Weekly Semaglutide Use Shows Promise Among Type 2 Diabetes Patients at a Polyclinic in Alahsa, Saudi Arabia: A Retrospective Study

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ABSTRACT

Background: Glucagon-like peptide-1 receptor agonist (GLP-1RAs) are vital for glycemic control and weight loss. Due to lack of extensive evidence on semaglutide efficacy in Saudi population, this study aimed to evaluate the effectiveness of once-weekly (OW) semaglutide in adults with type 2 diabetes.

Methods: This retrospective cohort study conducted in king faisal university polyclinic in 2023 which assessed patients with type 2 diabetes who started treatment with OW semaglutide alone or combined with other antidiabetic medications. Measurements taken before and six months after starting OW semaglutide which include glycated hemoglobin (HbA1c), body weight and other health variables.

Results: A total of 22 participants were enrolled in the study. After the intervention the HgA1c and body weight were significantly decreased ($p < 0.001$, $P < 0.001$) respectively. Additionally, there were notable decrease with statistical level in serum cholesterol, triglycerides (TG), low density lipoprotein (LDL) and alanine transferase (ALT) ($P = 0.001$, $p = 0.001$, $p = 0.013$, $p < 0.001$) whereas high density lipoprotein (HDL) and creatinine level did not show statistical difference ($p = 0.057$, $p = 0.829$).

Conclusion: This study examined the impact of OW semaglutide on individuals with type 2 diabetes, assessing HgA1c, body weight and other health metrics. Results showed significant health improvements post-intervention, suggesting key areas for further research. Future studies could explore OW semaglutide long-term effects on type 2 diabetes in the Saudi population.

1. Introduction

Diabetes mellitus is a widely recognized condition stemming from insufficient insulin production or the body's inability to utilize insulin effectively, resulting in elevated blood glucose levels. Globally, approximately 537 million adults are estimated to be affected by diabetes, with projections indicating a rise to 784 million by 2045. Type 2 diabetes stands as the predominant form of diabetes worldwide (1).

Regardless of the variety of pharmacological agents available for the treatment of type 2 diabetes, many patients face difficulties in maintaining glycemic control (2). Glucagon-like peptide-1 receptor agonists (GLP-1RAs) play a crucial role in managing blood sugar levels and promoting weight loss, with evident cardiac and renal benefits. They operate in a glucose-dependent manner, thereby minimizing the risk of hypoglycemia. Many associations across the world, including the American Diabetes Association, recommend using GLP-1RAs for individuals with type 2 diabetes with cardiovascular (CV) disease or at risk of CV disease (3,4).

The US Food and Drug Administration (FDA) has now approved the weekly injectable GLP-1RA semaglutide for treatment of type 2 diabetes mellitus (5). As per the SUSTAIN trials 1 and 6, semaglutide caused notable decreases in HgA1c, body weight, CV death, myocardial infarction and stroke (2,6).

A pooled analysis of 4 SURE studies concluded that OW semaglutide had the beneficial effects of controlling HgA1c levels and reducing body weight in patients with type 2 diabetes (7). A systematic review illustrated that

semaglutide is effective and safe in the treatment of type 2 diabetes, particularly for individuals with a high body mass index (BMI) or those who struggle with adhering to their daily diabetes medications (8). Another observational study examined various clinical factors among patients with type 2 diabetes who commenced treatment with semaglutide within a specific timeframe and attended one or more follow-up visits subsequent to initiation. The results indicated a significant decrease in HgA1c levels, body weight, lipid levels, and liver enzyme levels (9). Research on semaglutide's efficacy in Saudi Arabia is limited. Thus, we conducted a study at the King Faisal University (KFU) Polyclinic in Alahsa to assess the efficacy of once-weekly semaglutide in adults with type 2 diabetes. In addition to monitoring possible associations with other clinical variables like total cholesterol, TG, HDL, LDL, ALT, and creatinine levels, we recorded effects on HgA1c levels and body weight.

2. Materials and methods:

This retrospective cohort study was conducted in the KFU Polyclinic from March 2023 to November 2023. The 22 participants included in the study were selected from among type 2 diabetes patients who were registered at the KFU Polyclinic. Type 2 diabetes patients who recently started semaglutide alone or in addition to other anti-diabetic medications were registered in the study. No control group was included in the study, making it a single-arm study. The semaglutide dosage was initially 0.25 mg per week and was raised to 0.5 mg weekly after 4 weeks. If the effectiveness of a dose of 0.5 mg per week for at least 4 weeks was not satisfactory, the dosage was elevated to 1.0 mg per week. Participants who were pregnant, under the age of 18 years, receiving another GLP-1RA or dipeptidyl peptidase-4 (DPP4) inhibitors, or had a history of pancreatitis, thyroid cancer, severe gastrointestinal disorders, severe hypoglycemia, or severe renal dysfunction were not included.

The baseline was defined as the time point at which semaglutide was initially prescribed. Age, gender, and weight at baseline were recorded, and blood samples were collected after overnight fasting at baseline and then 6 months after starting semaglutide. Blood analyses included HgA1c, ALT, creatinine, total cholesterol, TG, HDL, and LDL. The primary endpoint was alterations in HgA1c levels and body weight over 6 months compared to the initial measurements. The secondary endpoint was any relationships and changes in other clinical variables like lipid profile, liver enzymes, and renal function. Ethical approval was obtained from the Local Committee for Scientific Research Ethics of KFU, and ethical considerations and the confidentiality of the study participants' information were maintained throughout the study.

3. Data management and statistical analysis:

Descriptive statistics were utilized to summarize demographic characteristics, medication usage patterns, and pre- and post-intervention health indicators among the study sample. Continuous variables are presented as means with standard deviations (SDs) or medians with interquartile ranges (IQRs), depending on data distribution. Categorical variables are expressed as frequencies and percentages. To assess the impact of the intervention on health outcomes, the paired-sample Wilcoxon signed-rank test was conducted. This non-parametric test was chosen due to the small sample size and the non-normal distribution of some variables. The test compared pre- and post-intervention measurements for each health indicator. Results were reported as mean ranks, sum of ranks, test statistics (Z), and associated p-values. A significance level of $\alpha = 0.05$ was used to determine statistical significance. All analyses were performed using statistical software (SPSS version 26), and tables were generated to present the findings comprehensively.

4. Results

Table 1 presents the demographic characteristics of the study sample, revealing a median age of 50.5 years with an IQR of 13.25. Participants were evenly split between those below and above 50 years of age, with 45.5% falling into each category. Female constituted a larger proportion of the sample (63.6%) than male (36.4%). Furthermore, 54.5% of participants were on statin medications, suggesting the prevalent use of these drugs for managing cholesterol levels and reducing CV risk. These demographic variables provide essential context for understanding the study population, facilitating potential subgroup analyses and interpretations regarding health outcomes or treatment effects.

Table 1. Demographic variables

Variables		n	%
Age (median±IQR)		50.5±13.25	
Age group	<50 years	10	45.5
	≥50 years	12	54.5
Gender	Male	8	36.4
	Female	14	63.6
Statin medication use	Yes	12	54.5
	No	10	45.5
	Total	22	100.0

Table 2 presents the different anti-diabetic medications used by participants in addition to semaglutide. Metformin was the most common medication, used by 13 (59.1%) participants, while empagliflozin and glargine were used by 10 (45.5%) and 6 (27.3%) participants, respectively. The varying percentages highlight differences in medication preference within the population, possibly reflecting individual patient needs, physician recommendations, or medication efficacy. This breakdown provides valuable insights into the pharmaceutical management of the surveyed cohort, offering useful information for healthcare practitioners and researchers aiming to understand medication utilization trends among individuals with certain medical conditions.

Table 2

Medication	n	%
Metformin	13	59.1
Empagliflozin	10	45.5
Glargine	6	27.3

Table 3 presents descriptive statistics for the pre- and post-test measurements of key health indicators among the sample of 22 individuals. Before the intervention, the mean HgA1c level was 8.20%, body weight averaged 98.14 kg, and the mean cholesterol level was 198.32 mg/dl. The TG level averaged 176.32 mg/dl, while HDL cholesterol and LDL cholesterol averaged 43.86 mg/dl and 120.68 mg/dl, respectively. The ALT level averaged 31.95 U/L, and the creatinine level averaged 0.69 mg/dl. Following the intervention, there were noticeable improvements in most indicators, with HgA1c decreasing to 6.50%, weight to 85.43 kg, and cholesterol to 168.36 mg/dl. TG decreased to 132.45 mg/dl, while HDL cholesterol increased to 47.14 mg/dl. These findings suggest a positive impact of the intervention on the participants' health outcomes, as indicated by improvements across several key metrics from pre- to post-test measurements.

Table 3. Descriptive statistics pre- and post-intervention (n=22)

	Mean	SD	Minimum	Maximum
Pre-intervention				
HgA1c (%)	8.20	1.92	6	13.5
Weight (kg)	98.14	17.66	73	141
Cholesterol (mg/dl)	198.32	57.82	105	325
TG (mg/dl)	176.32	90.18	70	449
HDL (mg/dl)	43.86	9.16	30	66
LDL (mg/dl)	120.68	46.53	27	196
ALT (U/L)	31.95	16.81	14	96
Creatinine (mg/dl)	0.69	0.23	0.3	1.2
Post-intervention				
Hga1c (%)	6.50	1.10	4.9	8.8
Weight (kg)	85.43	17.45	54	132
Cholesterol (mg/dl)	168.36	41.28	99	269
TG (mg/dl)	132.45	54.50	63	296
HDL (mg/dl)	47.14	9.05	30	76
LDL (mg/dl)	102.23	29.34	40.00	180.00
ALT (U/L)	23.82	7.47	16.00	45.00
Creatinine (mg/dl)	0.69	0.20	0.40	1.20

Table 4 outlines the outcomes of the Wilcoxon signed-rank test, a robust non-parametric method utilized to analyze paired data, comparing pre- and post-intervention measurements across a spectrum of health parameters. The results demonstrate noteworthy improvements in various health metrics subsequent to the intervention. Notably, significant reductions were observed in post-intervention levels of HgA1c ($p<0.001$), indicative of enhanced glycemic control, as well as in body weight ($p<0.001$), cholesterol ($p=0.001$), TG ($p=0.001$), LDL ($p=0.013$), and ALT ($p<0.001$), underscoring favorable shifts in CV and liver health markers. These findings suggest the intervention's effectiveness in ameliorating metabolic and physiological parameters. Conversely, no statistically significant alterations were detected in post-intervention HDL levels ($p=0.057$) or creatinine levels

(p=0.829), indicating a potential need for further intervention refinement or longer-term monitoring to discern significant changes in these specific biomarkers. Overall, the results underscore the multifaceted impacts of the intervention on diverse aspects of health, reflecting promising strides in metabolic and CV health management, although highlighting areas warranting continued attention and potential intervention optimization.

Table 4. Wilcoxon test results

		N	Mean Rank	Sum of Ranks	Z	P-value
Post Hga1c (%) - Pre HgA1c (%)	Negative Ranks	22	11.50	253.00	−4.110	<0.001
	Positive Ranks	0	0.00	0.00		
	Ties	0				
	Total	22				
Post Weight (kg) - Pre Weight (kg)	Negative Ranks	22	11.50	253.00	−4.109	<0.001
	Positive Ranks	0	0.00	0.00		
	Ties	0				
	Total	22				
Post Cholesterol (mg/dl) - Pre Cholesterol (mg/dl)	Negative Ranks	19	11.84	225.00	−3.199	0.001
	Positive Ranks	3	9.33	28.00		
	Ties	0				
	Total	22				
Post TG (mg/dl) - Pre TG (mg/dl)	Negative Ranks	17	13.24	225.00	−3.199	0.001
	Positive Ranks	5	5.60	28.00		
	Ties	0				
	Total	22				
Post HDL (mg/dl) - Pre HDL (mg/dl)	Negative Ranks	7	9.71	68.00	−1.901	0.057
	Positive Ranks	15	12.33	185.00		
	Ties	0				
	Total	22				
Post LDL (mg/dl) - Pre LDL (mg/dl)	Negative Ranks	16	12.69	203.00	−2.484	0.013
	Positive Ranks	6	8.33	50.00		
	Ties	0				
	Total	22				
Post ALT (U/L) - Pre ALT (U/L)	Negative Ranks	20	11.78	235.50	−3.542	<0.001
	Positive Ranks	2	8.75	17.50		
	Ties	0				
	Total	22				
Post Creatinine (mg/dl) - Pre Creatinine (mg/dl)	Negative Ranks	8	8.00	64.00	−0.216	0.829
	Positive Ranks	8	9.00	72.00		
	Ties	6				
	Total	22				

5. Discussion:

The distribution of different anti-diabetic medications among participants was close to that in a previous retrospective study, especially regarding the sodium-glucose co-transporter-2 inhibitor group (47.1%); however, it was 75% for metformin and 43.9% for insulin. In general, these variations might be explained by different guidelines, clinical decisions, and patient circumstances (9). The results from the post-semaglutide time point indicated a significant improvement in HgA1c levels (p<0.001) mirroring findings from numerous international studies (7–9). Additionally, the decrease in weight among participants post-intervention was substantial enough to yield a significant p-value of less than 0.001 (7–10). In this study, lipid metabolism showed improvement, as evidenced by significant reductions in fasting total cholesterol, TG, and LDL levels (p=0.001, p=0.001, p=0.013, respectively). However, there was no notable change in fasting HDL level.

According to one study, patients with type 2 diabetes who took semaglutide saw a significant reduction in their total cholesterol levels (9). Another retrospective study showed that total cholesterol and TG improved among type 2 diabetes patients who switched to semaglutide, with clinical significance (11). An article exploring the effect of semaglutide on the lipid profile of diabetic patients reported significant enhancements in total cholesterol, HDL, LDL, and TG (12). In general, we observed a favorable effect of semaglutide on the lipid profile of diabetic patients. Nonetheless, variations in previous trials suggest potential influences from factors such as lifestyle awareness, family history of dyslipidemia, and the use of statin medications, which may account for the differences. Liver enzyme function significantly diminished after the initiation of semaglutide. The same change was noted in other research evaluating the effect of semaglutide on liver enzymes in diabetic and/or obese patients (9,13,14). Weight reductions might play a role in the enhancement of liver enzyme function. One clinical factor we observed was serum creatinine, which showed no significant alteration (p=0.829). A Japanese retrospective study reported a similar outcome. The limited sample size in both studies may have influenced this observation (11).

6. Limitations:

The study conducted at the KFU Polyclinic may have limited generalizability due to its single-center design. The absence of a control group makes it difficult to attribute changes in health outcomes solely to the intervention. Selection bias is possible since participants were selected from those already attending the clinic. Excluding certain participants (e.g., those under 18 years or with specific conditions) limits the study's applicability to a broader diabetic population. Varying semaglutide dosages and a short 6-month follow-up period may affect the consistency and long-term insights of the results. Data collection only at baseline and 6 months might miss intermediate changes. The small sample size and non-normal distribution of variables required non-parametric tests, potentially limiting robustness. Some data may be subject to recall bias and inaccuracies. The study did not control for all confounding factors, such as dietary habits and physical activity levels.

7. Conclusion:

The current study sought to investigate the efficacy of OW semaglutide among persons with type 2 diabetes by measuring HgA1c, body weight, and other health outcomes. The data show that the intervention had a significant influence on the participants' health outcomes, as reflected by improvements in numerous important parameters from pre- to post-intervention assessments. Taken together, these findings point to areas that should be prioritized for further research and intervention enhancement. A further study could assess the long-term effects of OW semaglutide among persons with type 2 diabetes, particularly in the Saudi population.

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