

Effect of Glucagon Like Peptide 1| (GLP1) Analogues on Obese Egyptians With and Without Diabetes

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Abstract

Background: The Glucagon Like Peptide 1 (GLP1) receptor agonists are a new class for treatment of both type 2 diabetes and obesity.

Aim of Study: To evaluate efficacy of GLP1 analogues in both weight reduction and glycemic control in obese Egyptians with and without diabetes.

Patients and Methods: This intervention study was conducted from August 2017 to August 2018. Total of 40 patients were divided into 3 groups: Obese group, obese group with diabetes & obese group with diabetes after failure to lose 10% of their initial weight after bariatric surgery. Clinical data were collected, anthropometric measures and laboratory investigation included fasting blood glucose and HbA_{1c} in the beginning and every 3 months for a year were done.

Results: This study showed statistically significant body weight and BMI reduction in all groups, there was statistically significant reduction of fasting blood glucose, and HbA_{1c} in the 2nd & 3rd group.

Conclusion: GLP1 analogues are effective in treatment of obese patients with and without diabetes.

Key Words: GLP1 analogues – Type 2 diabetes – Obesity.

Introduction

MOST patients with type 2 diabetes are obese (diabesity) and this can explain the dramatic increase in the prevalence of type 2 diabetes last years. Insulin resistance may be the main link [1].

The Glucagon Like Peptide 1 (GLP1) receptor agonists are a new class of injectable drugs with double benefit as it can be used for treat both type 2 diabetes and obesity [2].

For this reasons, the aim of this research to evaluate the effect of GLP1 analogues on obese Egyptian patients with and without diabetes.

Patients and Methods

This intervention non-randomized controlled study had been conducted in Internal Medicine Outpatient Clinic at Zagazig University Hospitals from August 2017 to August 2018. We started the study on 40 subjects; after exclusion of patients with diabetes mellitus type 1 or patients with family history of medullary thyroid carcinoma and patients suffering from gastroparesies. Their ages ranged from 30 to 65 years; with mean \pm SD 48.6 \pm 9.6 years.

The patients divided into three groups:

- *Group I:* Obese group included 14 patients.
- *Group II:* Obese group with diabetes included 13 patients.
- *Group III:* Obese group with diabetes, after failure to lose 10% of their initial weight, 6 month after bariatric surgery included 13 patients.

Patients were subjected to thorough history taking and anthropometric measures were calculated including weight, BMI. Full clinical examination and routine investigations were done. Specific investigations included HbA_{1c}, fasting blood glucose ethical.

Written informed consent was taken from the patient to participate in the study. Approval for performing the study was obtained from Internal Medicine and Medical Biochemistry Departments, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval.

Statistical analysis:

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) Version 20. Quantitative variables were described using their means and standard deviations. Cate-

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gorical variables were described using their absolute frequencies. Kolmogorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify assumptions for use in parametric tests. To compare means, independent sample t test was used when appropriate. Nonparametric test (Mann Whitney) was used to compare means when data was not normally distributed and to compare medians in categorical data. To assess the best cutoff for study variables, ROC curve analysis was used. The level statistical significance was set at 5% ($p < 0.05$). highly significant difference was present if $p \leq 0.001$.

Results

This study included 40 patients divided into 3 groups, the 1st group was obese non diabetic consisted of 14 patients, 2nd group was obese diabetic and consisted of 13 patients and the 3rd group was obese diabetic who failed to lose 10% of their initial weight within 6 months after bariatric surgery and also consisted of 13 patients. In the three groups all variables were measured 4 times. 1st before using GLP-1 receptor agonist; subcutaneous injection of 3mg liraglutide and then every 3 months later for one year follow-up.

Table (1): Comparing serial BMI measures between the studied groups.

Variable	Group 1 (N=14) Obese patients	Group 2 (N=13) Obese with diabetes	Group 3 (N=13) Obese with diabetes after bariatric surgery	F-test	p -value!
Baseline BMI:					
Mean \pm SD	43.1 \pm 8.4	37.2 \pm 4.9	41.9 \pm 6.5	1.6	0.2
Range	(28.8-53.6)	(31.4-49.2)	(34.2-54.8)		
BMI after 3 months:					
Mean \pm SD	42.1 \pm 8.3	36.6 \pm 4.4	41.1 \pm 6.3	1.7	0.18
Range	(28.8-53.6)	(30.9-47.8)	(33.5-53.8)		
BMI after 6 months:					
Mean \pm SD	40.9 \pm 8.1	36.2 \pm 4.7	39.8 \pm 6.2	1.9	0.15
Range	(28-51.2)	(29.7-46.2)	(32.2-52.1)		
BMI after 9 months:					
Mean \pm SD	37.8 \pm 7.8	35.1 \pm 4.4	38.6 \pm 6.3	1.9	0.15
Range	(26.9-48.7)	(29.3-45)	(30.8-50.2)		
BMI after 12 months:					
Mean \pm SD	33.8 \pm 2.8	31.2 \pm 4.1	33.5 \pm 2.3	1.9	0.15
Range	(22.9-35.5)	(28.3-35)	(30.8-42)		
• ANOVA test for repeated measures	2.1	23	0.4		
• p -value [^]	0.04*	0.001**	0.001**		

*: Statistically significant difference ($p \leq 0.05$).

p -value! = For comparing the 3 groups.

p -value[^] = For comparing repeated BMI in each group.

This table shows that there was statistically significant difference (reduction) in BMI between the four times in the three studied groups. But, there was no statistically significant difference between the studied groups in BMI in the four times.

Table (2): Comparing serial fasting blood glucose measures between the studied groups.

Variable	Group 1 (14) Obese non diabetic	Group 2 (13) Obese diabetes	Group 3 (13) Obese diabetes after bariatric surgery	F-test	p -value!
• Baseline	93.5 \pm 19.9 (76-154)	251.5 \pm 49.9 (174-310)	235 \pm 66.8 (98-370)	20.9	0.001 **
• FBG 1st time	85.2 \pm 9.8 (76-115)	147.6 \pm 35.9 (98-240)	137.2 \pm 29.2 (76-190)	42.9	0.001 **
• FBG 2nd time	85.2 \pm 6.2 (77-94)	119.1 \pm 26.2 (86-190)	124 \pm 16.6 (78-140)	20.8	0.001 **
• FBG 3rd time	88.2 \pm 14.2 (70-129)	122.5 \pm 25.3 (90-201)	117.5 \pm 15.3 (74-135)	13.9	0.001 **
• FBG 4th time	86.2 \pm 11.3 (70-121)	118.5 \pm 20.1 (90-180)	100.5 \pm 10.2 (72-120)	11.2	0.001 **
• ANOVA test for repeated measures	1.1	39	31		
• p -value [^]	0.3	0.001 **	0.001 **		

**: Statistically highly significant difference ($p \leq 0.001$).

This table shows that there was highly statistically significant difference between the three studied groups in FBG in the four times. Also, there was statistically significant difference in FBG between the four times in each of the three studied groups.

Table (3): Comparing serial HBA_{1c} measures between the studied groups.

Variable	Group 1 (14) Obese non diabetic	Group 2 (13) Obese diabetes	Group 3 (13) Obese diabetes after bariatric surgery	F-test	p -value!
• Baseline	5.1 \pm 0.6 (4.2-6.3)	10.1 \pm 1.2 (8.1-12)	8.8 \pm 1.7 (4.9-12)	10.7	0.001 **
• HBA _{1c} 1st time	4.8 \pm 0.4 (4.2-5.9)	7.9 \pm 0.5 (7-9)	7.5 \pm 0.8 (5.2-8.3)	59.7	0.001 **
• HBA _{1c} 2nd time	4.9 \pm 0.4 (4.5-6.2)	7.4 \pm 0.3 (7-8.2)	7.2 \pm 0.6 (5-7.8)	101.5	0.001 **
• HBA _{1c} 3rd time	5.1 \pm 0.5 (4.5-6.5)	7.3 \pm 0.2 (7-8.3)	7.2 \pm 0.5 (5.2-7.8)	97.1	0.001 **
• HBA _{1c} 4th time	4.9 \pm 0.3 (4.5-6.2)	6.6 \pm 0.5 (5.8-6.9)	6.7 \pm 0.6 (5.2-7.5)	95.1	0.001 **
• ANOVA test for repeated measures	0.5	36	7.6		
• p -value [^]	0.6	0.001**	0.001 **		

**: Statistically highly significant difference ($p \leq 0.001$).

This table shows that there was highly statistically significant difference between the studied groups in HbA_{1c} in the four times. Also, there was statistically significant difference in HbA_{1c} between the four times in the 2nd and 3rd studied groups but not statistically significant in the 1st group.

Discussion

Obesity is one of the most important public health issue worldwide [3].

The Glucagon Like Peptide 1 (GLP1) receptor agonists are a new class of injected drugs for the treatment of both type 2 diabetes and obesity, they are associated with considerable HbA_{1c} reduction and weight loss with a low risk of hypoglycemia [2].

Therefore, the present study was designed to estimate the role of GLP1 analogues in obese patients with and without diabetes including patients who failed to lose weight after bariatric surgery.

We found statistically significant reduction in weight, BMI in all studied groups in every 3 months evaluation for one year. But, there was no statistically significant difference between the studied groups in BMI in the four times, which means reflect the efficacy of GLP1 analogues in obese patient either with diabetes or without even after failure to lose weight after bariatric surgery.

This in agreement with previous study showed that weight loss with liraglutide which is dose dependent to 3.0mg once daily in obese subjects without diabetes in comparison to placebo or orlistat [4].

Also in agreement with our results, study evaluated the efficacy of liraglutide in patients with prior bariatric surgery who experienced either suboptimal weight loss or weight regain after their procedures with recommended dose 0.6mg SC once daily increasing to maximal dose of 3mg/day and after 3 months of follow-up, mean weight and BMI reduction were 8.38 ± 9.19 Kg and 2.94 ± 3.14 Kg/m respectively [5].

Similarly significant body weight reductions in patients randomized to 3mg liraglutide when compared with placebo at 56 weeks alongside increased 5% and 10% responder rates [6].

Interestingly, supraphysiological doses of GLP-1 reduce appetite and food intake in both lean and

obese subjects, physiological GLP-1 doses reduces appetite and food intake in only lean subjects [7]. GLP-1 has been found to delay gastric emptying in healthy lean, obese and T2DM subjects [8].

In the present study; there was statistically significant reduction in FBG and HbA_{1c} in patient with diabetes (2nd and 3rd groups). This may be explained by body weight reduction in agreement with recent clinical trial showed that about 50% of patients with T2DM achieved remission to non-diabetic state after weight loss and this may be associated with the early and sustained improvement of beta cells function [9].

In obese patients with T2DM even modest weight loss have been shown to improve glycemic control and patients who lose weight achieve target HbA_{1c} more likely those with stable weight [10].

We can conclude that GLP1 receptor agonists are effective tool in both glycemic control and weight reduction even in patients who failed to lose weight after bariatric surgery.

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Conflicts of interest:

The authors declare that they have no competing interests.

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تأثير محفزات مستقبلات الببتيد شبيه الجلوكاجون على مرضى السمنة المصريين المصابين وغير المصابين بالسكري

السمنة هي حالة طبية تتراكم فيها الدهون الزائدة في الجسم إلى أمدى الذي قد يكون له تأثير سلبي على الصحة، وعادة ما يعتبر الناس بدنيين عندما يزيد مؤشر كتلة الجسم لديهم عن ٣٠ كجم/م^٢.

إن محفزات مستقبلات الببتيد شبيه الجلوكاجون هي فئة جديدة من الأدوية التي تعطى عن طريق الحقن لعلاج مرض السمنة ومرض السكري من النوع الثاني وهي تقوم بزيادة تأثير هورمون انكريتين وتحفيز إفراز الأنسولين، وتبطل حركة المعدة وتحفز الشبع مما يؤدي إلى إنقاص الوزن وإنخفاض مستوى الهيموجلوبين السكري.

الهدف من الدراسة: هو دراسة تأثير محفزات مستقبلات الببتيد شبيه الجلوكاجون على مرضى السمنة المصريين المصابين وغير المصابين بالسكري من ناحية التأثير على الوزن ومستوى الجلوكوز بالدم والهيموجلوبين السكري.

طرق وأدوات الدراسة: أجريت هذه الدراسة في العيادة الخارجية لقسم الباطنة العامة جامعة الزقازيق في الفترة من أغسطس ٢٠١٧ إلى أغسطس ٢٠١٨.

أشترك في الدراسة ٤٠ شخص تم تقسيمهم كالآتي:

١- ١٤ شخص يعانون من السمنة.

٢- ١٣ شخص يعانون من السمنة والسكري.

٣- ١٣ شخص يعانون من السمنة والسكري بعد فشل إنقاص ١٠٪ من وزنهم بعد ٦ شهور من إجراء جراحة لعلاج السمنة.

تم أخذ التاريخ المرضي والفحص السريري الشامل للمرضى في المجموعات الثلاث.

تم عمل متابعة كل ثلاثة أشهر لجميع المرضى لمتابعة الوزن ومستوى الجلوكوز الصائم بالدم والهيموجلوبين السكري.

النتائج: تعمل أدوية محفزات مستقبلات الببتيد شبيه الجلوكاجون بشكل فعال في إنقاص الوزن في مرضى السمنة وتخفيض مستوى الجلوكوز بالدم وتقليل مستوى الهيموجلوبين السكري في مرضى السكري من النوع الثاني.

التوصيات: يوصى باستخدام محفزات مستقبلات الببتيد شبيه الجلوكاجون في مرضى السمنة كما يوصى باستخدام هذه الأدوية في مرضى السكري من النوع الثاني المصابين بالسمنة.