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Original Research

Effects of Adding Semaglutide to Basal-Bolus or Mixed Insulin Therapy: A Retrospective Chart Review

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Abstract

Background: Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), has demonstrated beneficial effects when incorporated into basal insulin therapy. Despite mounting evidence from diverse geographical regions supporting its efficacy in more intricate insulin regimens for patients with type 2 diabetes (T2DM), there remains a scarcity of real-world data from our region. This study aims to assess the impact of adding Semaglutide to the basal-bolus or mixed insulin therapy over a 12-month period on glycated hemoglobin (HbA1c), weight, and total daily dose (TDD) of insulin. **Methods:** A retrospective chart review was conducted at a military medical center in Riyadh from January 2021 to September 2022. The study included all adult patients with T2DM who experienced clinical benefit from the addition of Semaglutide to basal-bolus or mixed insulin therapy during this timeframe. Measurements of HbA1c, weight, and TDD were obtained at baseline, 3, 6, and 9 months. Descriptive statistics and one-way ANOVA tests were utilized for statistical analysis. **Results:** The study cohort comprised 152 patients, of whom 105 (69.1%) were female, with a mean age of 57.7+11.4 years. There was a significant reduction in mean HbA1c levels from 9.32 at baseline to 8.62, 8.28, and 8.36 at three, six, and nine months, respectively (p-value <0.001). Moreover, mean weight in kilograms (kg) decreased from 94.8 kg at baseline to 93.54, 92.46, and 91.94 kg at three, six, and nine months, respectively (p-value > 0.005). **Conclusion:** This study demonstrates that the addition of Semaglutide to the current treatment regimen of patients with T2DM leads to improvements in HbA1c levels, accompanied by observed reductions in weight over nine months in individuals utilizing basal-bolus or mixed insulin therapy. Further studies with extended follow-up periods are warranted to validate these findings.

Keywords: Semaglutide; Basal Insulin, Bolus Insulin, Mixed Insulin, T2DM, Saudi Arabia

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INTRODUCTION

Type 2 diabetes mellitus (T2DM), a complex metabolic disorder, is characterized by a progressive decline in pancreatic beta cell function and insulin resistance, resulting in hyperglycemia [1,2]. As the disease advances, patients usually transition from oral antidiabetic drugs to injectable therapies, such as insulin, to meet their increasing insulin requirements [2,3]. Insulin treatment, however, may fail to maintain glycemic targets due to potential adverse effects such as hypoglycemia and weight gain [2,4,5].

To mitigate these challenges, newer injectable therapies, including glucagon-like peptide 1 receptor agonists (GLP-1 RA), have been developed, offering several advantages, such as weight loss, cardiovascular protection, and improved glycemic control [5-7]. Current diabetes guidelines even recommend a GLP-1 agonist as a second-line therapy option after metformin for patients with T2DM [4-6].

Semaglutide, a GLP-1 RA, stands out due to its unique properties [7]. It shares a 94% amino acid sequence homology with native GLP-1 RA and has been structurally engineered to enhance resistance to degradation by dipeptidyl peptidase-4 and improve binding to albumin [7,8]. These modifications result in a half-life of approximately a week, making once-weekly subcutaneous administration possible [7,8].

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Clinical trials have demonstrated the beneficial effects of Semaglutide, including significant reductions in glycated hemoglobin (HbA1c) and body weight when added to basal insulin therapy [9,10]. A meta-analysis has found that integrating a GLP-1 RA into various pre-existing insulin regimens decreased HbA1c levels by 0.47%, a weight reduction, and similar rates of hypoglycemic events [11]. Another study in 2019 assessed the effects of adding GLP-1 RA to three distinct insulin therapies: basal insulin alone, basal-bolus combinations, and U-500 insulin [12].

However, there is limited real-world evidence in Saudi Arabia on its use in conjunction with more complex insulin regimens like basal-bolus or mixed insulin. Therefore, this study aims to explore the impacts of adding Semaglutide to different insulin regimens (basal-bolus and mixed insulin) in a population of patients with T2DM, focusing on variables such as HbA1c and weight loss.

METHODS

Study Design and Settings, and Population

A single-center retrospective cohort study was conducted at a military medical city, in the central region of Saudi Arabia, from January 1, 2021, to September 30, 2022. The study included patients over 18 years of age with T2DM managed by a primary care physician or endocrinologist/diabetologist. All patients had Semaglutide added to their existing basal-bolus insulin regimen. Exclusion criteria were those who had received Semaglutide for less than 3 months, individuals with type 1 diabetes, contraindications to GLP-1 agonists, those utilizing an insulin pump, or women who were pregnant or had gestational diabetes.

Data Collection

For data collection, a list of patients diagnosed with type 2 DM and treated with Semaglutide was obtained from the patient's electronic medical records. Patient baseline data for HbA1c, weight, and TDD of insulin were reviewed at 3, 6, and 9 months. Outcomes were collected from patients' medical electronic profiles using an Excel sheet v. 2022.

Study Variables

The outcome variables assessed in this study were changes in HbA1c, body weight, and TDD after initiating treatment with Semaglutide. Specifically, HbA1c levels were evaluated at baseline before starting Semaglutide and subsequently at three months, six months, and nine months after Semaglutide initiation. Body weight in kilograms (kg) was measured at the same time intervals. Additionally, TDD of insulin in units per day (units/day) was documented at baseline before Semaglutide and after adding Semaglutide.

Statistical Analysis

Data were analyzed using SPSS version 25 after variables were cleaned and coded in an Excel sheet. Descriptive statistics, including means, standard deviations, percentages, and frequencies, were calculated. A repeated measures ANOVA was conducted to compare changes in HbA1c from baseline to 3 months, six months, and nine months. P-value < 0.05 was considered statistically significant.

Ethical Approval

The study protocol was reviewed and approved by the Prince Sultan Military Medical City Scientific Research Center HP-01-R079 with number 1659, dated December 1, 2022, before the study was conducted.

RESULTS

Patients who were primarily screened to be enrolled in the study were 3814. Only 152 patients met the inclusion criteria. Of those, 47 (30.9%) patients were males and 105 (69.1%) were females. The mean age of the participants was 57.5 ± 11.4 (Table 1).

The data showed that the majority of patients 101(32.9%), 69 (22.5%), 40 (13%), 16 (5.2%) 15 (4.9%) and 12 (3.9) were suffering from hypertension, dyslipidemia, obesity, ischemic heart disease thyroid disorder, and renal disease respectively. Whereas, less frequent comorbidities included bronchial asthma (2.3%) heart failure (1.6%), liver disease (1.3%), and multiple strokes (1.0%). Further, rare comorbidities that affected 0.3% of patients included Hodgkin lymphoma, bronchial asthma, hysterectomy, erectile dysfunction, atrial fibrillation, neuroendocrine tumors, gout, osteoarthritis, benign prostatic hyperplasia, obstructive sleep apnea, fibromyalgia, inflammatory bowel disease, cholecystectomy, major depressive disorder, old ischemic stroke, post-stroke epilepsy, depression, and epilepsy. Only 2.6% of patients had no comorbidities. Overall, hypertension, dyslipidemia, and obesity were the most prevalent comorbid conditions among the studied sample of 152 patients (Table 2).

The data show that patients on basal-bolus therapy were 103 of the total sample. Of those, 87 patients were on insulin Aspart plus insulin glargine and only 14 patients were on insulin Lispro plus insulin glargine. On the other hand, 49 (32.2%) patients were on mixed insulin therapy (Aspart + Protamine). Patients' data showed that the majority of patients (84.8%) were using additional non-insulin diabetes medications, most commonly metformin (78.3%). Other non-insulin medications included empagliflozin (9.9%), metformin plus empagliflozin (5.9%), linagliptin (4.6%), and vildagliptin (1.3%). Basal-bolus insulin regimens were most common, with insulin aspart plus glargine being the predominant combination. (Table 3).

Table 1: Sociodemographic characteristics of patients (n = 152)

Sociodemographic characteristics		**N**	**%**
Gender	Male	47	30.9
	Female	105	69.1
		Mean	SD
Age		57.5	11.4

SD: Standard deviation

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Table 2: Comorbidities of patients (n = 152).

Comorbidities	N	%
HTN	101	32.9
RENAL DISEASE	12	3.9
IHD	16	5.2
HF	5	1.6
Liver Disease	4	1.3
Thyroid disorder	15	4.9
DLP	69	22.5
Obesity	40	13
Osteoporosis	2	0.7
BA	7	2.3
Multiple strokes	3	1
Other Comorbidities	22	7.1
No Comorbidities	11	3.6

HTN: Hypertension. IHD: Ischemic heart disease. HF: Heart failure. DLP: Dyslipidemia. BA: Bronchial Asthma. AF: Atrial fibrillation.

Table 3: Medications type among patients

Medication Type	N	%
Type of insulin		
Basal + bolus	103	67.8
Mixed Insulin	49	32.2
Basal + bolus		
Aspart + Glargine	87	84.5
Aspart + Detemeir	0	0
Lispro + Glargine	14	13.6
Lispro + Detemeir	0	0
No determine	2	1.9
Mixed Insulin		
Aspart + Protamine	49	100
Other	0	0
Other diabetic medication		
Yes	129	84.8
No	23	15.2
Type of other diabetic medication		
Metformin	119	78.3
Empafliglozin	15	9.9
Metformin + Empafliglozin	9	5.9
Linagliptin	7	4.6
Vildagliptin	2	1.3

The data in Table 4 show the effect of adding semaglutide to insulin on glycemic control, TDD, and weight over a nine-month period. At baseline, the mean HbA1c was 9.32 ± 1.61, the mean TDD was 87 units ± 41.99, and the mean weight was 94.8 ± 19.48 kg. After three-month, significant reductions were observed in mean HbA1c, (8.62% ± 1.553), however, the mean weight showed a reduction but not significant (93.54 ± 17.59 kg), while mean TDD remained stable at 85.08 ± 39.33 units. After six months, improvements were seen in mean HbA1c reaching 8.28 ± 1.626 and weight reduction to 92.46 ± 17.71 kg, although TDD did not change with a mean of 87.26 ± 43.25 units. At nine months, mean HbA1c, weight, and TDD were 8.36 ± 1.511, 91.94 ± 18.16 kg, and 86.68 ± 42.68 units, respectively. Overall, glycemic control and weight improved over the 9-month follow-up, with the most significant reductions occurring in glycemic control by the first 3–6 months. TDD remained relatively unchanged over time.

A one-way ANOVA test assessed differences in HbA1c, weight, and TDD over time in patients on basal-bolus insulin regimens in Table 5. HbA1c value was changed significantly from baseline to 3, 6, and 9 months ($F = 7.556$, $P < 0.001$). Mean HbA1c decreased from 9.31% at baseline to 8.65%, 8.35%, and 8.45 at 3, 6, 9 months respectively. No significant differences were found in weight or TDD over time. Weight remained stable from baseline (mean 93.7 kg) to 9 months (mean 90.9 kg) ($F = 0.534$, $p = 0.660$). TDD also did not significantly change from baseline (mean 86.9 units) to 9 months (mean 85.2 units) ($F = 0.046$, $p = 0.987$).

A one-way ANOVA test was conducted to assess differences in HbA1c, weight, and TDD over time for patients on Semaglutide added to mixed insulin regimens as seen in Table 6. There was a significant difference in HbA1c from baseline to 3, 6, and 9 months ($F = 8.453$, $p<0.001$). Mean HbA1c decreased from 9.3% at baseline to 8.1% at six months and 8.2% at nine months. No significant differences were found in weight or TDD over time. Weight remained stable from baseline (mean 97.0 kg) to 9 months (mean 94.2 kg) ($F = 0.234$, $p = 0.873$). TDD also did not significantly change from baseline (mean 87.1 units) to 9 months (mean 89.8 units) ($F = 0.360$, $p = 0.782$). In summary, patients on Semaglutide added to mixed insulin regimens significantly reduced HbA1c over time, while weight and insulin dose remained unchanged.

DISCUSSION

DM is a major global health concern [13]. This issue has garnered significant attention, especially in Gulf countries including Saudi Arabia (SA), which is among the top 10 countries with the highest prevalence of diabetes [13]. In 2019, SA had 4.3 million diabetic patients, ranking fourth among Middle Eastern and North African (MENA) nations [14,15]. Achieving targeted glycemic control levels, particularly HbA1c, is the most effective way to prevent and mitigate the effects of type 2 diabetes [15]. Therefore, this retrospective study aimed to report on the effects and practical use of Semaglutide in Saudi patients with T2DM who received Semaglutide in addition to either mixed insulin therapy or basal-bolus therapy.

The data analysis for this study involving T2DM patients on insulin therapy revealed that adding a once-weekly Semaglutide injection to their current regimen resulted in

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Table 4: Changes in HbA1c, weight, and TDD of insulin over nine months

Measurement	N	Mean	SD	F	p-value
HbA1c baseline	152	9.32	1.613	13.575	0.000*
HbA1c 3 months	152	8.62	1.553		
HbA1c 6 months	152	8.28	1.626		
HbA1c 9 months	152	8.36	1.511		
Weight baseline	152	94.8	19.48	0.727	0.536
Weight 3 months	152	93.54	17.586		
Weight 6 months	152	92.46	17.711		
Weight 9 months	152	91.94	18.158		
TDD of insulin baseline	152	87.013	41.9918	0.084	0.969
TDD of insulin 3 months	152	85.079	39.3343		
TDD of insulin 6 months	152	87.2582	43.24915		
TDD of insulin 9 month	152	86.684	42.6828		

SD: Standard deviation. TDD: Total daily insulin dose.

* P-value < 0.05 (significant)

Table 5: One-way ANOVA test for differences between patients who had basal + bolus.

Measurement	Mean	SD	F	p-value
HbA1c				
HbA1c baseline	9.31	1.5	7.556	0.000*
HbA1c 3 months	8.65	1.6		
HbA1c 6 months	8.35	1.6		
HbA1c 9 months	8.45	1.6		
Weight				
Weight baseline	93.7	18.9	0.534	0.66
Weight 3 months	92.8	16.3		
Weight 6 months	91.8	16.4		
Weight 9 months	90.9	16.6		
TDD				
TDD of insulin (baseline)	86.9	43.4	0.046	0.987
TDD of insulin (3 months)	85.3	40.5		
TDD of insulin (6 months)	84.9	45.2		
TDD of insulin (9 month)	85.2	44.4		

SD: Standard deviation. TDD: Total daily insulin dose.

* P-value < 0.05 (significant).

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Table 6: One-way ANOVA test for differences between patients who mixed insulin.

Measurement	Mean	SD	F	p-value
HbA1c.				
HbA1c baseline	9.3	1.8	8.453	0.000*
HbA1c 3 months	9.3	1.8		
HbA1c 6 months	8.1	1.6		
HbA1c 9 months	8.2	1.4		
Weight				
Weight baseline	97	20.6	0.234	0.873
Weight 3 months	95.2	20		
Weight 6 months	93.9	20.5		
Weight 9 months	94.2	20.9		
TDD				
TDD of insulin (baseline)	87.1	39.2	0.36	0.782
TDD of insulin (3 months)	84.5	37.2		
TDD of insulin (6 months)	92.2	38.8		
TDD of insulin (9 months)	89.8	39.1		

SD: Standard deviation. TDD: Total daily insulin dose.

* P-value < 0.05 (significant).

significant improvements. There was a notable decrease in mean HbA1c, total body weight, and TDD of insulin over nine months. GLP-1 RAs are now a standard feature in management guidelines for T2DM, with their effects on HbA1c levels, body weight, and insulin dose being extensively studied [7-10,12,15]. In our study, the mean reduction in HbA1c was 0.96%, which is clinically significant considering that every 1% drop in HbA1c is associated with reductions in diabetes complications [16]. Additionally, higher baseline HbA1c levels were associated with greater overall reductions in HbA1c values [17]. The HbA1c improvement observed is consistent with previous randomized controlled trials showing 0.7–1.9% HbA1c reductions when Semaglutide is added to multiple daily injections (MDI) or premixed insulin therapy [18].

The observed weight loss in our study (-2.86 kg at nine months) aligns with findings from RCTs reporting average reductions of 2.5–6.5 kg [19-21]. The combination of basal insulin and GLP-1RA offers potent glucose-lowering effects and results in less weight gain compared to intensified insulin regimens [22]. Various studies have shown similar benefits when GLP-RA is added to MDI, with data indicating variable degrees of weight loss [18]. Linda et al. reported that body weight was significantly reduced in participants on MDI in the liraglutide group compared to the placebo group by an average of -3.8 kg [23]. Although Gyorffy's study found that the weight drop was not statistically significant, the overall trend indicated a decrease in weight that plateaued at the 12-month endpoint across various insulin regimens with the addition of a GLP-1 RA [12]. Exenatide, in combination with basal/MDI insulin in patients with T2DM, was associated with a mean weight loss of -5.2 kg (P-value<0.001), with 72% of evaluable patients losing weight over 12 months [24]. Another study exploring the use of GLP-1RA in T2DM patients on premixed insulin over 12 months showed an average weight change of -2.2 kg [25]. This variable degree of weight loss could be attributed to several factors, including proper GLP-RA dose instruction and titration, dietary factors, and lifestyle among diabetic patients in the Saudi Arabian population [26]. Additionally, insulin-induced weight gains due to its anabolic physiological effects, decreased metabolic rate, and reduced glycosuria after glycemic control are other determinant factors [27]. Overall, our study showed that the addition of GLP-1 RA therapy to MDI therapy appears to cause weight loss and prevent additional weight gain while being on intensified insulin therapy.

The improvements in HbA1c and body weight observed in our study are comparable to those reported in the SUSTAIN 5 trial, which showed a mean reduction in HbA1c levels between 1.4-1.85% and weight loss of 3.7-6.4 kg after 30 weeks of treatment when Semaglutide was added to basal insulin in patients with uncontrolled T2DM [17]. Notably, the maximum reductions in HbA1c and apparent weight loss in our study were achieved within the first 3–6 months of initiating Semaglutide, mirroring the rapid time-to-effect observed in clinical trials [21]. This rapid onset of benefits can be particularly advantageous for patients requiring immediate improvements in glycemic control, potentially enhancing patient motivation and adherence to treatment, which is vital in chronic disease management [28]. Furthermore, Semaglutide may provide an advantage by improving insulin sensitivity and reducing insulin requirements, thereby minimizing adverse effects like hypoglycemia and weight gain associated with high insulin doses [21,28].

As in clinical practice, it is recommended to reduce the total daily dose (TDD) of insulin initially or throughout the treatment

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in patients with controlled blood glucose [29], as studies have shown significant TDD reductions in patients on MDI with GLP-1 RAs [22, 25]. This study observed fluctuating insulin dose levels over the study period. However, in the study by Sassenrath et al., where a total of 8 studies evaluated the addition of a GLP-1 RA to MDI injections, only 3 studies that allowed insulin adjustment after the addition of GLP-1 RA showed an average TDD reduction [18]. Although our analysis did not reveal the anticipated decline in TDD and significant weight loss documented in previous studies, it aligns with Gyorffy et al., who reported no significant reduction in TDD and weight with the addition of a GLP-1 RA in specific insulin groups[12]. The characteristics of the studied population could account for the fluctuation in TDD, and the insignificant weight loss achieved. This suggests that the study population's inadequate control with suboptimal insulin doses or high insulin requirements was based on baseline demographics. Given that the effectiveness of GLP-1 RAs relies on multiple factors, including incretin effect and insulin production, it is conceivable that the advanced T2DM patients had impaired beta cell activity and thus were unable to sustain a response to the GLP-1 RA [21].

This study's strengths lie in its real-world setting and its focus on combining Semaglutide with more intensive and complex insulin regimens. However, the retrospective design and the use of a single center, along with our sample size, introduce certain limitations. These include potential selection bias, a lack of randomization, and the presence of confounding factors, which could impact the generalizability of the findings. Larger, multicenter randomized studies are needed to support these findings and fully understand the long-term implications of adding Semaglutide to complex insulin regimens. Further research is necessary to investigate the clinical outcomes and treatment approaches of combining a GLP-1 RA with different insulin regimens, especially in patients whose diabetes is poorly controlled and who require more intensive treatment plans.

CONCLUSION

Overall, adding once-weekly Semaglutide to basal-bolus or mixed insulin therapy led to significant improvements in HbA1c over 3, 6, and 9 interval periods in T2DM patients with fluctuating TDD of insulin and an overall trend down in body weight. The results of Semaglutide among the GLP-1 RA group further support its beneficial option for optimizing glycemic control when insulin fails to maintain diabetes treatment targets. It further indicates the potential of semaglutide as an adjunct therapy in T2DM, particularly for patients struggling with both uncontrolled glycemic control and obesity, highlighting the need for individualized treatment approaches and further research in this area.

AUTHOR CONTRIBUTIONS

A.A.J, K.M.A, B.A.A., M.A., D.F.A., E.E.A.,contributed to the data curation, writing—original draft, Writing—review & editing. H.A.B., I.M.D., W.M., A.H.A., to the conceptualisation, methodology, Writing—review & editing, supervision, and project administration. A.A.J. contributed formal analysis, writing—review & editing. All authors have read and agreed to the published version of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

References

1. Galicia-Garcia, U.; Benito-Vicente, A.; Jebari, S.; Larrea-Sebal, A.; Siddiqi, H.; Uribe, K.B.; Ostolaza, H.; Martín, C. Pathophysiology of Type 2 Diabetes Mellitus. Int. J. Mol. Sci. 2020, 21, 6275, doi:10.3390/ijms21176275
2. Padhi, S.; Nayak, A.K.; Behera, A. Type II Diabetes Mellitus: A Review on Recent Drug Based Therapeutics. Biomed. Pharmacother. 2020, 131, 110708, doi:10.1016/j.biopha.2020.110708.
3. Ortiz-Martínez, M.; González-González, M.; Martagón, A.J.; Hlavinka, V.; Willson, R.C.; Rito-Palomares, M. Recent Developments in Biomarkers for Diagnosis and Screening of Type 2 Diabetes Mellitus. Curr. Diab. Rep. 2022, 22, 95–115, doi:10.1007/s11892-022-01453-4.
4. American Diabetes Association Professional Practice Committee 6. Glycemic Targets: Standards of Medical Care in Diabetes—2022. Diabetes Care 2022, 45, S83–S96, doi:10.2337/dc22-s006.
5. Choi, J.G.; Winn, A.N.; Skandari, M.R.; Franco, M.I.; Staab, E.M.; Alexander, J.; Wan, W.; Zhu, M.; Huang, E.S.; Philipson, L.; et al. First-Line Therapy for Type 2 Diabetes with Sodium–Glucose Cotransporter-2 Inhibitors and Glucagon-like Peptide-1 Receptor Agonists: A Cost-Effectiveness Study. Ann. Intern. Med. 2022, 175, 1392–1400, doi:10.7326/m21-2941.
6. Wojtara, M.; Mazumder, A.; Syeda, Y.; Mozgała, N. Glucagon-like Peptide-1 Receptor Agonists for Chronic Weight Management. Adv. Med. 2023, 2023, 9946924, doi:10.1155/2023/9946924.
7. Mahapatra, M.K.; Karuppasamy, M.; Sahoo, B.M. Semaglutide, a Glucagon like Peptide-1 Receptor Agonist with Cardiovascular Benefits for Management of Type 2 Diabetes. Rev. Endocr. Metab. Disord. 2022, 23, 521–539, doi:10.1007/s11154-021-09699-1.
8. Kalra, S.; Sahay, R. A Review on Semaglutide: An Oral Glucagon-like Peptide 1 Receptor Agonist in Management of Type 2 Diabetes Mellitus. Diabetes Ther. 2020, 11, 1965–1982, doi:10.1007/s13300-020-00894-y.
9. Pratley, R.E.; Crowley, M.J.; Gislum, M.; Hertz, C.L.; Jensen, T.B.; Khunti, K.; Mosenzon, O.; Buse, J.B. Oral Semaglutide Reduces HbA1c and Body Weight in Patients with Type 2 Diabetes Regardless of Background Glucose-Lowering Medication: PIONEER

Subgroup Analyses. Diabetes Ther. 2021, 12, 1099–1116, doi:10.1007/s13300-020-00994-9.
10. Røder, M.E. Clinical Potential of Treatment with Semaglutide in Type 2 Diabetes Patients. Drugs Context 2019, 8, 1–11, doi:10.7573/dic.212585.
11. Wang, W.; Liu, H.; Xiao, S.; Liu, S.; Li, X.; Yu, P. Effects of Insulin plus Glucagon-like Peptide-1 Receptor Agonists (GLP-1RAs) in Treating Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Diabetes Ther. 2017, 8, 727–738, doi:10.1007/s13300-017-0282-3.
12. Gyorffy, J.B.; Keithler, A.N.; Wardian, J.L.; Zarzabal, L.A.; Rittel, A.; True, M.W. The Impact of GLP-1 Receptor Agonists on Patients with Diabetes on Insulin Therapy. Endocr. Pract. 2019, 25, 935–942, doi:10.4158/ep-2019-0023.
13. IDF Diabetes Atlas Available online: https://diabetesatlas.org/ (accessed on 8 June 2024).
14. Alhazmi, A.; Sane, F.; Lazrek, M.; Nekoua, M.P.; Badia-Boungou, F.; Engelmann, I.; Alidjinou, E.K.; Hober, D. Enteroviruses and Type 1 Diabetes Mellitus: An Overlooked Relationship in Some Regions. Microorganisms 2020, 8, doi:10.3390/microorganisms8101458.
15. Alsheikh, A.; Alshehri, A.; Alzahrani, S.; Jammah, A.A.; Alqahtani, F.; Alotaibi, M.; Aldahash, R.; Alhozali, A.M.; Alsabaan, F.; Almehthel, M.; et al. Evaluating the Clinical Effectiveness and Safety of Semaglutide in Individuals with Uncontrolled Type 2 Diabetes. Real-World Evidence from Saudi Arabia: The Observational, Multicenter, 15-Month EVOLUTION Study. Diabetes Ther. 2024, 15, 473–485, doi:10.1007/s13300-023-01516-z.
16. Stratton, I.M.; Adler, A.I.; Neil, H.A.; Matthews, D.R.; Manley, S.E.; Cull, C.A.; Hadden, D.; Turner, R.C.; Holman, R.R. Association of Glycaemia with Macrovascular and Microvascular Complications of Type 2 Diabetes (UKPDS 35): Prospective Observational Study. BMJ 2000, 321, 405–412, doi:10.1136/bmj.321.7258.405.
17. Rodbard, H.W.; Lingvay, I.; Reed, J.; de la Rosa, R.; Rose, L.; Sugimoto, D.; Araki, E.; Chu, P.-L.; Wijayasinghe, N.; Norwood, P. Semaglutide Added to Basal Insulin in Type 2 Diabetes (SUSTAIN 5): A Randomized, Controlled Trial. J. Clin. Endocrinol. Metab. 2018, 103, 2291–2301, doi:10.1210/jc.2018-00070.
18. Sassenrath, K.; Phillips, B.B.; Stone, R.H. Evaluation of GLP-1 Receptor Agonists in Combination with Multiple Daily Insulin Injections for Type 2 Diabetes. J. Pharm. Pract. 2022, 35, 979–990, doi:10.1177/08971900211010678.
19. Lingvay, I.; Catarig, A.-M.; Frias, J.P.; Kumar, H.; Lausvig, N.L.; le Roux, C.W.; Thielke, D.; Viljoen, A.; McCrimmon, R.J. Efficacy and Safety of Once-Weekly Semaglutide versus Daily Canagliflozin as Add-on to Metformin in Patients with Type 2 Diabetes (SUSTAIN 8): A Double-Blind, Phase 3b, Randomised Controlled Trial. Lancet Diabetes Endocrinol. 2019, 7, 834–844, doi:10.1016/s2213-8587(19)30311-0.
20. Kellerer, M.; Kaltoft, M.S.; Lawson, J.; Nielsen, L.L.; Strojek, K.; Tabak, Ö.; Jacob, S. Effect of Once-weekly Semaglutide versus Thrice-daily Insulin Aspart, Both as Add-on to Metformin and Optimized Insulin Glargine Treatment in Participants with Type 2 Diabetes (SUSTAIN 11): A Randomized, Open-label, Multinational, Phase 3b Trial. Diabetes Obes. Metab. 2022, 24, 1788–1799, doi:10.1111/dom.14765.
21. Kapitza, C.; Dahl, K.; Jacobsen, J.B.; Axelsen, M.B.; Flint, A. Effects of Semaglutide on Beta Cell Function and Glycaemic Control in Participants with Type 2 Diabetes: A Randomised, Double-Blind, Placebo-Controlled Trial. Diabetologia 2017, 60, 1390–1399, doi:10.1007/s00125-017-4289-0.
22. American Diabetes Association Standards of Care in Diabetes—2023 Abridged for Primary Care Providers. Clin. Diabetes 2023, 41, 4–31, doi:10.2337/cd23-as01.
23. Lind, M.; Hirsch, I.B.; Tuomilehto, J.; Dahlqvist, S.; Ahrén, B.; Torffvit, O.; Attvall, S.; Ekelund, M.; Filipsson, K.; Tengmark, B.-O.; et al. Liraglutide in People Treated for Type 2 Diabetes with Multiple Daily Insulin Injections: Randomised Clinical Trial (MDI Liraglutide Trial). BMJ 2015, h5364, doi:10.1136/bmj.h5364.
24. Sheffield, C.; Kane, M.; Busch, R.; Bakst, G.; Abelseth, J.; Hamilton, R. Safety and Efficacy of Exenatide in Combination with Insulin in Patients with Type 2 Diabetes Mellitus. Endocr. Pract. 2008, 14, 285–292, doi:10.4158/ep.14.3.285.
25. Ehrhardt, N.; Fazeli, S.; Rao, S.; Amdur, R. Use of Premixed Insulin, Metformin, and a Glucagon-like Peptide 1 Receptor Agonist as a Therapeutic Approach for Uncontrolled Type 2 Diabetes. Diabetes Spectr. 2020, 33, 182–189, doi:10.2337/ds19-0025.
26. Almutairi, O.O.; Alhomaid, T.A.; Alshuaibi, A.M.; Ahmad Alahmad, R.M.; Al Mardhamah, N.H.; Alamri, T. The Influence of Eating Habits on Type 2 Diabetes in Saudi Arabia: A Systematic Review. Cureus 2023, doi:10.7759/cureus.42638.
27. Gupta, A. Metabolic and Physiological Effects of Insulin. In Understanding Insulin and Insulin Resistance; Elsevier, 2022; pp. 203–230 ISBN 9780128202340.
28. Isaacs, D.M.; Kruger, D.F.; Spollett, G.R. Optimizing Therapeutic Outcomes with Oral Semaglutide: A Patient-Centered Approach. Diabetes Spectr. 2021, 34, 7–19, doi:10.2337/ds20-0016.
29. Chen, M.; Vider, E.; Plakogiannis, R. Insulin Dosage Adjustments after Initiation of GLP-1 Receptor Agonists in Patients with Type 2 Diabetes. J. Pharm. Pract. 2022, 35, 511–517, doi:10.1177/0897190021993625.