RACE OF GLPS: IMPACT ON WEIGHT AND GLYCEMIC CONTROL ON TYPE 2 DIABETES WITH SEMAGLUTIDE VERSUS LIRAGLUTIDE

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ABSTRACT

OBJECTIVES

Semaglutide is a glucagon-like peptide-1 receptor agonist that improves glycemic control and reduces body weight in patients with type 2 diabetes. This study aimed to evaluate the effect of Semaglutide with standard Metformin on glycemic control and BMI after 3 and 6 months of treatment. Additionally, we compared the glycemic control and weight benefits of Semaglutide vs. liraglutide.

METHODOLOGY

This longitudinal cohort study was conducted in a general practice clinic in Clifton and a family medicine health center in Ziauddin University, Karachi from April 2022 till April 2023. We enrolled 128 patients with type 2 diabetes who were treated with metformin alone. Patients received Semaglutide 2mg once weekly in addition to standard metformin 1gm bid for 6 months. HbA1C and BMI were measured at baseline, 3 months, and 6 months. We compared the glycemic control and weight loss of Semaglutide with a cohort of participants taking Liraglutide over a period of 6 months in the same catchment area in 2021 to determine which drug has an edge over the other.

RESULTS

Semaglutide was superior to Liraglutide in controlling sugars (HbA1c% reduction 1.13 vs 0.94) as well as in weight loss (10.6 vs 6.2kg) respectively. Single sample t-test showed a statistically significant difference from the hypothetical mean of HbA1C <6.5% (p-value <0.00) Paired t-test showed a strong correlation between initial weight and after 6 months' weight and HbA1C respectively. (p-value <0.00 & 0.004).

CONCLUSION

Semaglutide has proven to be substantially beneficial in reducing weight (10.6kgs) and achieving optimal glycemic control (1.13% HbA1C reduction) over the 6-month study period. Semaglutide is superior to Liraglutide in controlling sugars and weight.

KEYWORDS: *Semaglutide, Liraglutide, Weight loss, Glycemic Control*

INTRODUCTION

Obesity is a global public health challenge impacting most body systems. It is associated with hypertension, dyslipidemia, and insulin resistance which leads to type II diabetes mellitus, metabolic dysfunction associated with steatotic liver disease, cardiovascular disease, stroke, musculoskeletal disorders, cancers, and various mental health issues.[1] The prevalence of obesity has nearly tripled in the past few years and it is expected that the number will rise to approximately 2.7 billion by 2025.[2] Although diabetes is managed by oral anti-diabetic medications or injectable insulin lifestyle modification such as weight loss plays an important role in improving glycemic control and even reversing the progression of type II diabetes.[3] For patients with type II diabetes who are overweight or obese, initial recommendations for weight loss and physical activity are to lose 5 to 10 percent of initial body weight and to carry out at least 30 minutes of moderate physical

activity on most days of the week or 150 minutes/week.[4] Semaglutide is a glucagon-like-peptide-1 analog, a drug that is word of mouth and has created history. After being evaluated by multiple trials its efficacy and safety were ensured and it became available for commercial use, marking a significant milestone in the management of diabetes.[5] Semaglutide is approved for weight loss at a dose of 2.4mg once weekly in obese but in people with type II diabetes, it is approved at doses of up to 1mg administered subcutaneously once weekly which helps in controlling blood sugar levels as well as weight reduction.[6,7] Semaglutide interacts with specific enzyme inhibiting their activity and prolonging the activity of GLP-1 by enhancing insulin secretion hence reducing the peristalsis of the stomach, decreasing appetite, and promoting a feeling of fullness.[8] Additionally, this medication has proved to be cardio-protective, making it a valuable tool in the prevention and treatment of heart disease.[9,10] Furthermore, it has been proved in a recent study that patients experienced an average weight loss of 15% over 68 weeks by using Semaglutide therefore making it a preferable choice for individuals with type 2 diabetes and obesity.[11] Despite showing favorable results, Semaglutide does come with potential risks. The most commonly encountered side effects are diarrhea, nausea, and vomiting. Occasionally more serious side effects may occur such as pancreatitis, gastroparesis, kidney problems, or diabetic retinopathy. Therefore, it is advised that each patient using Semaglutide should discuss the potential risks and benefits with their healthcare provider before starting it.[12,13] These symptoms can be managed by starting with a low dose and gradually up-titrating it until the maximum dose is achieved with regular monitoring. Moreover, anti-nausea medications may be prescribed to help relieve these symptoms and improve the patient's overall health and well-being. Patients must report any severe or persistent side effects to their healthcare provider for further evaluation and management.[14] Semaglutide is contraindicated in patients suffering from medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2. In addition, caution should be exercised in patients with a history of pancreatitis or diabetic gastroparesis. It is crucial for healthcare professionals to thoroughly access the patient's medical history and current health status to minimize the risk of adverse effects and ensure the best possible outcome. This study is conducted to evaluate the effect of Semaglutide with standard Metformin on glycemic control and BMI after 3 and 6 months of treatment. Additionally, we compared the glycemic control and weight benefits of Semaglutide vs. liraglutide.[15,16]

METHODOLOGY

This was a longitudinal cohort study done in a general practice clinic in Clifton and a family medicine health care center in Ziauddin University, Karachi from April 2022 till April 2023 over a period of 1 year. All patients with uncontrolled Type 2 Diabetes, having no prior usage of insulin or any GLP 1 analog aged 15 years and older who consented to the study were recruited. Oral anti-diabetic agents apart from those who were on monotherapy with metformin 1gm twice daily along with lifestyle modification and who agreed to use Semaglutide as add-on therapy were recruited in the study. Participants with malignancy, pregnancy, and lactating women were excluded from the study. An ethics review committee of Ziauddin University Pakistan approved this study. The sample size was 128 subjects. At the start of the study, HbA1C was done and BMI was calculated after taking informed consent. Duration of diabetes, level of physical activity, and dietary habits were determined before and after 24 weeks BMI was evaluated and HbA1c was reassessed. Episodes of hypoglycemia and gastrointestinal side effects were evaluated as well. Semaglutide was started on the initial dose of 0.25mg once a week for 4 weeks, and then dosage was increased to 0.5mg once a week for 4 weeks then to 1mg once a week for 4 weeks then 2mg once a week for 4 weeks. Gastrointestinal side effects were evaluated and if bloating, early satiety, diarrhea, nausea, or vomiting occurred then they were categorized into mild, moderate, and severe. Exercise was assessed by at least 30 minutes of physical activity such as brisk walking, gymming, cycling, etc. Hypoglycemia was categorized, as either no, single, 3-4, or 5 episodes of fasting blood sugar of less than 60mg/dl. Data was compared to a cohort of patients (49) in a similar catchment area who took Liraglutide 1.8mg on top of Metformin for a period of 6 months in 2021. We compared the glycemic control, weight loss, and adverse effects including hypoglycemia of both GLP1 analogues to determine which drug has an edge over the other. Data was analyzed using SPSS software version 20. Numerical variables were analyzed by mean and standard deviation. Categorical variables were analyzed by frequencies and percentages.

RESULTS

Semaglutide was superior to Liraglutide in controlling sugars (HbA1c% reduction 1.13 vs 0.94) as well as in weight control (10.6 vs 6.2kg weight loss) respectively. The mean age of the participants was 45.65$\pm$11.45. Duration of Diabetes was 5.6$\pm$3.08yrs. Mean weight initially was 101.8kg$\pm$9.8, after 3 months was

97.6±13.6kg, and after 6 months was 91.2±10.8kg. Mean HbA1C initially was 8.2±0.47 and after 6 months was 7.13±0.75. Table 1 shows the demographic profile of the participants. Table 2 demonstrates the declining weight trajectory and glycemic control among participants using Semaglutide over 6 6-month span. Paired sample t-tests show a significant correlation between initial weight and HbA1C (p-value <0.00) as well as after 6 months' weight and hbA1c (p-value 0.004). Table 3 demonstrates the difference between Semaglutide and Liraglutide regarding glycemic control and weight. Figure 1 and 2 demonstrates diabetes complications and gastrointestinal adverse effects of Semaglutide respectively.

Table 1: Demographic Profile of the Participants

Characteristics	N(%) X±SD
Age in years	45.65±11.45
Duration of Diabetes in years	5.6±3.08
Screen time in hrs	2.8±1.1
Gender Male Female	 80(62.5) 48(37.5)
Exercise Occasionally Sometimes Mostly	 20(15.6) 72(56.3) 36(28.1)
Extreme sports Participates Does not participate	 16(12.5) 112(87.5)
Hypoglycemic episodes Occurred Did not occur	 16(12.5) 112(87.5)
Orthostasis Present Absent	 32(25) 96(75)
Comorbid HTN	56(43)

Table 2: Weight and Glycemic Change After Semaglutide Usage, T-Test, And Paired T-Test Applied

	Before Semaglutide	Single sample t-test p-value	After 3 months of Semaglutide	After 6 months of Semaglutide	Change after 6 months
HbA1C %	8.26±0.47	<0.00	7.9±0.38	7.13±0.75	1.13
Weight in kgs	101.8±9.98	<0.00	97.6±13.6	91.2±10.8	10.6
Paired t - test	<0.00	-	-	0.004	

Table 3: Comparison of Semaglutide and Liraglutide with Regards to Glycemic Control and Weight

	Semaglutide N=128	Liraglutide N=49	Difference
HbA1C%	1.13	0.94	0.19
Weight in kgs	10.6	6.2	4.4
Hypoglycemia	0	14.3%	

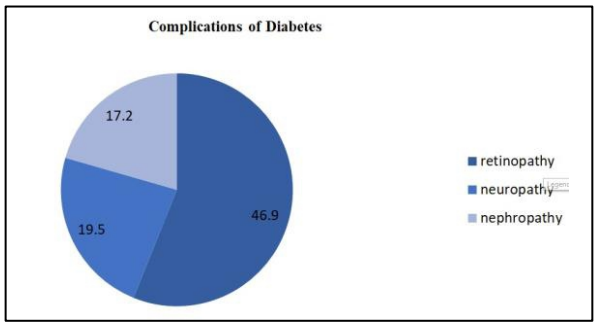

Figure 1: Microvascular complications of Diabetes

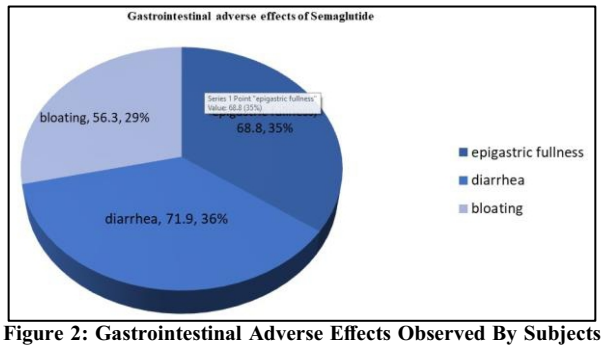

Figure 2: Gastrointestinal Adverse Effects Observed By Subjects Using Semaglutide

DISCUSSION

This study evaluates the combined effects of Semaglutide 2mg and Metformin 1gm bid over 6 months and concomitantly compares the outcomes with Liraglutide another GLP 1 receptor agonist, adding valuable insights into the management of adult-onset diabetes. We will further elaborate on the study's findings and their significance while drawing comparisons with existing research on the GLP-1 analog. Achieving optimal glycemic control is the objective in the management of diabetes.[17] This study signifies that the combination therapy of Semaglutide with standard Metformin led to a notable reduction in HbA1C levels over a period of 6 months. The mean reduction of 1.13% of HbA1C level observed in this study is clinically significant and aligns with the results of previous research on Semaglutide. A study was conducted about cardiovascular outcomes of Semaglutide by Marso et al. (2016) which revealed that Semaglutide not only lowers glycemic index but also has cardiovascular benefits, reducing the risk of major adverse cardiovascular events in patients with type 2 diabetes.[18] Additionally, weight reduction plays a key role in the management of diabetes mellitus, as obesity is a common comorbidity.[19] This study also highlights the decline in weight from 101.8kg at baseline to

91.2kg after 6 months. These results are consistent with the broader body of research on GLP-1 analogs. The impact of GLP-1 receptor agonist on body weight reduction is significantly higher than any other antidiabetic medication which was proven by Vilsboll et al. (2012) in a meta-analysis, the mechanism behind this weight loss involves central appetite suppression and delayed gastric emptying.[20] Our study noted that the treatment was well-tolerated by the participants, with mostly mild gastrointestinal symptoms. Although these side effects such as bloating, early satiety, diarrhea, nausea, or vomiting can be bothersome, they are typically transient and tend to diminish over time as the body adjusts to the medication.[21] This finding is consistent with a study by Davies et al. (2015) which stated that most gastrointestinal adverse events occurred initially in the treatment and decreased in frequency with continued use of semaglutide.[22] A noteworthy aspect of this study is the presence of comorbid hypertension in a significant portion of 43% of participants. This highlights the importance of considering the long-term health of individuals with type 2 diabetes and addressing associated conditions alongside glycemic control. Comorbidities should be simultaneously managed as they have a pivotal role in the overall health outcome of the patients.[23,24] The mean duration of diabetes of the participants in this study is 5.6 years. This suggests that the addition of Semaglutide to Metformin may be effective at all stages of the disease. Diabetes is a progressive condition so the treatment strategies should be up to date with the changing needs of patients. Research has shown that GLP-1 receptor agonists can be beneficial in both relatively early and moderately advanced stages of the disease, making them versatile agents in clinical practice.[25]

LIMITATIONS

This study was conducted on 128 participants over 1 year time period hence a larger sample size and longer duration of study could have added more value and variability.

CONCLUSIONS

In conclusion, this pre-post observational study provides further evidence of the effectiveness of Semaglutide with metformin for the treatment of type 2 diabetes mellitus. This study reports good tolerability, improved glycemic control, and weight reduction, corresponding with previous research. Moreover, few other studies further highlight the potential of semaglutide to improve cardiovascular outcomes for diabetic patients. However, it's essential to acknowledge the limitations of this study, including its relatively short duration and the need for larger and longer-term trials to confirm these findings and asse ss sustained benefits and safety. Nevertheless, this study contributes valuable insights to the growing body of knowledge on effective strategies for managing type 2 diabetes. Semaglutide, as a GLP-1 receptor agonist, holds promise as an important therapeutic option in the multifaceted approach to diabetes care, offering both glycemic control and potential cardiovascular benefits to patients. Future research should continue to explore its role in different patient populations and in the context of evolving diabetes management guidelines.

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REFERENCES

1. Celik O, Yildiz BO. Obesity and physical exercise. Minerva Endocrinology. 2021;46(2).
2. Boutari C, Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. Metabolism. 2022;133:155217-.
3. Stone S, Drobycki N, Johnson M. Abstract NS5: Use of a Multidisciplinary Approach to Successfully Improve Inpatient Diabetes Self-Management Education and Diabetes Medication Reconciliation at Discharge for Persons With Diabetes and Stroke at a Major Academic Medical Center. Stroke. 2020;51(Suppl_1).
4. Jakicic JM, Apovian CM, Barr-Anderson DJ, Courcoulas AP, Donnelly JE, Ekkekakis P, et al. Physical Activity and Excess Body Weight and Adiposity for Adults. American College of Sports Medicine Consensus Statement. Medicine & Science in Sports & Exercise. 2024;56(10):2076-91.
5. Røder ME. Clinical potential of treatment with semaglutide in type 2 diabetes patients. Drugs Context. 2019;8:212585-.
6. Williams DM, Staff M, Bain SC, Min T. Glucagon-like Peptide-1 Receptor Analogues for the Treatment of Obesity. touchREV Endocrinol. 2022;18(1):43-8.
7. Mahapatra MK, Karuppasamy M, Sahoo BM. Semaglutide, a glucagon like peptide-1 receptor agonist with cardiovascular benefits for management of type 2 diabetes. Rev Endocr Metab Disord. 2022;23(3):521-39.
8. Krieger J-P. Intestinal glucagon-like peptide-1 effects on food intake: Physiological relevance and emerging mechanisms. Peptides. 2020;131:170342.
9. Ryan DH, Lingvay I, Colhoun HM, Deanfield J, Emerson SS, Kahn SE, et al. Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity (SELECT) rationale and design. American Heart Journal. 2020;229:61-9.
10. Husain M, Bain SC, Holst AG, Mark T, Rasmussen S, Lingvay I. Effects of semaglutide on risk of cardiovascular events across a continuum of cardiovascular risk: combined post hoc analysis of the SUSTAIN and PIONEER trials. Cardiovasc Diabetol. 2020;19(1):156-.
11. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. New England Journal of Medicine. 2021;384(11):989-1002.

12. Shu Y, He X, Wu P, Liu Y, Ding Y, Zhang Q. Gastrointestinal adverse events associated with semaglutide: A pharmacovigilance study based on FDA adverse event reporting system. Front Public Health. 2022;10:996179-.
13. Niman S, Hardy J, Goldfaden RF, Reid J, Sheikh-Ali M, Sutton D, et al. A Review on the Efficacy and Safety of Oral Semaglutide. Drugs R D. 2021;21(2):133-48.
14. Smits MM, Van Raalte DH. Safety of Semaglutide. Front Endocrinol (Lausanne). 2021;12:645563-.
15. Chao AM, Tronieri JS, Amaro A, Wadden TA. Clinical Insight on Semaglutide for Chronic Weight Management in Adults: Patient Selection and Special Considerations. Drug Des Devel Ther. 2022;16:4449-61.
16. Kane MP , Triplitt CL, Solis-Herrera CD. Management of type 2 diabetes with oral semaglutide: Practical guidance for pharmacists. Am J Health Syst Pharm. 2021;78(7):556-67.
17. Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, et al. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. JAMA. 2022;327(2):138-50.
18. Raff E, Hramiak I, Mann JF, Frandsen KB, Daniels G, Kristensen P, et al. Liraglutide and Renal Outcomes in Type 2 Diabetes: Results of the LEADER Trial. Canadian Journal of Diabetes. 2017;41(5):S5.
19. Pavlou V, Cienfuegos S, Lin S, Ezpeleta M, Ready K, Corapi S, et al. Effect of Time-Restricted Eating on Weight Loss in Adults With Type 2 Diabetes: A Randomized Clinical Trial. JAMA Netw Open. 2023;6(10):e2339337-e.
20. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. BMJ. 2022;376:o109-o.
21. Liu L, Chen J, Wang L, Chen C, Chen L. Association between different GLP-1 receptor agonists and gastrointestinal adverse reactions: A real-world disproportionality study based on FDA adverse event reporting system database. Front Endocrinol (Lausanne). 2022;13:1043789-.
22. Wharton S, Calanna S, Davies M, Dicker D, Goldman B, Lingvay I, et al. Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss. Diabetes Obes Metab. 2022;24(1):94-105.
23. Handelsman Y, Butler J, Bakris GL, DeFronzo RA, Fonarow GC, Green JB, et al. Early intervention and intensive management of patients with diabetes, cardiorenal, and metabolic diseases. Journal of Diabetes and its Complications. 2023;37(2):108389.
24. Pati S, Pati S, Akker Mvd, Schellevis FFG, Jena S, Burgers JS. Impact of comorbidity on health-related quality of life among type 2 diabetic patients in primary care. Prim Health Care Res Dev. 2020;21:e9-e.
25. Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes - state-of-the-art. Mol Metab. 2021;46:101102-.

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