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Research Article

Efficacy and Safety of GLP-1 Receptor Agonists in Obesity Management among Otherwise Healthy Adults

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ABSTRACT

Background: Obesity is a chronic and progressive condition that can have metabolic, cardiovascular and psychosocial consequences. Glucagon-like peptide-1 receptor agonists have been shown to be useful weight management drugs, but the body of evidence for their chronic, daily use in otherwise healthy adults is still relatively small.

Objective: To determine the efficacy and safety of GLP-1 receptor agonists in obesity management among otherwise healthy adults.

Methods: This is a prospective observational study carried out at Bacha Khan Medical College, Mardan from January 2025 to June 2025. Total 82 adult (18–60 years) individuals with body mass index ≥30 kg/m² were recruited using non-probabilistic consecutive sampling. They were given either semaglutide or liraglutide in addition to diet and physical activity advice. Body weight, BMI, waist circumference, blood pressure, fasting glucose, HbA1c and lipid profile were measured. Proportions losing 5%, 10%, 15% and 20% of their weight were calculated. Treatment adherence and adverse effects were also recorded. The p value <0.05 was regarded as statistically significant.

Results: The mean age of participants was 36.8 ± 9.4 years, and 52.4% were female. Mean body weight decreased from 98.7 ± 13.6 kg at baseline to 87.9 ± 12.8 kg at follow-up, with a mean reduction of 10.8 ± 5.4 kg (p<0.001). BMI decreased from 35.9 ± 4.2 to 32.0 ± 4.0 kg/m², while waist circumference declined by 9.6 ± 5.7 cm (both p<0.001). At least 5% weight loss was achieved by 68.3% of participants, 43.9% achieved at least 10%, and 18.3% achieved at least 15%. Semaglutide produced greater mean percentage weight loss than liraglutide (12.4 ± 5.0% versus 8.6 ± 4.3%; p=0.001). Significant improvements were also observed in blood pressure, glycaemic indices, and lipid profile. Adverse effects occurred in 52.4%, most commonly nausea and constipation, while 4.9% discontinued treatment because of intolerance. No acute pancreatitis or serious hypoglycaemia was observed.

Conclusion: GLP-1 receptor agonists produced clinically meaningful weight loss and favourable metabolic changes among otherwise healthy adults with obesity. Semaglutide was more effective than liraglutide, while adverse effects were predominantly mild and gastrointestinal. Regular adherence, longer treatment duration, and physical activity contributed to improved treatment response.

Keywords: Glp-1 Receptor Agonists, Obesity, Semaglutide, Liraglutide, Weight Loss, Body Mass Index, Adverse Effects.

INTRODUCTION

Obesity is a chronic relapsing and multifactorial disease that is caused by the interaction of biological, behavioural, environmental and socioeconomic factors. It is defined as an abnormal amount of fat that may affect a person's function, health and quality of life. Obesity is highly linked with the

development of type 2 diabetes, hypertension, dyslipidaemia, cardiovascular disease, sleep-disordered breathing and various malignancies; however, adverse metabolic changes can occur prior to the clinical diagnosis of these conditions. Therefore, it is important to manage obesity in the early stages in order to avoid future complications [1-3].

The basis of obesity management is still lifestyle modification, with a focus on reducing energy intake, eating a better diet and increasing physical activity, and providing behavioural support. Sub-optimal weight loss, however, is often achieved with lifestyle interventions and weight maintenance is challenging due to physiological changes that stimulate hunger, decrease satiety, and facilitate weight regain. This means that more and more adults are being recommended to take medications to lose weight, even when lifestyle changes have not been effective or have not led to satisfactory weight loss [4, 5].

Glucagon-like peptide-1 is an incretin hormone released after food intake. It stimulates glucose-dependent insulin release, inhibits glucagon secretion, slows down the emptying of the stomach and influences the centres in the central nervous system regulating appetite. GLP-1 receptor agonists mimic these actions, and decrease energy intake by increasing satiety (fullness) and decreasing hunger and food cravings. Liraglutide is taken once a day, while semaglutide is taken once a week as it has a longer half-life. Both drugs were first developed to control glycaemia but have also been shown to have significant weight reducing properties in adults with obesity [6, 7].

The effectiveness of GLP-1 receptor agonists for long-term weight loss has been proven in large clinical trials. In the STEP 1 trial, adults with overweight or obesity (without diabetes) lost a mean of 14.9% of their body weight after 68 weeks on semaglutide, when taken once weekly with lifestyle intervention . In the STEP 8 trial, the weight loss with semaglutide was significantly more than with once-daily liraglutide, with mean weight loss of -15.8% and -6.4%, respectively. These data suggest that GLP-1 receptor agonists can offer greater weight loss than diet and exercise changes alone [8, 9].

The effects of GLP-1 receptor agonists can go beyond weight loss. Clinical studies have shown that the waist circumference, blood pressure, fasting glucose, HbA1c and atherogenic lipid levels have all been reduced. In addition, the SELECT trial demonstrated cardiovascular disease benefit in adults with overweight or obesity, despite the lack of diabetes, and also demonstrated reduction in major adverse cardiovascular events. While adults with no apparent signs of cardiometabolic disease, enhancing these risk factors may help to prevent or slow future complications [10].

Although effective, GLP-1 receptor agonists are known to be associated with gastrointestinal side effects such as nausea, vomiting, diarrhoea, constipation, abdominal discomfort and dyspepsia. These effects are especially common during treatment initiation and dose escalation, and can cause a reduction in dose, delayed dose escalation, or treatment discontinuation. Very uncommon but significant complications include gallbladder disease, dehydration, and possible pancreatitis. Another important issue is weight gain following treatment cessation. The data from STEP 1 showed that participants experienced a significant proportion of weight loss rebound after stopping the semaglutide treatment, reinforcing the need to consider obesity pharmacotherapy as a possible long-term treatment [11].

Most of the evidence available has been obtained in highly controlled randomized trials with fixed doses, regular follow-up, and intensive lifestyle support. This may differ in actual clinical practice given the affordability of medications, availability, adherence to treatment, tolerance to dose, differing lifestyle and shorter duration of treatment exposure. Also, there is little local data on the efficacy and safety of semaglutide and liraglutide in adults not yet diagnosed with diabetes or other significant chronic conditions who have obesity [12, 13].

The present study was therefore conducted to evaluate the efficacy and safety of GLP-1 receptor agonists in obesity management among otherwise healthy adults. The primary objective was to assess changes in body weight, BMI, and waist circumference. Secondary objectives were to determine the proportions of participants achieving clinically meaningful weight-loss targets, compare outcomes between semaglutide and liraglutide, examine changes in cardiometabolic parameters, document adverse effects, and identify factors associated with successful weight reduction.

METHODOLOGY

This prospective observational study was conducted at Bacha Khan Medical College, Mardan, from January 2025 to June 2025. The study aimed to evaluate the efficacy and safety of glucagon-like peptide-1 receptor agonists in the management of obesity among otherwise healthy adults. A total of 82 participants were enrolled through non-probability consecutive sampling. All eligible adults presenting to the outpatient department for obesity management during the study period were assessed for inclusion. Before enrolment, the purpose and procedures of the study were explained to each participant, and written informed consent was obtained.

Patients were adults (18-60 years) with a BMI of 30 kg/m² or more, who were prescribed a GLP-1 receptor agonist for weight management. Participants had to be without any previously diagnosed diabetes mellitus, cardiovascular disease, chronic kidney disease, chronic liver disease, thyroid disorder, active malignancy or other major systemic illness. They were excluded if they had experienced pancreatitis, had an active gallbladder disease, medullary thyroid carcinoma, multiple endocrine neoplasia type 2, or hypersensitivity to GLP-1 receptor agonists. Other exclusion criteria were pregnancy or breastfeeding, other drugs for weight loss, and drugs that significantly alter body weight. The number of participants who were not included in the final efficacy analysis included those who discontinued treatment for reasons other than adverse effects, or those who were not completed with the planned follow-up.

Demographic and clinical data were collected on a structured data-collection form at enrolment. Demographic variables measured included age, sex, baseline body weight, height, body mass index, waist circumference, blood pressure, smoking status, physical activity, obesity class, and family history of obesity. The body weight measurement was done on a calibrated digital weighing scale to the nearest 0.1kg without shoes or heavy garments. Stadiometer was used to record height to the nearest 0.1 cm (wall mounted stadiometer). BMI was computed as weight (kg) divided by height (m²). Waist circumference was taken at the end of normal expiration between the lowest rib and the iliac crest using a nonstretchable measuring tape.

In each group, participants were treated with either semaglutide or liraglutide based on the clinical judgment of the prescribing physician, availability, patient preference, affordability and tolerability. Semaglutide was started at a low dose every week and carefully escalated as per the recommended protocol, while liraglutide was started at a low dose per day and slowly increased to the maximum tolerated dose. For those who experienced gastrointestinal intolerance, dose was not escalated or reduced. Attendees were also provided with universal counseling on calorie restriction, healthy diet, portion control and incremental increases in physical activity. They were encouraged to engage in at least 150 minutes of moderate-intensity physical activity per week, unless otherwise limited by MSD or other temporary factors.

Assessments were carried out on a monthly basis during the study period. Body weight, BMI, waist circumference, treatment dose, adherence, missed doses, physical activity and adverse effects were recorded at each visit. Treatment adherence was evaluated with patient interviews, prescription records and self-reported missed doses. Regular adherence was defined as taking 80% or more of the prescribed doses. Dose reduction, temporary interruption and permanent treatment discontinuation was documented, with the specific reason documented.

The main efficacy measure was the percentage of body weight loss from baseline to follow-up. Secondary efficacy endpoints were absolute weight loss (kg), BMI change, waist circumference change, and percentage of participants who lost a minimum of 5%, 10%, 15%, and 20% of body weight. The response to treatment was defined as poor (weight loss less than 5%), moderate (between 5-10%), good (between 10-15%) and excellent (15% or more). Secondary metabolic outcomes included changes in systolic blood pressure, diastolic blood pressure, fasting blood glucose, glycated haemoglobin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglyceride levels.

Safety was assessed by reporting all adverse effects of treatment on follow-up. Special emphasis was placed on: nausea, vomiting, constipation, diarrhoea, abdominal discomfort, dyspepsia, headache, dizziness, fatigue, injection site reactions, dehydration, hypoglycaemia, gall bladder related symptoms, and suspected pancreatitis. Adverse events were graded as mild, moderate, or serious based on their impact on the patient's ability to function normally and

whether the patient's ability to function was compromised by dosage adjustment or medical intervention. The following serious adverse events were recorded separately: hospital admission, dose reduction, temporary treatment interruption or permanent discontinuation of treatment due to intolerance. Those who reported severe abdominal pain, persistent vomiting, jaundice and/or symptoms suggestive of pancreatitis or gall bladder disease were referred for prompt clinical evaluation and appropriate laboratory and/or radiological tests.

Laboratory tests were done at baseline and end of follow-up, with an 8 to 12 hour overnight fast. Standard laboratory methods were used to measure fasting blood glucose, HbA1c, total, LDL, HDL, and triglycerides. The blood pressure was measured after a seated resting period of at least five minutes. These readings were taken at a time interval of about 2 minutes and an average reading was taken.

IBM SPSS Statistics was used to enter and analyse the data. Continuous variables e.g., age, weight, BMI, WC, BP and biochemical parameters were expressed as mean and standard deviation. Categorical variables were presented as frequency and percentage such as sex, obesity class, type of medication, treatment adherence, weight-loss category, and adverse effects. For normally distributed continuous measures, the paired-samples t-test was used to compare baseline and follow-up measures. Non-normally distributed paired data were analyzed using Wilcoxon signed rank test. The mean treatment outcomes for both groups were compared using independent-samples t-tests, with categorical comparisons made using the chi-square test orFisher's exact test. Univariate analysis was used to explore relationships between the participant characteristics and weight loss. Success was considered as a loss of at least 10% of the body weight recorded before the treatment. Variables that were clinically relevant or had a univariate p value < 0.20 were included in a multivariable logistic regression model. Odds ratios (with 95% CI) were calculated to determine independent factors associated with successful weight loss. The p value < 0.05 was used as a threshold for statistical significance.

RESULTS

Eighty-two adults with obesity participated in the study and were analyzed. The average age of the subjects was 36.8 ± 9.4 years (ranging from 20 to 58 years). The females comprised 52.4% and males 47.6% of the study population. At baseline, the mean body weight was 98.7 ± 13.6 kg, the mean body mass index was 35.9 ± 4.2 kg/m², and the mean waist circumference was 111.5 ± 10.8 cm. The majority of the participants were obese. Most participants had class II obesity. The baseline characteristics showed that 28.0% of participants had class I obesity, 47.6% had class II obesity, and 24.4% had class III obesity. 50 patients were treated with semaglutide, while 32 were given liraglutide. Standardized counseling for diet and physical activity (PA) was provided to all the participants during the treatment.

Table 1. Baseline demographic and clinical characteristics of participants (n = 82)

Variable	Frequency (%) or Mean ± SD
Age, years	36.8 ± 9.4
Male	39 (47.6)
Female	43 (52.4)
Baseline body weight, kg	98.7 ± 13.6
Baseline BMI, kg/m²	35.9 ± 4.2
Waist circumference, cm	111.5 ± 10.8
Systolic blood pressure, mmHg	128.4 ± 10.6
Diastolic blood pressure, mmHg	81.7 ± 7.9
Fasting blood glucose, mg/dL	94.8 ± 8.7
HbA1c, %	5.4 ± 0.3
Class I obesity	23 (28.0)
Class II obesity	39 (47.6)
Class III obesity	20 (24.4)
Semaglutide treatment	50 (61.0)
Liraglutide treatment	32 (39.0)
Regular adherence to treatment	70 (85.4)

Treatment with GLP-1 receptor agonists resulted in substantial decreases in BMI, waist circumference and weight. The mean body weight at baseline was 98.7 ± 13.6 kg and at the end of follow-up was 87.9 ± 12.8 kg, with a mean weight loss of 10.8 ± 5.4 kg. The average body weight loss percentage was 10.9 ± 5.1%. There was a 3.9 ± 1.9 kg/m² decrease in BMI and a 9.6 ± 5.7 cm decrease in WC, all of which were significant.

Table 2. Comparison of anthropometric measurements before and after treatment

Variable	Baseline Mean ± SD	Follow-up Mean ± SD	Mean Change	p-value
Body weight, kg	98.7 ± 13.6	87.9 ± 12.8	−10.8 ± 5.4	<0.001
BMI, kg/m²	35.9 ± 4.2	32.0 ± 4.0	−3.9 ± 1.9	<0.001
Waist circumference, cm	111.5 ± 10.8	101.9 ± 10.2	−9.6 ± 5.7	<0.001

Of the 82 participants, 68.3% lost 5% of their baseline body weight. 43.9% of the participants lost at least 10% of their body weight and 18.3% lost at least 15%. Four participants lost 20% or more of their body weight. The overall rate of excellent response to treatment was 13.4% and good response was 31.7%.

Table 3. Distribution of participants according to weight-loss response

Weight-loss outcome	Frequency (%)
Less than 5% weight loss	26 (31.7)
At least 5% weight loss	56 (68.3)
At least 10% weight loss	36 (43.9)
At least 15% weight loss	15 (18.3)
At least 20% weight loss	4 (4.9)
Poor response: <5%	26 (31.7)
Moderate response: 5% to <10%	20 (24.4)
Good response: 10% to <15%	25 (30.5)
Excellent response: ≥15%	11 (13.4)

Treatment had a mild but statistically significant effect on lowering SBP, FBG, HbA1c, TCHOL, LDL, and triglycerides. Treatment resulted in a slight increase in HDL cholesterol. Diastolic blood pressure decreased as well, but not by as much as for systolic blood pressure.

Table 4. Changes in cardiovascular and metabolic parameters

Variable	Baseline Mean ± SD	Follow-up Mean ± SD	p-value
Systolic blood pressure, mmHg	128.4 ± 10.6	122.1 ± 9.5	<0.001
Diastolic blood pressure, mmHg	81.7 ± 7.9	78.6 ± 7.1	0.002
Fasting blood glucose, mg/dL	94.8 ± 8.7	89.6 ± 7.8	<0.001
HbA1c, %	5.4 ± 0.3	5.2 ± 0.3	<0.001
Total cholesterol, mg/dL	194.6 ± 31.5	181.2 ± 28.7	<0.001
LDL cholesterol, mg/dL	121.8 ± 26.9	109.7 ± 24.5	<0.001
HDL cholesterol, mg/dL	43.7 ± 8.2	46.1 ± 8.5	0.006
Triglycerides, mg/dL	157.4 ± 42.8	136.6 ± 37.5	<0.001

Participants treated with semaglutide had a bigger mean percentage body weight loss compared to those treated with liraglutide. The average weight lost in the semaglutide group was 12.4% ± 5.0% and 8.6% ± 4.3% in the liraglutide group. In the same vein, more of those taking semaglutide lost a minimum of 10% of their body weight. There was no significant difference in adherence to treatment between the two groups.

Table 5. Comparison of treatment outcomes between semaglutide and liraglutide

Outcome	Semaglutide (n = 50)	Liraglutide (n = 32)	p-value

Mean weight reduction, kg	12.2 ± 5.3	8.6 ± 4.7	0.002
Mean percentage weight loss	12.4 ± 5.0	8.6 ± 4.3	0.001
Reduction in BMI, kg/m²	4.4 ± 1.9	3.1 ± 1.6	0.003
Reduction in waist circumference, cm	10.8 ± 5.8	7.7 ± 5.0	0.015
Achieved ≥5% weight loss	39 (78.0)	17 (53.1)	0.018
Achieved ≥10% weight loss	27 (54.0)	9 (28.1)	0.021
Regular treatment adherence	44 (88.0)	26 (81.3)	0.401

Forty-three participants reported at least one adverse effect. The majority of events were mild or moderate, and were experienced during the dose escalation phase. The most common side effects reported were nausea, constipation, vomiting, abdominal discomfort and diarrhea. Five participants needed to be dose-reduced and four stopped treatment due to continued gastrointestinal intolerance. No cases or severe hypoglycemia or acute pancreatitis were noted.

Table 6. Frequency of treatment-related adverse effects

Adverse effect	**Frequency (%)**
Any adverse effect	43 (52.4)
Nausea	25 (30.5)
Constipation	14 (17.1)
Vomiting	10 (12.2)
Abdominal pain or discomfort	9 (11.0)
Diarrhea	8 (9.8)
Headache	7 (8.5)
Dizziness	5 (6.1)
Fatigue	5 (6.1)
Injection-site reaction	3 (3.7)
Suspected gallbladder-related symptoms	2 (2.4)
Hypoglycemia	1 (1.2)
Dose reduction due to intolerance	5 (6.1)
Treatment discontinuation due to adverse effects	4 (4.9)
Serious adverse event	0 (0.0)
Acute pancreatitis	0 (0.0)

Body weight reduction of at least 10% from baseline was deemed successful for treatment. Adherence to treatment, use of semaglutide, longer treatment duration and engagement in regular physical activity were all significantly associated with successful weight loss. There was no significant difference in the relationship between age, sex or baseline BMI and treatment success.

Table 7. Factors associated with achieving at least 10% weight loss

Factor	**Achieved ≥10% Weight Loss n (%)**	**Did Not Achieve ≥10% Weight Loss n (%)**	**p-value**
Regular treatment adherence	34 (94.4)	36 (78.3)	0.041
Semaglutide use	27 (75.0)	23 (50.0)	0.021
Regular physical activity	25 (69.4)	20 (43.5)	0.019
Treatment duration ≥6 months	29 (80.6)	25 (54.3)	0.013
Female sex	21 (58.3)	22 (47.8)	0.345
Baseline BMI ≥35 kg/m²	23 (63.9)	27 (58.7)	0.633
Age ≥40 years	14 (38.9)	19 (41.3)	0.823
Presence of adverse effects	20 (55.6)	23 (50.0)	0.617

Regular treatment adherence, semaglutide treatment, regular physical activity, and treatment duration of 6 months or more were independent factors associated with achieving at least 10% weight loss. The persons who were regular in adherence had about 3 times

higher likelihood of successful weight loss than poor adherence.

Table 8. Multivariable logistic regression for predictors of at least 10% weight loss

Predictor	Adjusted Odds Ratio	95% Confidence Interval	p-value
Regular treatment adherence	3.18	1.05–9.62	0.041
Semaglutide use	2.74	1.08–6.95	0.034
Regular physical activity	2.61	1.04–6.56	0.041
Treatment duration ≥6 months	3.09	1.18–8.10	0.022
Female sex	1.34	0.53–3.39	0.539
Baseline BMI ≥35 kg/m²	1.29	0.50–3.31	0.598
Age ≥40 years	0.91	0.35–2.34	0.839

Overall, GLP-1 receptor agonist therapy resulted in clinically significant weight loss, BMI reduction and a reduction in waist circumference in otherwise healthy adults with obesity. Semaglutide led to a higher weight loss than liraglutide. Gastrointestinal side effects were relatively frequent, but mild and did not lead to withdrawal from treatment.

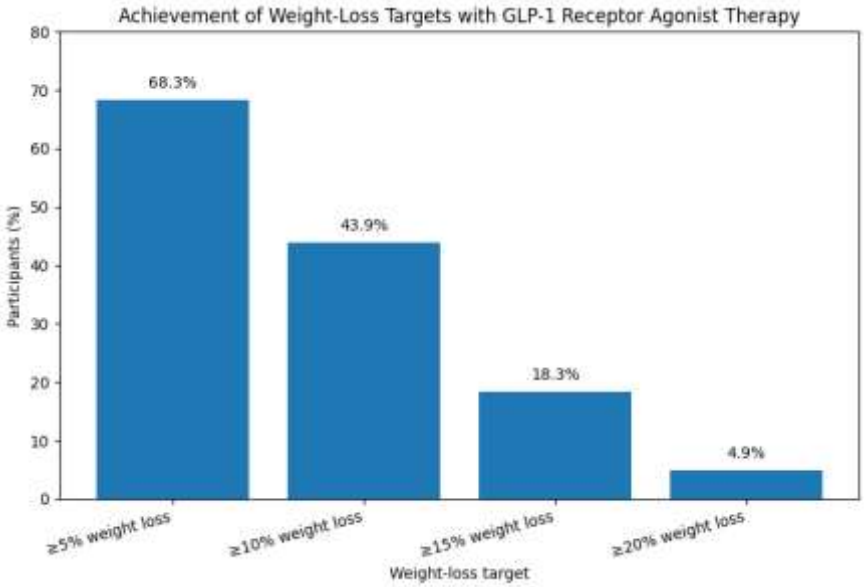

Figure 1. Proportion of participants achieving different weight-loss targets following treatment with GLP-1 receptor agonists among otherwise healthy adults with obesity (n = 82).

DISCUSSION

The present study evaluated the efficacy and safety of glucagon-like peptide-1 receptor agonists in 82 otherwise healthy adults with obesity. Treatment produced significant reductions in body weight, body mass index, and waist circumference. The mean body weight decreased by 10.8 kg, representing an average reduction of 10.9% from baseline. More than two-thirds of the participants achieved at least 5% weight loss, while 43.9% achieved a reduction of 10% or greater. These findings demonstrate that GLP-1 receptor agonists can produce clinically meaningful weight reduction among adults without diabetes or other major systemic illnesses. The observed improvement in anthropometric measurements also indicates that the treatment affected both overall and central adiposity.

The weight loss seen in this study was in line with the proven efficacy of semaglutide and liraglutide, but lesser than some large randomized clinical trials. In a STEP 1 trial, Wilding et al. reported a mean weight loss of 14.9% with once-weekly semaglutide 2.4 mg in adults with overweight or obesity who did not have diabetes after 68 weeks of treatment. During that trial, 86.4% of the subjects lost 5% or more of their body weight, 69.1% lost 10% or more of their body weight, and 50.5% lost 15% or more of their body weight [14]. The lower response rates in the current study could be attributed to the shorter follow-up period, differences in maximum tolerated doses, treatment adherence, drug affordability, and the

combination of both semaglutide and liraglutide users. The STEP 5 trial also showed that weight loss achieved with semaglutide was sustained up to 104 weeks of treatment [15].

Participants who took semaglutide lost more body weight, BMI, and waist size than those who took liraglutide. The mean (SD) percentage weight loss was 12.4% in the semaglutide group and 8.6% in the liraglutide group. Likewise, 54.0% of the semaglutide group lost 10% or more of their body weight, compared to 28.1% of the liraglutide group. This is consistent with the STEP 8 trial where once-weekly semaglutide achieved a mean weight loss of 15.8%, while once-daily liraglutide resulted in a mean weight loss of 6.4% after 68 weeks [16]. The longer half-life, weekly dosing, more potent appetite suppression and/or convenience of treatment with semaglutide compared with other GLP-1RA may help account for its increased effectiveness. The comparison in the current study, however, was not carried out in a randomized allocation of treatment, and these comparisons could have been influenced by differences in adherence, dose received, patient preference, availability and/or affordability.

The results with liraglutide were also in line with the previous data that showed its efficacy in obesity control. Among people without diabetes who were overweight or obese, Pi-Sunyer et al. found that the liraglutide 3.0 mg plus diet and exercise therapy group experienced significantly more weight loss than the placebo group [17]. The weight reduction seen with liraglutide was less than with semaglutide in this trial, however a significant number of individuals continued to benefit from this treatment. Thus, liraglutide might remain a valuable alternative for patients intolerant to semaglutide or unable to obtain once weekly therapy or who prefer a different method of dose-escalation.

Besides weight loss, improvements were seen in various blood markers such as SBP, DBP, FBG, HbA1C, total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides. The weight loss benefits of GLP-1 receptor agonist therapy appear to be more than just about weight, with these improvements. Favorable reductions in WC, BP, glucose tolerance, and cardiovascular risk factors related to lipids were also reported for the STEP 1 and STEP 5 trials [14, 15]. While the present study participants were not diabetic, a decrease in fasting glucose and HbA1c levels could indicate an increased insulin sensitivity and decreased risk of metabolic dysfunction in the future. These blood pressure and lipid profile improvements could help provide long-term cardiovascular protection.

The SELECT trial has also been supportive regarding cardiovascular benefit. Lincoff et al. showed that semaglutide was associated with a significant decrease in major adverse cardiovascular events in adults with overweight or obesity, and also showed that it was associated with cardiovascular disease without diabetes [18]. But in the present study, participants were healthy and had no known cardiovascular disease. Hence, the present results should not be taken as proof of cardiovascular event reduction. However, the metabolic benefits (body weight, blood pressure, glucose control and lipid profile) indicate a possible positive impact on future cardiometabolic risk.

Adherence to the treatment regimen, use of semaglutide, participation in physical activity and the duration of treatment >6 months were independently linked to weight loss ≥10%. The odds of successful weight reduction were over 3 times higher in the group with regular adherence than in the group with low adherence. This findings underscore the importance of consistency in treatment, right dosage, and lifestyle changes that accompany GLP-1 receptor agonists' clinical efficacy. Real-world data also indicate that weight loss is higher with semaglutide compared to liraglutide, and among those who continue to be on a regimen with the drug [19]. This may be, at least in part, due to various treatment interruptions, reduced drug doses, treatment discontinuation due to cost considerations, and inconsistent follow-up between clinical trials and routine care.

Safety of the present study was acceptable overall. Just over half of the individuals reported at least one adverse effect, but a majority of adverse events were mild or moderate. The most common complaints were nausea, constipation, vomiting, abdominal discomfort and diarrhoea. The event is consistent with pooled analysis of STEP trials where gastrointestinal adverse events were the most commonly reported treatment related events, and typically reported during dose escalation [20]. A small fraction of the participants in the present study did need to reduce their dose or stop their treatment. None of the medical staff recorded either

acute pancreatitis, severe hypoglycaemia, or any other serious adverse event. But it is important to note that the lack of serious events should be taken with a grain of salt as uncommon complications may not be recognized in a relatively small population of subjects that has been followed for only six months.

The continuation of therapy appears to be important for maintaining treatment benefits. The STEP 1 extension showed that participants lost a significant amount of weight again in one year after stopping semaglutide and a number of the cardiometabolic benefits returned to baseline levels[21]. This finding confirms that obesity can be a chronic disease, and that a short treatment course may not be enough. It is therefore important that patients are counselled on a potential risk of weight regain after discontinuation, the need for lifelong lifestyle modification, and the need for regular clinical monitoring during and after treatment.

There are some limitations in the present study. It was conducted at a single institution and included a relatively small sample, which may limit the generalizability of the findings. Random treatment allocation, placebo comparison and blinding were not built into the observational design. Thus, the choice of treatment and clinical outcomes could have been affected by price, availability, choice, compliance, or doctor's bias. Dietary intake, physical activity and missed doses were partly reported and may have been influenced by recall bias. No long term follow-up was performed for 6 months to evaluate long term weight maintenance, weight regain after withdrawal, or rare adverse events. Larger samples, standardised dosage, longer follow-up periods, body-composition measures, quality-of-life measures, and detailed assessment of adherence and cost-effectiveness of treatment should all be included in future multicentre, randomised studies.

CONCLUSION

GLP-1 receptor agonist therapy produced clinically meaningful reductions in body weight, BMI, and waist circumference among otherwise healthy adults with obesity. Treatment was also associated with favourable changes in blood pressure, glucose regulation, and lipid profile. Semaglutide produced greater weight loss than liraglutide, while regular adherence, physical activity, and longer treatment duration were important predictors of successful treatment. Gastrointestinal adverse effects were common but usually mild and manageable, and treatment discontinuation was infrequent. GLP-1 receptor agonists may therefore represent an effective and generally well-tolerated component of comprehensive obesity management when combined with dietary modification, physical activity, gradual dose escalation, and appropriate clinical monitoring.

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