GAVIN PUBLISHERS

Emergency Medicine Investigations

Fang R, et al.Emerg Med Inves 2017: J128.

Case Report

The Effectiveness of Exenatide in an Unusual Case of Obese Type 2 Diabetes Mellitus with Brain Hemorrhage

Xuexue Deng, Shuqiong Fu, Ronghua Fang*

Department of General Medicine, West China Hospital Sichuan University, China

***Corresponding author:** Ronghua Fang, Department of General Medicine, West China Hospital Sichuan University, Postal code: 610041, Chengdu City, Sichuan Province, China, Tel: +86 028 854 213 48; E-mail: fangronghua@126.com

Citation: Deng X, Fu S, Fang R (2017) The Effectiveness of Exenatide in an Unusual Case of Obese Type 2 Diabetes Mellitus with Brain Hemorrhage. Emerg Med Inves 2017: J128.

Received Date: 25 December, 2016; **Accepted Date:** 31 January, 2017; **Published Date:** 7 February, 2017

Abstract

The selection of effective therapeutic agents for the treatment of diabetes in obese patients is limited. Exenatide, a Glucagon-Like Peptide-1 receptor agonist, has been shown to improve glycemic control and reduce excess body weight in patients with Type 2 Diabetes Mellitus (T2DM). However, its efficacy in the management of the obese T2DM patients with brain hemorrhage receiving nasogastric tube feeding has not been reported. In the present case report, we describe an unusual case of T2DM and obesity with nasogastric tube feeding due to loss of consciousness, in whom glycemic control was successfully achieved after addition of exenatide as an adjunctive therapy to arcarbose and insulin injection. In addition, the patient's body weight, liver function, and inflammatory parameters related to pulmonary infection were significantly improved, and no hypoglycemia was observed. In conclusion, the use of exenatide is recommended in the treatment of obese T2DM patients with brain hemorrhage.

Keywords: Brain Hemorrhage; Exenatide; Glucagon-like Peptide-1; Nasogastric Tube Feeding; Obesity; Type 2 Diabetes Mellitus

Introduction

Diabetes is a major health problem in China with an estimated 92.4 million adults suffering from Type 2 Diabetes Mellitus (T2DM). Major changes in lifestyles, such as insufficient physical activity, adoption of a Western diet, and sedentary occupations, have been the main contributors to the increasing prevalence of this disease [1]. Patients with T2DM generally have Cardio Vascular Disease (CVD) risk factors such as obesity, dyslipidemia, hypertension, and early atherosclerotic lesions, and therefore, are more likely to develop CVD than individuals without diabetes. Furthermore, studies have indicated that diabetes patients are at greater risk for progression to various cardiovascular comorbidities, including chronic renal disease, end-stage kidney disease, coronary artery disease, and brain ischemia [2]. Although diet and exercise intervention have shown efficacy in decreasing Fasting Plasma Glucose (FPG), Postprandial Blood Glucose (PBG), Glycated Hemoglobin (HbA1c), and T2DM-associated complications, a large portion of patients eventually require glucose-lowering therapy with medication, the side effects of which, such as weight gain, have been widely reported to aggravate dyslipidemia and hypertension. Few studies have reported on improving glycemic control without increasing CVD risk factors from further weight gain or loss of patient compliance because of hypoglycemia [3].

Exenatide, a 39-amino-acid peptide, is a chemically synthetic form of exendin-4, which is extracted from in the saliva of the Gila monster [4]. Studies have found that exenatide acts similarly to human Glucagon-Like Peptide-1 (GLP-1), one of the key molecules in the modulation of glucose metabolism and insulin production. Indeed, exenatide has been reported to lower levels of A1C by-1.3% to-1.9% [5] and, in turn, improve glycemic control in patients with T2DM. Further studies have shown that exenatide treatment significantly reduced the risks of developing CVD, as assessed by body weight, lipid levels, blood pressure, and hepatic dysfunction measured by Alanine Amino Transferase (ALT) in patients with T2DM [6-7]. Since April 2005 when exenatide was approved by the Food and Drug Administration (FDA) for T2DM patients, it has been used either alone or in combination with other existing medications to effectively treat T2DM, especially patients

who did not respond to the oral medication well. Until now, its use in T2DM patients with brain hemorrhage receiving nasogastric tube feeding has not been reported.

In this case report, we describe a case of T2DM in a an obese patient with brain hemorrhage receiving nasogastric tube feeding whose glycemic levels, body weight, and hepatic function were successfully improved by the use of exenatide as an adjunctive therapy.

Case Report

Patient Description

A 47-year-old Chinese man was admitted to the Neurosurgery Department of West China Hospital for loss of consciousness and an experience of cardiopulmonary arrest. Two years prior to admission, he was diagnosed with T2DM and hypertension, which were poorly managed due to noncompliance with treatment.

Computed Tomography (CT) examination of the head showed an extensive hemorrhage in the left thalamus. The patient was treated with a tracheotomy, nasogastric tube feeding, measures to prevent infection in the lungs, and a dehydrating agent to reduce intracranial pressure. Twenty-eight days later, the patient had loss of consciousness, his vital signs were stable, and within normal ranges, and the patient was then transferred to the Department of General Medicine in our hospital.

Clinical Examination

The physical examination revealed a height of 176 cm, body weight of 100 kg, Body Mass Index (BMI) of 32.28 kg/m2, and blood pressure of 138/90 mmHg. Laboratory tests showed a FBG of 9-11 mmol/L and PBG of 18-22 mmol/L.

Treatment and Outcome

Monitoring of blood glucose, along with his medical history of T2DM, indicated a need for therapy to reduce blood glucose. Changes in waist, abdominal girth, FBG, PBG, Triglycerides (TG), total cholesterol (TC), High-Density Lipoprotein-Cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), Alanine Amino Transferase (ALT, Aspartate Amino Transferase (AST), Procalcitonin (PCT), Interleukin-6 (IL-6), and C-Reactive Protein (CRP), as measured over the three time points (prior to treatment, 1 month, and 4 months after the use of exenatide) are shown in Table 1. Insulin as part injection and adjustment of the insulin dosage according to the blood glucose levels were first considered. The patient was given insulin glargine 10U injection at bedtime. However, his FBG remained within 8.5-12 mmol/L, and his PBG remained high at 15-18 mmol/L and occasionally over 20 mmol/L even after adjustment for the insulin dosage. The patient had dyslipidemia (TG=2.28 mmol/L, TC=5.03 mmol/L, HDL-C=0.59 mmol/L, LDL-C=3.00 mmol/L) as well as impaired liver function (ALT=109 IU/L, AST=44 IU/L) and recurrent pulmonary infection (inflammatory indicators PCT=0.18 mg/ ml, IL-6=10.64 pg/ml, CRP=8.64 mg/L) developed. Then we added acarbose and exenatide to the treatment plan; the patient was given 50 mg acarbose via nasogastric tube feeding three times daily, injected with 5 μg exenatide twice daily (morning and evening), and given insulin glargine 10 U injection at bedtime. The patient responded well to treatment, with a FBG 7-8 mmol/L and PBG values of 5-11 mmol/L (after breakfast and dinner) and 11-15 mmol/L (after lunch) without experiencing hypoglycemia at midnight, suggesting a significant improvement in glycemic control. One month after exenatide was started, decreases in markers for inflammation were observed (PCT=0.099 mg/ ml, IL-6=10.66 pg/ml, CRP=5.19 mg/L). In addition, the impaired liver function improved significantly (ALT= 76 IU/L, AST= 41 IU/L). But the lipid control was even worsen (TG=2.33 mmol/L,TC=5.63 mmol/L) .The dose of acarbose was increased to 100 mg for the lunch-time tube feeding at 3 months after the start of exenatide, but his blood glucose levels did not reach normal ranges. The treatment plan was adjusted to include 50 mg acarbose in the tube feeding three times daily, 10 μg of exenatide twice daily injection (morning and evening), and insulin glargine 10U injection at bedtime. Laboratory tests showed FBG=6-8 mmol/L and PBG=5-11 mmol/, without recurrence of hypoglycemia before sleep or at 3 am. After the use of exenatide for 4 months, the patient's glycemic levels were well controlled with a FBG=6.96 mmol/L and PBG=8.79 mmol/L. The patient's dyslipidemia, inflammation, and impaired liver function also showed much improvement (TG=1.15 mmol/L, TC=4.00 mmol/L, HDL-C=0.91 mmol/L, LDL-C=2.60 mmol/L, PCT=0.05 mg/ ml, IL-6=6.79 pg/ml, and CRP=2.64 mg/L as well as ALT=13 IU/L and AST=12 IU/L). Physical examination revealed decreases in the waist circumference from 100 to 86 cm and the abdominal girth from 105 to 85 cm. Exenatide's registration number was H20140821 and produced by Baxter Pharmaceutical Solutions LLC in the patient. There were no nausea, vomiting, abdominal pain, abdominal distension, and allergic reaction related to the injection of exenatide.

Parameter	Before	1 month	4 months
Waist (cm)	100	92	86
Abdominal Girth (cm)	105	98	85
FBG (mmol/L)	11.82	9.11	6.96
PBG (mmol/L)	17.3	14.04	8.79
TG (mmol/L)	2.28	2.33	1.15
TC (mmol/L)	5.03	5.63	4
HDL-C (mmol/L)	0.59	0.77	0.91
LDL-C (mmol/L)	3	3.48	2.6
ALT (IU/L)	109	76	13

AST (IU/L)	44	41	12
PCT (mg/ml)	0.18	0.099	0.05
IL-6 (pg/ml)	10.64	10.66	6.79
CRP (mg/L)	8.64	5.19	2.64
FBG: Fasting Plasma Glucose; PBG: Postprandial Plasma Glucose; TG: triglycerides; TC: Total Cholesterol; HDL-C: High-Density Lipoprotein; LDL-C: Low-Density Lipoprotein; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; PCT: Procalcitonin; IL-6: Interleukin 6; CRP: C-Reactive Protein			

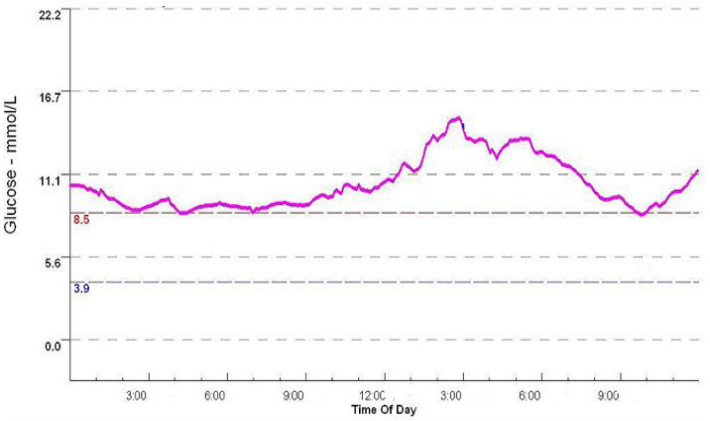
Table 1: Comparison of parameters of glucose and lipid metabolism and markers for liver function and inflammation before and after the use of exenatide.

Discussion

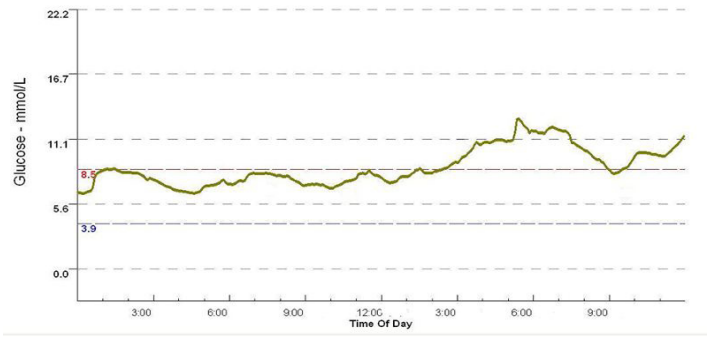
Management of T2DM in obese patients is particularly challenging as most glucose-lowering agents result in weight gain.

In this case report, for the first time, we reported the effectiveness and safety of exenatide as an adjunctive therapy in combination with insulin injection and acarbose for glycemic control in an obese T2DM patient under the rare condition of nasogastric tube feeding due to loss of consciousness. Researchers reported that oral feeding can shorten hospital stay and eliminate of the psychologic and traumatic side effects of nasogastric feeding, decrease large numbers of bacteria colonize the oral cavity and stomach [7,8]. Furthermore, improvement in liver function and reduction in risk factors associated with cardiovascular disease were demonstrated in our patient.

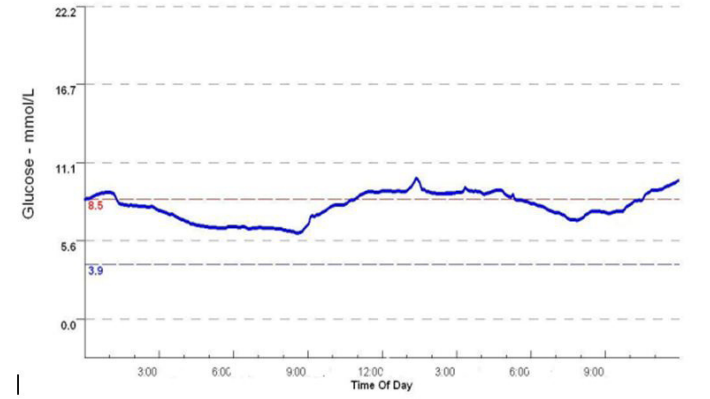
Changes in lifestyle such as proper diet and aerobic excise have been known to yield good results, including glycemic control, lowering cardiovascular risk factors, etc. However, patients who do not achieve successful glycemic control following lifestyle intervention or who exhibit low compliance may need anti-diabetic medication or even weight loss surgery in some cases [9]. Oral anti-diabetic medications like metformin are among the first-line glucose-lowering agents, and if the response is poor in the first 3 months, this therapy is followed by the initiation and then intensification of insulin therapy [10,11]. It has been widely reported that weight gain and hypoglycemia are common, and weight gain increases the risk of developing CVD during insulin therapy [12,13]. In this uncommon case, management of the patient's T2DM by lifestyle intervention was unlikely. Metformin, which has been recommended as the first oral anti-diabetic agent for patients with obese T2DM, was not suitable for delivery via nasogastric tube feeding and had a potential side effect of causing or worsening liver and kidney dysfunction. Thus, the use of metformin should be considered with caution in patients with liver and kidney problems. Therefore, metformin was excluded from our initial treatment plan for our patient. Acarbose was used as an oral anti-diabetic agent alone and in combination with insulin injection, and neither treatment accomplished successful glycemic control for the patient (Figure 1).



A: Before the start of exenatide.



B: One month after the start of exenatide.



C: Four months after the start of exenatide (1 mmol/L=18 mg/dl).

Figure 1: Continuous glucose monitoring in the patient before and after the use of exenatide. Exenatide injection was given at the dose of 5μg twice a day within the 60 min before the morning and evening meals in the first three months, and in the fourth month, the dose of exenatide was increased at the dose of 10μg

twice a day within the 60 min before the morning and evening meals. Data were presented as mean ± Standard Deviation (SD). Continuous Glucose Monitoring (CGM) indicated that the glucose fluctuations were attenuated to 9.2 ± 2.7, 8.8 ± 2.5, and 5.5 ± 1.9 mmol/L, respectively, at three time points of before, 1 month, and 4 months after exenatide was started (Figure 1). (A) Before the start of exenatide; (B) One mother after the use of exenatide; (C) Four months after the use of exenatide

Exenatide was only recently approved by the FDA for use as either a primary monotherapy or in combination with other existing anti-diabetic medications to treat T2DM. Studies on its mechanisms have shown that exenatide acts through at least five directions, including enhancement of insulin secretion, suppression of hepatic glucagon degradation, slowing of gastric emptying, appetite reduction, and lowering hepatic fat [14-15]. As a result, exenatide is able to improve glycemic control, promote weight loss, and reduce cardiovascular risk factors in patients with T2DM [6]. In view of its advantages and the uncommon health condition of our patient, exenatide was selected as an adjunctive therapy to our treatment plan for the patient. As expected, the patient showed adequate glycemic control without resultant weight gain and drug side effects like hypoglycemia. Moreover, liver function was improved and cardiovascular risk factors were reduced in the patient. Of course, the improvement in glycemic control was obviously multi factorial. Demonstrate the causal relationship with the use of exenatide. The improvement can be due to the effect of acarbose, or a change in tube feeding regime, or even due to control of pulmonary infection. Considering the specific condition of the patient, we believed regarding the endpoint of weight loss induced besides related to exenatide, the patient had been lying on the bed for a long time (5 months), lack of nutrition and exercises, which will affect the outcome of weight loss.

We postulated that exenatide may have been effective in our patient through the known mechanisms and possibly other unidentified ones. Because we have very few experience of treatment with exenatide resulting in weight loss in regular patient or patient with obesity in clinical, so our study has limitations as well. It remains unclear whether exenatide alone can result in similar clinical outcomes in our patient.

In conclusion, exenatide is recommended as an adjunctive therapy to treat obese T2DM patients with brain hemorrhage receiving nasogastric tube feeding.

References

1. Yang W, Lu J, Weng J, Jia W, Ji L, et al. (2010) Prevalence of diabetes among men and women in China. N Engl J Med 362:1090-1101.
2. Bergenstal RM, LiY, Porter TK, Weaver C, Han J (2013) Exenatide once weekly improved glycaemic control, cardio metabolic risk factors and a composite index of an HbA1c < 7%, without weight gain or hypoglycaemia, over 52 weeks. Diabetes Obesity and Metabolism 15: 264-271.
3. Zinman B, Schmidt WE, Moses A, Lund N, Gough S (2012) Achieving a clinically relevant composite outcome of an HbA1c of <7% without weight gain or hypoglycaemi in type 2 diabetes: a meta-analysis of the liraglutide clinical trial programme. Diabetes Obes Metab 14: 77-82.
4. Aramadhaka LR, Prorock A, Dragulev B, Bao Y, Fox JW (2013) Connectivity maps for biosimilar drug discovery in venoms: The case of Gila Monster Venom and the anti-diabetes drug. Toxicon 69: 160-167.
5. Blevins T, Pullman J, Malloy J, Yan P, Taylor K, et al. (2011) DURATION-5: exenatide once weekly resulted in greater improvements in glycemic control compared with exenatide twice daily in patients with type 2 diabetes. J Clin Endocrinol Metab 96: 1301-1310.
6. Klonoff DC, Buse JB, Nielsen LL, Guan X, Bowlus CL, et al. (2008) Exenatide effects on diabetes, obesity, cardiovascular risk factors and hepatic biomarkers in patients with type2 diabetes treated for at least 3 years. Curr Med Res Opin 24: 275-286.
7. Saydam L, Kalcioglu T, Kizilay A (2002) Early oral feeding following total laryngectomy. Am J Otolaryngol 2: 277-281.
8. Matsuura T, Suzuki K, Yamakoshi M, et al. (1997) Study of bacterial flora in the oral cavity and stomach of elderly patients receiving nasogastric tube feeding. Kansenshogaku Zasshi. 71: 397-404.
9. Bergenstal RM, Wysham C, MacConell L, Malloy J, Walsh B, et al. (2010) Efficacy and safety of exenatide once weekly versus sitagliptin or pioglitazone as an adjunct to metformin for treatment of type 2 diabetes (DURATION-2): a randomised trial. Lancet 376: 431-439.
10. Kishimoto M, Noda M (2014) Effects of Exenatide in a Morbidly Obese Patient with Type 2 Diabetes Diabetes Ther 5:323-332.
11. NICE (2009) Type 2 Diabetes: The management of type 2 diabetes. CG87NICEGuideline.
12. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, et al. (2009) Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 32:193-203.
13. Kotsis VT, Stabouli SV, Papamichael CM, Zakopoulos NA (2006) Impact of obesity in intima thickness of carotid arteries. Obesity 14:1708-1715.
14. Egan JM, Clocquet AR, Elahi D (2002) The insulinotropic effect of acute exendin-4 administeredto humans: comparison of nondiabetic state to type 2 diabetes. J Clin Endocrinol Metab 87:1282-1290.
15. Kolterman OG, Kim DD, Shen L, Ruggles JA, Nielsen LL, (2005) Pharmacokinetics, pharmacodynamics, and safety of exenatide in patients with type 2 diabetes mellitus. Am J Health Syst Pharm 62: 173-181.
16. Kolterman OG, Buse JB, Fineman MS, Gaines E, Heintz S, et al. (2003) Synthetic exendin-4 (exenatide) significantly reduces postprandial and fasting plasma glucose in subjects with type 2 diabetes. J Clin Endocrinol Metab 88: 3082-3089.