatment with liraglutide, the LDL cholesterol level was significantly reduced at 12 months, while HDL cholesterol tended to increase [47]. In our study, a significant change from baseline reduction was observed in the LDL and total cholesterol levels, -0.33 ± 0.65 mmol/L ($P < 0.001$) and -0.38 ± 0.67 mmol/L ($P < 0.001$), respectively. This difference could be partially explained by the small sample size; however, this finding could also be due to a normal lipid profile at the baseline [48].

In an exposure-response analysis of the Satiety and Clinical Adiposity - Liraglutide Evidence (SCALE) trials [49], it was revealed that liraglutide had gender-dependent influences on weight loss. On average, women had a greater reduction in body weight with liraglutide than men [50]. However, the authors attributed this difference to the dose variation, since a higher proportion of women compared to men were exposed to higher doses. In our study, all the participants were exposed to the same dosage, and as a result, we did not find a difference between them. Weight reduction after 12

months, glycemic control parameters, BP, and lipid profiles did not differ significantly among male and female patients.

We observed in the multiple regression analyses that concomitant treatment with Metformin, insulin, or Orlistat was not associated with a significant weight loss. On the contrary, the non-Saudis showed a significant positive correlation with weight reduction, although this might be explained partially by the small sample size, genetic and cultural variations [14]. Several studies among the Saudi community observed the high prevalence of socioeconomic risk factors that lead to the development of obesity [51, 52]. It can also be attributed to rapid urbanization in the last three decades that contributes to changes in eating and physical habits. A high fat and sugar diet with low physical activity leads to an increase in the prevalence of obesity among the Saudi population, which may eventually lead to CVD development [53].

Limitations and strengths of the study

This was an observational study representing actual clinical practice at KKUH and faced several limitations. The data was collected from EMRs and could be exposed to documentation errors. Lack of complete information in some patients' files limited us from recording diagnoses of hypertension and dyslipidemia, and other concomitant medications. We did not measure any safety profile or adherence to this medication. Due to the small sample size and the fact that it is a single center study where liraglutide is only prescribed by endocrinologists, we cannot generalize our findings to the Saudi population.

Conclusion

Liraglutide shows several beneficial effects including a reduction in body weight, improvement in glycemic control and a reduction in BP, LDL, and total cholesterol. Liraglutide and other GLP-1 agonists are promising treatments in the management of obese and overweight patients, especially diabetics.

Acknowledgements

We would like to thank our family and friends. Special thanks for support by the College of Medicine Research Center, Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia.

Disclosure of conflict of interest

None.

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