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Long-Term Efficiency of Twice-Daily Exenatide in Type 2 Diabetes Mellitus: A Real-Life Study

ORIGINAL ARTICLE
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ABSTRACT

Objective: Exenatide (twice daily) has been used as a glucagon-like peptide-1 receptor agonist in patients with diabetes with inadequate glycemic control for over a decade. In this paper, we aimed to investigate the long-term glycemic control and change in body weight in patients treated with exenatide.

Methods: A total of 287 patients who were treated with exenatide twice daily between 2012 and 2022 were included in this retrospective study. The changes in glycated hemoglobin (HbA1c) levels and body weight were assessed over time after exenatide administration. The administered insulin dosage and metabolic parameters were documented. The baseline data were compared over a period of 3 months to 3 years.

Results: The study included 101 (36%) males and 186 (64%) females, with an average age of 56.4 ± 10.7 years. The baseline HbA1c level was 8.0 ± 1.8%, and the body mass index was 38.8 ± 5.9 kg/m^2. The HbA1c level had decreased by 1.29% from the baseline at 3 months ($P < .001$), which continued up to 3 years (−0.63%, $P = .010$). During the 3-year period, body weight continued to decrease significantly (−12.1, $P < .001$). Glucose levels were significantly reduced, but the lipid levels and glomerular filtration rate after exenatide treatment were similar. Notably, exenatide administration resulted in a decrease in insulin dosage for patients treated with insulin.

Conclusion: Exenatide therapy produced continued improvements in glycemic control and progressive weight loss for 3 years in patients with diabetes in a real-life setting.

Keywords: Exenatide, glucagon-like peptide-1 receptor agonist, type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic, progressive disease characterized by insulin resistance and hyperglycemia, which lead to multiple micro- and macro-vascular complications. In Türkiye, the prevalence of T2DM is approximately 16.5%, and it has been showing an increasing trend over the years.[1] The pathogenesis of diabetes includes insulin resistance and progressive pancreatic beta-cell failure, which deteriorate glycemic control and require the intensification of glucose-lowering therapies.[2] Despite improvements in the treatment options for T2DM, achieving adequate glycemic control remains a frequent challenge.[3]

Glucagon-like peptide-1 receptor agonist (GLP-1 RA) has emerged as a treatment option for diabetes over the last decade. GLP-1 RAs enhance glucose-dependent pancreatic insulin production and inhibit pancreatic glucagon by mimicking the effects of endogenous incretins. Additionally, they decrease postprandial glycemia and promote satiety by delaying stomach emptying, which results in weight loss.[4] GLP-1 RAs are suggested as an alternative to insulin for inadequate control with oral antidiabetic drugs (OADs) in patients with T2DM.[5]

Exenatide is the first GLP-1 RA to be proven effective as an adjunct therapy for T2DM. The glucose-lowering mechanism of exenatide is similar to that of other GLP-1 RAs. Additionally, exenatide increases beta-cell responsiveness to glucose and promotes islet cell neogenesis, or pancreatic beta-cell proliferation.[6-8] An exenatide dose of 5-10 µg twice a day reportedly reduces glycated hemoglobin (HbA1c) levels in patients with inadequate glycemic control with metformin and/or sulfonylurea.[9] This improvement was also observed in patients treated with basal insulin.[10]

Currently, 9 formulations of injectable GLP-1 RAs have been approved for the treatment of T2DM in Europe. Despite randomized clinical trials and real-life observational studies,

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long-term data regarding the efficacy of exenatide treatment is still represented by a limited number of studies.[11-15]

Herein, we aimed to investigate long-term glycemic control and evaluate changes in body weight in patients treated with exenatide.

Materials and Methods

This retrospective study included patients with T2DM who were treated with twice-daily exenatide at the Dokuz Eylül University Research and Application Hospital between December 2012 and December 2022. This study has been approved by the Ethics Committee of Dokuz Eylül University Faculty of Medicine (Approval number: 2021/26-02, Approval date: September 22, 2021). This study was conducted retrospectively, and therefore, informed consent was not obtained from the patients. The medical records of these patients who had been treated with various OADs (metformin, sulfonylureas, sodium–glucose transport protein-2 inhibitors, or thiazolidinediones) with or without insulin (basal or intensive insulin regimen) before exenatide use were reviewed. Of the 628 patients scrutinized, 341 were excluded due to insufficient data; thus, 287 were included in the study. Patients who were younger than 18 years of age and had been diagnosed with type 1 diabetes or gestational diabetes have been excluded.

The following data about the patients was documented: demographic characteristics, duration of diabetes, comorbidities, insulin dose, and OADs used. The following data were collected after the initiation of exenatide up until discontinuation or the last visit: weight, body mass index (BMI), HbA1c level, fasting plasma glucose (FPG) level, lipid parameters, urine albumin–creatinine ratio (uACR), and glomerular filtration rate (GFR). In addition, duration, side effects, and reasons for discontinuing exenatide treatment were also noted. The baseline data were compared with those obtained 3, 6, 12, 24, and 36 months after initiating exenatide treatment. The changes in HbA1c levels over time and the long-term effects of exenatide on the patients' weight, lipid levels, and other biological parameters were evaluated. Additionally, any changes in the insulin dosage or the discontinuation of insulin therapy in patients who were already receiving insulin treatment after the initiation of exenatide were also investigated.

Statistical Analysis

Descriptive statistics, frequencies, percentages, means, and standard deviations of the collected data were obtained. The suitability for the normal distribution of variables was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. The differences between normally distributed variables were evaluated using the paired *t*-test, while the Wilcoxon signed-rank test was employed for non-normally distributed variables. Categorical variables were scrutinized utilizing Fisher's exact test and chi-square test. All data were analyzed using the Statistical Package for the Social Sciences Statistics software, version 29.0 (IBM Corp., Armonk, NY, USA). Statistical significance in all tests was quantified at the $P < .05$ level.

MAIN POINTS

- Over the last decade, glucagon-like peptide-1 receptor agonists have emerged as a viable treatment option for diabetes. We investigated the long-term glycemic control and changes in body weight in patients with diabetes treated with exenatide.
- Our study showed that patients experienced a continued improvement in glycated hemoglobin levels and weight reduction for up to 3 years in a real-life setting.
- We also observed a decrease in the amount of insulin units administered when exenatide was added, and some patients were able to discontinue insulin altogether.

Results

Baseline Characteristics of the Patients

The study comprised a total of 287 patients diagnosed with T2DM, among whom 101 (35%) were male and 186 (64%) were female. The mean age of the patients was 56.4 ± 10.7 years, and the mean duration of diabetes was 11.9 ± 8 years. The baseline HbA1c level was 8.0 ± 1.8%. The patients' mean body weight and BMI were 106 ± 18 kg and 38.8 ± 5.9 kg/m^2, respectively. Microalbuminuria was observed in 46 (16%) patients, and 12 patients had a GFR < 60 mL/min/1.73 m^2. There were 191 (66%) patients using OAD, and 96 (33%) patients were treated with basal or basal–bolus insulin regimens with the OADs (Table 1).

The mean duration of exenatide treatment was 25.2 ± 12.4 months (minimum–maximum: 1-132 months). Of the 287 included patients, 84 (29%) were treated with exenatide for less than 1 year. After 3 years, only 71 (25%) patients were still being administered exenatide. During the follow-up period, exenatide treatment was discontinued in 80 (28%) patients. The 3 most common reasons for discontinuation

Table 1. Demographic Data and Baseline Characteristics of the Patients

Characteristic	Value
Age (years), mean ± SD	56.4 ± 10.7
Sex, n (%)	
Female	186 (64.8)
Male	101 (35.1)
Duration of diabetes (years), mean ± SD	11.9 ± 8
Body weight (kg), mean ± SD	106 ± 18
Body mass index (kg/m^2), mean ± SD	38.8 ± 5.9
Comorbidities, n (%)	
Hypertension	191 (66.6)
Coronary artery disease	39 (13.6)
Cerebrovascular disease	6 (2.1)
Peripheral arterial disease	5 (1.7)
Microvascular disease, n (%)	
Polyneuropathy	56 (19.5)
Nephropathy	53 (18.5)
Retinopathy	15 (5.2)
Baseline treatment (number of OADs), n (%)	
None	20 (7)
1	102 (35.5)
2	82 (28.6)
≥3	83 (28.9)
Baseline treatment (insulin), n (%)	
None	191 (66.6)
Basal insulin ± OAD	50 (17.4)
Basal–bolus insulin ± OAD	46 (16)

SD, standard deviation; OAD, oral antidiabetic drug

were noncompliance (n = 19), nausea (n = 15), and poor glycemic control (n = 9).

Diabetes and Glycemic Control

The HbA1c level significantly decreased 3 months after exenatide administration in all patients (−1.29% vs. baseline; $P < .001$) (Figure 1). At the 6th, 12th, 24th, and 36th months, the reduction in HbA1c levels compared to the baseline was 0.73%, 0.68%, 0.77%, and 0.63%, respectively ($P < .05$) (Table 2). After 1 year, an HbA1c level < 7% was achieved in 58% of the patients. Additionally, when patients with a history of diabetes for >10 years were evaluated (n = 122), a significant decrease in HbA1c level from baseline was observed up to 3 years after exenatide treatment (−0.63% at 1 year, −0.81% at 2 years, and −0.83% at 3 years; $P < .05$). The HbA1c value decreased more in the first and second years in patients with an HbA1c >9% than in those with an HbA1c <9% (vs. baseline −2.64% at 1 year, $P = .006$ and −2.69% at 2 years, $P = .002$).

The change in HbA1c from baseline was evaluated based on age [in those >65 years old (n = 69) versus in those <65 years old (n = 218)] to determine if there were any age-specific differences in the response to exenatide treatment. In elderly patients, exenatide's effects were sustained. After 1 year, the mean change in HbA1c was −0.59% and −0.71% in patients aged >65 and <65 years, respectively. Furthermore, both groups had a significant decrease in HbA1c levels from the baseline ($P < .001$). The reduction in the HbA1c level was similar between both sexes. There was no difference in the decrease in HbA1c levels between those with morbid obesity (BMI ≥40 kg/m^2) and those without.

The FPG levels decreased significantly 3, 6, 12, and 24 months after exenatide administration ($P < .001$). After 2 years, the FBG level had been reduced by 24.4 mg/dL from the baseline. The levels of triglycerides, low-density lipoprotein (LDL), creatinine, and the glomerular filtration rate after exenatide administration did not show any significant changes from the baseline ($P > .05$). There was a decrease in the uACR in people with albuminuria (uACR > 30 mg/g, n = 46) after 1 year ($P = .028$) (Table 2).

Body Weight

The patients' body weight continued to decrease for up to 3 years after the initiation of exenatide treatment (Figure 2). The mean body weight decreased by 9.7 kg, 11.7 kg, and 12.1 kg from the baseline at 1, 2, and 3 years, respectively (Table 2). After 1 year, the weight loss was greater in patients with morbid obesity (n = 40) than those without ($P = .007$). This difference continued for up to 2 years ($P = .029$). In those with morbid obesity, the mean body weight was reduced by 13.7 kg, 15.7 kg, and 15.8 kg after 1, 2, and 3 years of exenatide administration, respectively. Age (<65 vs. ≥65 years), sex, and duration of diabetes (<10 years vs. ≥10 years) did not affect weight loss.

Table 2. Changes in the Clinical and Biological Parameters Over Time

	0-12 Months	0-24 Months	0-36 Months
Delta HbA1c (%) (Nb of evaluated patients)	−0.68* (87)	−0.77* (67)	−0.63* (39)
Delta body weight (Kg) (Nb of evaluated patients)	−9.7* (97)	−11.7* (81)	−12.1* (71)
Delta BMI (kg/m^2)	−3.4*	−4.1*	−4.2*
Changes in FPG (mg/dL)	−21.0*	−24.7*	−13.1
Changes in triglycerides (mg/dL)	−4.6	−8.8	−21.2
Changes in LDL (mg/dL)	0.1	1.3	2.3
Changes in GFR (mL/min/1.73 m^2)	−1.6	−1.36	−4.1
Changes in uACR (mg/g)**	−97.5**	NA	NA

Results are presented as differences of means. Paired sample *t*-test was used for the statistical analyses. Two-sided *P*-values < .05 were considered statistically significant.
BMI, body mass index; FBG, fasting plasma glucose; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein; NA, not applicable; uACR, urine albumin−creatinine ratio.
*The change was statistically significant between the time points.
**Values of change in uACR in those who had albuminuria (uACR >30, n = 46).

Insulin Dose and Number of Oral Antidiabetic Drugs

The OADs and/or insulin regimens remained unchanged from the treatment before exenatide administration, except for cases where dipeptidyl peptidase-4 inhibitors were discontinued if they were being used. The mean number of OADs used by the patients had decreased significantly from 1.7 to 1.4 by the end of the study ($P < .001$). Among the 96 patients using any insulin regimen before exenatide administration, insulin was discontinued by the end of the study in 17 (18%). During the follow-up period, the mean HbA1c level significantly decreased after 2 years in patients treated with any insulin regimen (−0.94% vs. baseline, $P = .002$). The mean insulin dose decreased from 43.2 ± 28.2 units to 29.4 ± 18.5 units in patients who continued insulin administration ($P < .001$).

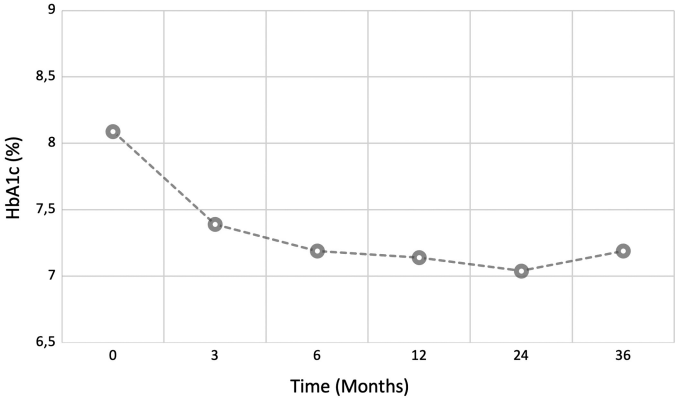

Figure 1. Evolution of the mean HbA1c concentration from baseline until 3 years after exenatide administration.

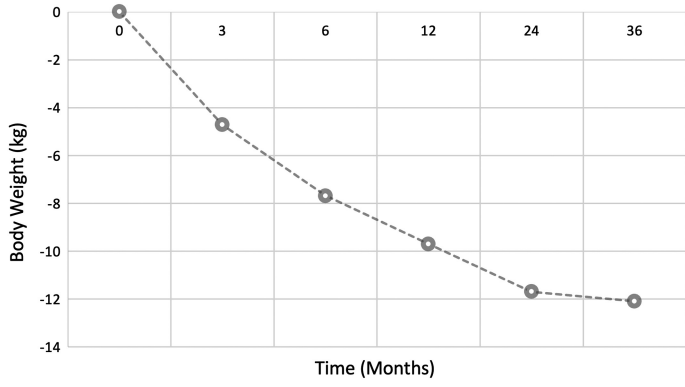

Figure 2. Mean changes in the body weight from baseline until 3 years after exenatide administration.

Discussion

In the last decade, GLP1 RAs have been utilized to treat T2DM and have demonstrated effectiveness in achieving glycemic control and weight loss. Dulaglutide and lixisenatide (in combination with glargine) are GLP-1 RAs approved for the treatment of diabetes by the Turkish Ministry of Health; however, only twice-daily exenatide administration is currently covered by the universal healthcare system in Turkey. Most observational and randomized trials have relatively short follow-up periods, and no real-life studies have been carried out in Turkey. Consequently, our objective was to evaluate the long-term effectiveness of exenatide in the treatment of T2DM over 3 years in a real-life setting.

The patients in this study indicated inadequate glycemic control (baseline HbA1c level: 8%), and a significant proportion were classified as obese (BMI 38.8 kg/m^2). Similar to previous studies, we identified a significant reduction in HbA1c levels with exenatide administration, beginning in the third month and continuing up to 3 years.[4,11,12] In our study, the HbA1c level was reduced by 1.2% after 3 months and by 0.6% after 3 years from the mean baseline of 8.0%. In 2 long-term studies involving 131 and 217 patients, the HbA1c level was reduced by 1.0% at 3 years.[11,12] Patients with a higher baseline HbA1c level (>9%) had a more significant reduction in HbA1c level (−2.6% at 1 year), which is consistent with the findings of previous reports. After 1 year, a glycemic target of HbA1c ≤7% was achieved in 58% of the patients; this value was 46% in an extension of the exenatide trial study.[12]

Exenatide's beneficial effect was also identified in elderly patients (>65 years), consistent with the findings of a previous report 12. In this current study, the reduction in HbA1c levels was relatively lower than in previous studies. This variance could be because certain studies included open-label extensions of controlled trials, whereas our approach involved a retrospective evaluation of the efficacy of exenatide.[12,14] Furthermore, we determined that the reduction in HbA1c levels was similar between sexes and independent of the body weight or duration of diabetes.

In the present study, the FPG level was decreased significantly up to 2 years after exenatide, in agreement with the findings of a previous study.[12] On the other hand, LDL and triglyceride levels were similar to their baseline levels. Exenatide trials have shown an improvement in the lipid profile;[14] however, similar to real-world studies, we determined that these were not long-term improvements.[11] Randomized trials have demonstrated that exenatide has the potential to decrease albuminuria in individuals with diabetic kidney disease.[16,17] Our research found that exenatide did not lead to a deterioration in the GFR over the long term and it even resulted in a reduction in uACR among patients with albuminuria after the first year.

Exenatide was associated with progressive weight loss caused by delaying stomach emptying and enhancing satiety. In our study, the reduction in body weight began at 3 months and continued until 3 years. Exenatide-induced weight loss has been proven in randomized trials and long-term studies of 1-4 years.[11-14,18,19] Deng et al[20] reported that baseline BMI did not affect the change in body weight. However, we found that more significant weight loss was seen in patients with a BMI >40 kg/m^2, consistent with the findings of some long-term studies.[12,14] Furthermore, we found that variables such as age, sex, and duration of diabetes did not affect the changes in body weight. The mean body weight and BMI reduction after 3 years of exenatide treatment were higher in our study than in randomized trials or real-life studies. This might be because the patients in our study had a higher BMI than those in previous studies.

In our study, adding exenatide to basal or intensive insulin regimens was associated with improved glycemic control, and HbA1c levels decreased significantly after 2 years. Insulin units administered decreased when exenatide was added. Furthermore, insulin was discontinued in 18% of patients on insulin treatment. Similar improvements in HbA1c levels were reported in a case series of 23 patients on a high-dose insulin regimen and a randomized trial of exenatide administration in addition to insulin glargine.[21,22] Additionally, the number of OADs used had decreased during the follow-up period. Therefore, it may be hypothesized that decreasing the number of antidiabetic medications or ceasing insulin use may improve patient compliance with exenatide therapy.

Due to the retrospective design of the study, it has some limitations. The number of patients included in the study decreased as the duration of exenatide administration increased. The hospital registry system was used to obtain patient data; hence, certain data such as side effects, body weight, and BMI of some participants could not be retrieved. Additionally, because the pandemic occurred during the last 2 years of the study, many patients with T2DM could not attend their routine visits. As a result, several patients' laboratory results were also missing from the statistical analysis.

In conclusion, exenatide therapy has been found to provide sustained improvements in glycemic control and progressive weight loss for up to 3 years in a real-life setting, consistent with the findings of previous randomized trials. Therefore, when conventional antidiabetic medications or insulin regimens are unable to achieve adequate glycemic control, exenatide can be considered as an additional alternative for diabetes treatment.

Data Availability Statement: The datasets used and/or analyzed in this study are available upon reasonable request from the corresponding author.

Ethics Committee Approval: This study has been approved by the Dokuz Eylül University Faculty of Medicine Ethics Committee (Approval number: 2021/26-02, Approval date: September 22, 2021).

Informed Consent: Due to the retrospective design of the study, informed consent was not obtained.

Peer-review: Externally peer-reviewed.

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References

1. Satman I, Omer B, Tutuncu Y, et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. *Eur J Epidemiol*. 2013;28(2):169-180. [CrossRef]

2. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359(15):1577-1589. [CrossRef]
3. Ali MK, Bullard KM, Saaddine JB, Cowie CC, Imperatore G, Gregg EW. Achievement of goals in U.S. diabetes care, 1999-2010. *N Engl J Med*. 2013;368(17):1613-1624. [CrossRef]
4. Guerci B, Charbonnel B, Gourdy P, et al. Efficacy and adherence of glucagon-like peptide-1 receptor agonist treatment in patients with type 2 diabetes mellitus in real-life settings. *Diabetes Metab*. 2019;45(6):528-535. [CrossRef]
5. Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia*. 2022;65(12):1925-1966. [CrossRef]
6. Xu G, Stoffers DA, Habener JF, Bonner-Weir S. Exendin-4 stimulates both beta-cell replication and neogenesis, resulting in increased beta-cell mass and improved glucose tolerance in diabetic rats. *Diabetes*. 1999;48(12):2270-2276. [CrossRef]
7. Zummo FP, Cullen KS, Honkanen-Scott M, Shaw JAM, Lovat PE, Arden C. Glucagon-like peptide 1 protects pancreatic β-cells from death by increasing autophagic flux and restoring lysosomal function. *Diabetes*. 2017;66(5):1272-1285. [CrossRef]
8. Zhou S, Sun Y, Xing Y, et al. Exenatide ameliorates hydrogen peroxide-induced pancreatic β-cell apoptosis through regulation of METTL3-mediated m(6)A methylation. *Eur J Pharmacol*. 2022;924:174960. [CrossRef]
9. Norris SL, Lee N, Thakurta S, Chan BK. Exenatide efficacy and safety: a systematic review. *Diabet Med*. 2009;26(9):837-846. [CrossRef]
10. Buse JB, Bergenstal RM, Glass LC, et al. Use of twice-daily exenatide in Basal insulin-treated patients with type 2 diabetes: a randomized, controlled trial. *Ann Intern Med*. 2011;154(2):103-112. [CrossRef]
11. Hemmer A, Maiter D, Buysschaert M, Preumont V. Long-term effects of GLP-1 receptor agonists in type 2 diabetic patients: a retrospective real-life study in 131 patients. *Diabetes Metab Syndr*. 2019;13(1):332-336. [CrossRef]
12. Klonoff DC, Buse JB, Nielsen LL, et al. Exenatide effects on diabetes, obesity, cardiovascular risk factors and hepatic biomarkers in patients with type 2 diabetes treated for at least 3 years. *Curr Med Res Opin*. 2008;24(1):275-286. [CrossRef]
13. Matthaei S, Reaney M, Mathieu C, et al. Patients with Type 2 diabetes initiating exenatide twice daily or insulin in clinical practice: CHOICE study. *Diabetes Ther*. 2012;3(1):6. [CrossRef]
14. Ratner RE, Maggs D, Nielsen LL, et al. Long-term effects of exenatide therapy over 82 weeks on glycaemic control and weight in over-weight metformin-treated patients with type 2 diabetes mellitus. *Diabetes Obes Metab*. 2006;8(4):419-428. [CrossRef]
15. Simó R, Guerci B, Schernthaner G, et al. Long-term changes in cardiovascular risk markers during administration of exenatide twice daily or glimepiride: results from the European exenatide study. *Cardiovasc Diabetol*. 2015;14:116. [CrossRef]
16. van Ruiten CC, van der Aart-van der Beek AB, IJzerman RG, et al. Effect of exenatide twice daily and dapagliflozin, alone and in combination, on markers of kidney function in obese patients with type 2 diabetes: a prespecified secondary analysis of a randomized controlled clinical trial. *Diabetes Obes Metab*. 2021;23(8):1851-1858. [CrossRef]
17. Wang X, Zhang H, Zhang Q, et al. Exenatide and renal outcomes in patients with Type 2 diabetes and diabetic kidney disease. *Am J Nephrol*. 2020;51(10):806-814. [CrossRef]
18. Blonde L, Klein EJ, Han J, et al. Interim analysis of the effects of exenatide treatment on A1C, weight and cardiovascular risk factors over 82 weeks in 314 overweight patients with type 2 diabetes. *Diabetes Obes Metab*. 2006;8(4):436-447. [CrossRef]
19. DeFronzo RA, Ratner RE, Han J, Kim DD, Fineman MS, Baron AD. Effects of exenatide (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. *Diabetes Care*. 2005;28(5):1092-1100. [CrossRef]
20. Deng H, Lin S, Yang X, et al. Effect of baseline body mass index on glycemic control and weight change with exenatide monotherapy in Chinese drug-naïve type 2 diabetic patients. *J Diabetes*. 2019;11(7):509-518. [CrossRef]
21. Sönmez A, Dinç M, Taşlıpınar A, et al. Add on exenatide treatment is beneficial in poorly controlled obese Type 2 diabetics under intensive insulin regimens. *Exp Clin Endocrinol Diabetes*. 2017;125(4):256-261. [CrossRef]
22. Rosenstock J, Shenouda SK, Bergenstal RM, et al. Baseline factors associated with glycemic control and weight loss when exenatide twice daily is added to optimized insulin glargine in patients with type 2 diabetes. *Diabetes Care*. 2012;35(5):955-958. [CrossRef]